INTERNAL MEDICINE

A CASE REPORT ON BRONCHOMEGALY: INFECTIOUS COMPLICATIONS IN THE NEW ERA

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ABSTRACT

INTRODUCTION: Bronchomegaly is characterized by dilatation of the main bronchi due to atrophy of the elastic fibers and smooth muscle cells. The diagnosis is confirmed through radiological imaging and bronchoscopy. It is associated with recurrent lower respiratory tract infections (LRTIs). Most patients present with chronic productive cough, hemoptysis, and dyspnea.

CASE PRESENTATION: A 46-year-old female presented with chest tightness, cough, purulent expectoration, and hemoptysis. The patient had a history of bronchomegaly and bronchiectasis, having experienced multiple exacerbations of the latter. She has undergone video-assisted thoracoscopic surgery (VATS) for the treatment of an encapsulated pleural effusion. During her previous hospitalization, bronchoscopy showed obstruction of several bronchi by multiple mucus plugs, some of which were partially removed during the procedure. Physical examination revealed bilateral decreased breath sounds. After admission, due to the chronic nature of the patient's condition, she was referred for a chest computed tomography (CT) which revealed a consolidation in the right middle lobe. Fiberoptic bronchoscopy revealed complete obstruction of B8 by a mucus plug, which could not be removed. Bronchoalveolar lavage (BAL) samples taken during the procedure tested positive for Pseudomonas aeruginosa. Four days after admission, the patient complained of sore throat and fever. An antigen test confirmed a positive result for influenza A. Seven days after admission, microbiological analysis of the sputum revealed the presence of Staphylococcus aureus. The therapeutic regimen of the patient included Ciprinol® 100 mg 2 x 3 amp. i.v. for 11 days, Pipetazon 3 x 1 fl. i.v. for 7 days, Tamiflu® 2 x 1 tb. for 5 days, bromhexine 3 x 2 amp. i.v., inhalations with physiological serum, methylprednisolone 40 mg i.v., famotidine 40 mg x 1 tb. daily. The patient was discharged on the eleventh day of hospitalization in improved condition.

CONCLUSION: Bronchomegaly manifests with reduced mucociliary clearance and the accumulation of secretions, which increases the risk of recurrent lower respiratory tract infections. Further complicated by bronchiectasis, it can lead to more frequent infections with more severe manifestations. The lack of respiratory rehabilitation and prolonged postponement of a medical appointment may lead to severe and irreversible consequences.

Keywords: *bronchomegaly, bronchiectasis, respiratory infections, case report*

PURULENT LUNG INFECTIONS: CHALLENGES IN DIAGNOSIS AND TREATMENT—A CASE REPORT

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ABSTRACT

INTRODUCTION: A pulmonary abscess is an infection of the lungs that causes destruction of the tissue, leading to cavity formation with purulent fluids. Purulent lung infections are rare but severe, often resulting from a polymicrobial infection.

CASE PRESENTATION: A 41-year-old woman presented with productive cough and purulent expectoration. She had a medical history of bronchial asthma and diabetes mellitus. The patient has undergone three in vitro fertilization procedures, with the first two resulting in livebirth and the last one being unsuccessful. During the second procedure, she was diagnosed with thrombophilia, however, she was not undergoing anticoagulation therapy. Upon hospitalization, a computed tomography (CT) scan was performed, revealing bilateral cavitary lesions, with the size of the biggest one being 97/64 mm. Due to the development of acute respiratory failure (ARF) and deterioration of her state, she was transferred to the intensive care unit (ICU) for five days. After an evaluation of the case by the national consultant, she was transferred to the Clinic of Pneumology and Phthisiology. During her hospital stay, the patient underwent two fiberoptic bronchoscopies, which did not show any endoscopic signs of neoplastic changes but revealed abundant mucopurulent discharge. Bronchoalveolar lavage samples collected during the procedure tested positive for Enterococcus faecium. A consultation with a rheumatologist and cardiologist was conducted to exclude systemic disease, vasculitis and pulmonary thromboembolism. Two HIV tests were performed, both coming back negative. Her treatment plan included Meronem® 3 x 1 g for 14 days, Vancomycin 2 g for 14 days, Sulcef® 2 g for 8 days, antifungal treatment with Diflucan® 1 flacon for 12 days, low-molecular-weight heparin, symptomatic treatment, and oxygen therapy. On the eight day of her hospitalization, follow-up CT scan was performed, revealing a decrease in the size of the lesions. She was discharged in an improved condition.

CONCLUSION: Acute respiratory failure, primarily caused by pulmonary infections, is the leading reason for ICU admissions. While identifying the cause of ARF significantly improves survival rates, it can be extremely challenging due to the interplay of underlying diseases, treatments, and infections, which create complex clinical presentations, requiring broad differential diagnosis and multidisciplinary approach.

Keywords: *pulmonary infection, abscess, case report*

MYCOBACTERIUM AVIUM COMPLEX (MAC)-ASSOCIATED RESPIRATORY INFECTION

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ABSTRACT

INTRODUCTION: Tuberculosis (TB) continues to be a global concern, especially with the rise of infections caused by non-tuberculous mycobacteria (NTM). In 2022, 35,000 TB cases were reported in Europe, particularly in Eastern Europe. Alongside Mycobacterium tuberculosis, other NTM species, like those from the Mycobacterium avium complex (MAC), cause similar respiratory issues and clinical presentation. Epidemiological data is insufficient to calculate incidence or prevalence. However, in the USA it has been established that NTM infections have an annual increase of 8%. Mycobacterium avium complex infections are particularly common in individuals over 65 and those with compromised immune systems, such as postmenopausal women. It is also very common in patients diagnosed with bronchiectasis. This case report discusses an 80-year-old woman diagnosed with MAC-associated tuberculosis.

CASE PRESENTATION: The patient, an 80-year-old woman, has had symptoms for two years, including cough, purulent sputum, weight loss, and night sweats. She has also experienced fatigue and shortness of breath, alongside pre-existing conditions, such as chronic heart failure, dyslipidemia, and bronchiectasis. In 2022, sputum cultures revealed acid-fast bacteria, though TB tests, including QuantiFERON® and HIV, were negative. A chest X-ray in 2020 revealed reticular and patchy shadows bilaterally. A computed tomography (CT) scan from the same year and a follow-up in 2022 confirmed bilateral lung consolidations and bronchiectasis. The patient was treated with standard TB medications, including rifampicin, isoniazid, and ethambutol. Despite the treatment, symptoms persisted, leading to further investigation in 2023.

In October 2023, the patient presented with hemoptysis and worsening respiratory symptoms. Examination revealed poor physical condition, decreased lung mobility, resonant percussion sounds and crackles during auscultation. Lab results showed elevated erythrocyte sedimentation rate (ESR) and slightly raised c-reactive protein (CRP). Candida krusei was isolated in sputum culture. Bronchoscopy with bronchioalveolar lavage was recommended but the patient declined. The patient received antifungal treatment with fluconazole and was referred for further testing.

CONCLUSION: This case highlights the diagnostic challenges posed by NTM infections, emphasizing the importance of distinguishing between TB and NTM for appropriate treatment. Strengthening follow-up and anti-epidemic measures, particularly in countries with rising NTM cases, is crucial to prevent complications and secondary infections.

Keywords: *clinical case, MAC-associated respiratory infection, tuberculosis, comorbidity, therapy, complications*

EMERGENCY TREATMENT OF ANAPHYLACTIC SHOCK

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ABSTRACT

INTRODUCTION: Anaphylactic shock is a life-threatening allergic reaction that requires immediate medical intervention. The purpose of this research is to outline globally recognized methods for emergency response to this type of shock.

AIM: This work aims to showcase the guidelines for dealing with emergency situations involving anaphylactic shock and the medicaments needed to do so.

Research Methodology/Methods and Materials: Information was gathered from various sources regarding the subject of the research and the most important aspects were synthesized. The collected data included insights from diverse perspectives, which contributes to a deeper understanding of the topic under investigation.

RESULTS: The study resulted in outlining the most effective approach for managing emergency situations involving anaphylactic shock and a variety of rapid response kits that provide quick and easy access to the necessary medications in such cases.

CONCLUSION: This research presents globally recognized emergency response strategies that highlight the crucial need for fast and effective intervention in anaphylactic shock cases. It also emphasizes the importance of clear protocols and rapid access to life-saving medications, simplified by various response kits. These findings aim to enhance preparedness and improve outcomes in managing life-threatening allergic reactions.

Keywords: *anaphylactic shock, emergency, treatment*

ACUTE PERICARDITIS: A RARE INITIAL MANIFESTATION OF ADRENAL INSUFFICIENCY

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ABSTRACT

INTRODUCTION: Acute pericarditis, with or without pericardial effusion, is an inflammatory condition affecting the outermost layer of the heart—the pericardial sac, and is characterized by sharp chest pain, which often worsens with deep breathing or lying down, and may be accompanied by fever, pericardial friction rub, and electrocardiographic changes. It remains idiopathic in the majority of cases (80–90%). Infectious, autoimmune, neoplastic causes are mainly responsible for remaining instances. There have been several reports of patients who presented with such cardiac manifestations in the context of adrenal insufficiency due to APS 2 syndrome, Addison's disease, isolated adrenocorticotropic hormone (ACTH) deficiency or following a treatment with pembrolizumab.

CASE PRESENTATION: We present the case of a 61-year-old female patient with a history of triple-negative breast cancer, who underwent surgical intervention and completed eight cycles of neoadjuvant chemotherapy, including immunotherapy with pembrolizumab. She was diagnosed with adrenal insufficiency, likely drug-induced, although an autoimmune origin related to her immunotherapy should also be considered. Her initial presentation included sharp chest pain from two days prior, which varied with breathing and position, along with an episode of atrial fibrillation with a heart rate of 148 bpm, blood pressure of 80/40 mmHg, and a small pericardial effusion. The onset of her symptoms coincided with the cessation of her corticosteroid replacement therapy. Restoration of sinus rhythm was achieved, and the reinitiation of corticosteroids, combined with anti-inflammatory treatment, proved beneficial for her recovery.

CONCLUSION: Although the connection between pericardial involvement and adrenal insufficiency remains unclear, and the underlying mechanisms are not fully understood, all reported cases showed favorable outcomes following the initiation of corticosteroid therapy. The theoretical explanation is that tamponade physiology may develop easily in the setting of lower baseline cortisol levels. With this case, we want to highlight a rare clinical manifestation of adrenal insufficiency, emphasizing the importance of early recognition and treatment of these patients due to their increased risk of hemodynamic instability and shock in acute settings.

Keywords: *acute pericarditis, adrenal insufficiency, immunotherapy, corticosteroid therapy*

ARTERIAL HYPERTENSION IN ADRENAL INCIDENTALOMA WITH MILD AUTONOMIC CORTISOL SECRETION

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ABSTRACT

INTRODUCTION: The majority of incidentally discovered adrenal tumours are benign adrenocortical adenomas. Their incidence varies, being highest in the age group of over 70 years, reaching up to 10%. These can be non-functioning adrenal tumours or they can be associated with autonomous cortisol secretion on a spectrum that ranges from rare clinically overt adrenal Cushing syndrome to the much more prevalent mild autonomous cortisol secretion (MACS) without signs of Cushing syndrome. An adrenal incidentaloma is a formation discovered incidentally in the absence of suspected adrenal disease. Mild autonomous cortisol secretion is diagnosed in 20–50% of patients with adrenal adenomas. It is associated with cardiovascular morbidity, frailty, fragility fractures, decreased quality of life, and increased mortality.

CASE PRESENTATION: We present a 60-year-old female patient with poorly controlled hypertension, admitted to the clinic with complaints of easy fatigability and weight gain. The patient presented with an incidentally detected right-sided adrenal lesion, measuring 40 x 34 mm, on chest computed tomography (CT). On physical examination, the woman was found to be in a mildly impaired general condition, with a BMI of 29. No visible exophthalmos was observed; Graefe sign (-); swollen adrenal gland sign (-). The chest was symmetric with bilateral vesicular breathing and normal heart sounds. Her blood pressure was 160/100. Her abdomen was soft, not painful. No stretch marks were detected. At home she was treated with perindopril and hydrochlorothiazide. Laboratory studies confirmed the presence of mild autonomic cortisol secretion.

The medical treatment for MACS is to normalize cortisol levels using medications such as cortisol-lowering drugs like ketoconazole. The only curative treatment is surgery, removing the adrenal tumor.

CONCLUSION: Modern imaging, increases the incidence of adrenal incidentalomas. Among the hormonally active ones, cortisol-secreting ones are the most common. Mild autonomous cortisol secretion requires evaluation of multiple comorbidities such as hypertension, diabetes mellitus, and obesity. In patients with resistant hypertension and MACS, surgical treatment should be considered.

Keywords: *adrenal incidentaloma, MACS, arterial hypertension*

A CASE OF LATE SEQUELAE OF POLIOMYELITIS

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ABSTRACT

INTRODUCTION: Poliomyelitis is a viral disease caused by polioviruses and is characterized by acute asymmetric flaccid paralysis that frequently affects the musculoskeletal system. Childhood polio can lead to muscle imbalances and contractures that disrupt normal limb growth, potentially resulting in a shorter leg, which can cause spinal deformities, such as scoliosis. Prolonged immobility can also give rise to severe complications in the cardiovascular and pulmonary system. This case report aims to emphasize the challenges of managing post-polio sequelae and enhancing the effectiveness of medical treatment for this condition.

CASE PRESENTATION: We present a case of a 72-year-old male admitted to St. Marina University Hospital with shortness of breath, palpitations, productive cough with white sputum, and chest pain related to elevated blood pressure (190/70 mmHg). Complaints started 10 days prior to admission. These symptoms persisted despite regular medication intake with atenolol 25 mg and nifedipine 20 mg, both of which were prescribed twice daily. The patient's medical history included mild aortic insufficiency and mitral valve prolapse, and poliomyelitis in childhood with residual late sequelae. Examination revealed abnormal inspiratory crepitations and a high-frequency decrescendo-diastolic murmur in the 3rd intercostal space. X-ray imaging displayed an asymmetrical thorax, enlarged cardiac silhouette, kinking of the aorta, severe S-shaped scoliosis, and suspected lung infiltration. Blood tests showed elevated inflammatory markers. Electocardiographic findings indicated sinus rhythm with a leftward positional axis view and preserved repolarisation. Echocardiography revealed a dilated aortic root with moderate aortic regurgitation.

CONCLUSION: One of the primary symptoms of poliomyelitis is impaired limb growth due to premature calcification of the growth plates. In our patient, the shortened left lower limb led to severe S-shaped scoliosis, resulting in a thoracic deformity, reduced lung volume, and compression of the heart and aorta. This explains the observed cardiovascular and pulmonary pathologies, as well as the patient's respiratory predisposition. Careful pharmacotherapy selection is essential because of the risk of aortic kinking and high blood pressure, which increase the risk of aortic dissection. This case highlights the importance of comprehensive multidisciplinary care to address the multifaceted challenges of post-polio sequelae.

Keywords: *poliomyelitis, scoliosis, post-polio sequelae, cardiopulmonary pathologies, treatment*

CLINICAL CASE OF ENDOCARDITIS WITH ACCOMPANYING MARFAN SYNDROME

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ABSTRACT

INTRODUCTION: Marfan syndrome is a systemic connective tissue disorder that predisposes individuals to severe vascular pathologies, such as aortic dissection and aneurysms. Patients with this condition face a high risk of life-threatening complications that require a multidisciplinary approach and frequent interventions. This clinical case illustrates the challenges in diagnosing and treating a patient with Marfan syndrome and multiple vascular complications, following their last hospitalization for a diagnosis of endocarditis.

The case presents a patient with Marfan syndrome who has undergone five hospitalizations related to serious vascular complications, including aortic dissection, aneurysms, and endoleaks, aiming to discuss therapeutic approaches, difficulties in monitoring, as well as their current diagnosis and treatment pitfalls from previous interventions.

CASE PRESENTATION: A clinical case of a 40-year-old man is described, hospitalized at various times (2009, 2014, 2023, and 2024) with diverse complaints, including acute respiratory failure, syncope, abdominal and chest pain, fever, and hemoptysis. Clinical, imaging, and surgical methods were utilized for diagnosis and treatment, including aortic valve replacement, aortic reconstruction, and treatment of endoleak following stent placement.

During the first hospitalization (2009), a successful surgical intervention with aortic valve replacement and reconstruction of the ascending aorta was performed. In 2014, the patient was diagnosed with an aneurysm of the abdominal aorta and distal thoracic aorta. He was admitted in 2023 with syncope, and in 2024, he presented with fever and hemoptysis after endovascular correction of an endoleak in the right subclavian artery. Despite multiple surgical and endovascular interventions, the patient's condition remains stable but requires active monitoring. Due to the absence of antibacterial prophylaxis, endocarditis developed, leading to two adjustments in antibiotic treatment, combining three different medications.

CONCLUSION: This clinical case demonstrates the complexity and challenges in of treating patients with Marfan syndrome and serious vascular pathology. Complex conditions like aortic dissection and aneurysms require a multidisciplinary approach, frequent reinterventions, and long-term monitoring. Proper treatment significantly improves the patient's quality of life, but the risk of complications remains high.

Keywords: *Marfan syndrome, aortic dissection, aneurysm, aortic valve replacement, endoleak, endocarditis*

HEART FAILURE IN A YOUNG THALASSEMIA MAJOR PATIENT: A CASE STUDY

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ABSTRACT

INTRODUCTION: Thalassemia major is a rare autosomal recessive anemia with a prevalence more common in Bulgaria than in Western Europe. Improved access to blood transfusions and chelation therapy has significantly enhanced the prognosis and life expectancy in these patients, underscoring the need for strict monitoring and early intervention to prevent serious complications.

This case report showcases thalassemia major complicated by severe iron overload and cardiomyopathy and focuses on the challenges of managing chronic iron accumulation despite chelation therapy.

CASE PRESENTATION: A case of a 27-year-old patient diagnosed with thalassemia major and, due to repeated need of blood transfusions, suffering from progressive severe iron overload is presented. Treatments since 2010 have also included chelation therapy with different medications. In June 2022, an MRI showed significant deposition of iron both in the heart (8.5 ms) and liver (1.1 ms). Due to low patient compliance with the chelation therapy, iron deposition unfortunately continued.

In October 2015 the patient presented with decompensated heart failure for the first time—right and left ventricular systolic dysfunction, pleural effusions, ascites, transient liver cytolysis, and diabetes mellitus, attributed to the iron overload. After the commencement of adequate diuretic, chelation and insulin therapy, the patient was stabilized; however, the iron burden remained a cause for concern. By September 2024, the patient presented with another cardiac decompensation, needing hospitalization. Magnetic resonance imaging (MRI), performed in April 2024, demonstrated further iron deposition in both the heart and liver, 6.85 and 1.1 ms, respectively. Additionally, hypogonadotropic hypogonadism (with follicle-stimulating hormone (FSH) of 1.68 mIU/mL and testosterone of 5.3 mmol/L) and hypopituitarism developed. Once more intensification of chelation, combined with substitution therapy, led to substantial improvement.

CONCLUSION: This case enlightens the pressing need for the initiation of early and aggressive chelation therapy in thalassemia major to prevent irreversible complications from iron overload, specifically cardiomyopathy. Routine monitoring of iron deposition with proactive medical management will maintain cardiac, hepatic, and endocrine functions to reduce the risks of iron overload.

Keywords: *thalassemia major, iron overload, cardiomyopathy, chelation therapy, case report*

ACUTE SUPPURATIVE THYROIDITIS PROGRESSING TO THYROID ABSCESS: A CASE REPORT WITH LITERATURE REVIEW

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ABSTRACT

INTRODUCTION: Acute suppurative thyroiditis (AST) is a rare yet potentially life-threatening endocrine disorder caused by bacterial infection. The conventional approach to managing this condition typically involves surgical intervention alongside targeted antibiotic therapy. The thyroid gland's unique characteristics, including its rich blood supply, effective lymphatic drainage, high iodine content—which possesses bactericidal properties—and its anatomical separation from surrounding neck structures, contribute to its resistance to infections.

CASE PRESENTATION: In this article, we discuss the case of a 63-year-old woman diagnosed with a thyroid abscess. She presented with symptoms including fever, painful swelling in the neck, sore throat, tachycardia, restricted neck mobility, and dysphagia. Laboratory analysis identified Staphylococcus aureus as the causative microorganism. Treatment commenced with intravenous antibiotics and progressed to incision and drainage of the abscess.

CONCLUSION: This comprehensive management approach led to an uncomplicated recovery for the patient.

Keywords: *thyroid gland, abscess, Staphylococcus aureus, acute thyroiditis, treatment*

A CHALLENGING CASE OF PERSISTENT HYPOGLYCEMIA: A CASE REPORT

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ABSTRACT

Hypoglycemia is the term used to define a low blood glucose level of less than 70 mg/dL (3.9 mmol/L). Since 1938, the symptoms of Whipple's triad have been used to describe hypoglycemia: 1) symptoms consistent with hypoglycemia, 2) a low plasma glucose concentration measured with a precise method, 3) relief of symptoms after the plasma glucose level is raised. Typically, hypoglycemic episodes can present with hunger, sweating, anxiety, and fatigue at first, but later progress to confusion, blurred vision, loss of consciousness, and seizures, even death, if left untreated. Most commonly hypoglycemia is seen in individuals on insulin treatment; errors in dosage, increased exercise, a change in insulin injection site and starvation are all aggravating factors for these patients. Other risk factors include alcohol use, infection, adrenal insufficiency. Despite understanding the immense neurologic, cardiovascular and cognitive damage that severe hypoglycemia can cause, there is still difficulty in understanding and diagnosing nondiabetic sources of such episodes. This article introduces a case of persistent nondiabetic hypoglycemia of unclear origin. Throughout the course of 10 years, this patient has undergone multiple magnetic resonance images (MRIs) of the pituitary gland and abdomen, single-photon emission computed tomography/computed tomography (SPECT/CT), and intraoperative ultrasound, which all contributed to the initial diagnosis of a pancreatic tail insulinoma. In fact, more than 90% of insulinomas originate from the pancreatic beta cells, with probability of around 30% in the head, body, and tail. Less than 2% are extrapancreatic, most commonly on the duodenal wall. However, having undergone a partial pancreatectomy and total splenectomy, the patient's condition remained unchanged, opening the possibility of alternate mechanisms or other cryptogenic origin of beta cell tumor causing the patients hypoglycemia.

Keywords: *hypoglycemia, insulinoma, insulin, cryptogenic, tumor, beta cells*

ABDOMINAL PAIN AND FEVER: IS ONE RARE CAUSE ENOUGH? A CASE REPORT

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ABSTRACT

INTRODUCTION: Monogenic autoinflammatory diseases are a rare cause of recurrent abdominal pain, fever, and acute phase response. Constant vigilance is of utmost importance for the correct diagnosis to be made. On the other hand, such patients are not unsusceptible to other conditions, even life-threatening ones.

CASE PRESENTATION: The patient, a 55-year-old female, presented to our clinic in December 2017. She has had complaints of recurrent episodes of fever and abdominal pain all her life. She was consulted by gastroenterologists, surgeons, and was admitted to the hospital numerous times, treated with antibiotics and spasmolytics and even underwent cholecystectomy, without any effect. As she fulfilled the clinical criteria for familial Mediterranean fever, genetic testing was performed, confirming the diagnosis. Treatment with colchicine was initiated with full resolution of the attacks.

In August 2024 the patient presented with complaints of another typical attack—fever, lumbar and abdominal pain, acute phase reaction. Physical examination revealed marked jaundice and the patient was admitted urgently once again. Laboratory and imaging tests showed mechanical jaundice, choledocholithiasis, and cholangitis. Surgery was performed on the next day with full recovery within the next couple of weeks.

CONCLUSION: Our case underlines the challenges in diagnosing and managing rare conditions, specifically autoinflammatory diseases. Additionally, we present the relatively rare event of choledocholithiasis, 9 years post cholecystectomy, in the same patient, emphasizing the need to keep an open mind regarding our patients' symptoms.

Keywords: *post-cholecystectomy, familial Mediterranean fever, autoinflammatory, choledocholithiasis, case report*

EOSINOPHILIC FASCIITIS AFTER COVID-19 INFECTION: A CASE REPORT

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ABSTRACT

INTRODUCTION: Eosinophilic fasciitis is a rare condition with an unclear etiology, affecting mainly middle-aged active patients. It involves often symmetrical thickening of the muscular fascia and subcutaneous tissue, accompanied by varying degrees of eosinophilic infiltration, acute phase reaction and peripheral eosinophilia. The onset is typically acute, presenting with localized swelling and painful, symmetrical stiffness in the limbs. The condition can quickly advance to fibrosis, potentially restricting joint mobility and causing substantial disability.

CASE PRESENTATION: A 47-year-old female patient with complaints of pain and stiffness in the muscles of the shoulder girdle, arms, abdominal muscles and hips for three months is presented. Limited motion in shoulders and elbows gradually developed. Past medical history showed COVID-19 infection one month prior to the occurrence of the disease. On physical examination, right wrist arthritis, limited active and passive movements in both elbows and to a lesser degree—in the knees, were established. The skin was involved with induration along the entire ulnar surface of the right forearm and elbow and less pronounced but similar changes on the left arm. Acute phase reactant levels were increased, as well as the absolute eosinophil count on complete blood count. Diagnosis of primary eosinophilic fasciitis was established, supported by magnetic resonance imaging findings of fascial thickening and right forearm biopsy showing inflammatory infiltrate in the fascia with involvement of eosinophils, fibrin depositions, and focal necrotic changes. Treatment with high-dose glucocorticoids was initiated with later addition of the steroid-sparing agent methotrexate. There was an almost full resolution of skin changes and subjective symptoms after six months.

CONCLUSION: The underlying pathological process of eosinophilic fasciitis is not fully understood with infections, malignancy, medications most often implicated as triggering factors. Recent evidence suggests that COVID-19 infection may trigger the onset of autoimmune and autoinflammatory diseases, and several case reports and small series have proposed its connection with eosinophilic fasciitis. The diagnosis is difficult, and the condition has to be differentiated from all scleroderma-like conditions among others. Early treatment initiation may greatly improve the prognosis but it is often delayed, resulting in permanent skin changes, contractures, and loss of mobility in these patients.

Keywords: *eosinophilic fasciitis, COVID-19, case report*

A CLINICAL CASE OF ROSAI DORFMAN DISEASE

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ABSTRACT

INTRODUCTION: Rosai-Dorfman disease (RDD) is a rare non-Langerhans histiocytosis characterized by the accumulation of activated histiocytes within the affected tissues. It is a widely heterogeneous entity with a range of clinical phenotypes occurring in isolation or in association with autoimmune or malignant diseases. Classic RDD presents with massive bilateral painless lymphadenopathy. Extranodal involvement is also common (40% of the cases), involving skin (10%), nasal cavity (11%), bone (5–10%), orbital tissue (11%), and central nervous system (5%, predominantly dural).

CASE PRESENTATION: A case of a 66-year-old male patient is presented. He had palpable bilateral axillary and inguinal lymphadenopathy with lymph nodes enlarged up to 3 cm in diameter, splenomegaly, and complaints of fatigue and general malaise. The laboratory results revealed normocytic, normochromic anemia, leukopenia, thrombocytosis with elevated lactate dehydrogenase (LDH), gamma-glutamyl transferase (GGT), direct hyperbilirubinemia, and hypergammaglobulinemia. Biopsy of an axillary lymph node was performed with the morphological picture of interfollicular and capsular fibrosis with characteristic lesional histiocytes, which demonstrate variable frequency of emperipolesis and are positive for S100, CD68, and negative for CD1a. Based on the histology of the lymph node, the diagnosis of RDD was established. The imaging showed generalized lymphadenopathy on both sides of the diaphragm with the largest measuring 37/22 mm and splenomegaly; no extramedullary involvement was observed. The bone marrow biopsy revealed infiltration with RDD. The patient was discussed for initiating polychemotherapy.

CONCLUSION: Rosai-Dorfman disease is a rare and heterogeneous disorder presenting many diagnostic and therapeutic challenges. The heterogeneity of the clinical presentation raises suspicion for various differential diagnoses which include lymphomas, tuberculosis, metastatic carcinoma, malignant melanoma, juvenile xanthogranuloma, etc. Similarly, our patient presented with a clinical picture which resembles lymphoproliferative disease and the histological pattern with defining immunohistochemical phenotype was the confirmation of RDD.

Keywords: *Rosai Dorfman disease, histiocytosis*

CHRONIC MYELOID LEUKEMIA WITH B-LYMPHOID BLAST PHASE: A CASE REPORT

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ABSTRACT

INTRODUCTION: Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm that accounts for 15–20% of adult leukemias. It is associated with a reciprocal translocation between chromosomes 9 and 22, t (9;22), which results in the BCR-ABL1 fusion gene. With a biphasic clinical course, the majority of CML cases (> 90%) are diagnosed in the chronic phase (CP) of the disease, whereas 2.2% of the cases present with de novo blast phase (BP), from which 30%—with B-phenotype blast cells.

CASE PRESENTATION: Here, we present a case report of an adult male patient, who experienced long-term fatigue, abdominal discomfort and early satiety, enlarged spleen and a hyperleukocytosis of 140x10^9/L. A bone marrow aspiration was performed, where flowcytometry detected 36.6% blast cell population with phenotype of B lymphoblasts. Molecular genetics testing (PCR) was done afterwards. It showed a presence of a molecular equivalents of BCR-ABL transcript b2a2 variant (p210). Treatment with protocol HCVAD + imatinib was started and, after the second course of the protocol, reassessment of the disease was made, where B lymphoblasts were not detected by flowcytometry, while polymerase chain reaction (PCR) showed presence of BCR-ABL transcripts. The patient was treated with two more courses of the same protocol, followed by reassessment of the disease, which showed negative minimal residual disease (MRD) but no molecular response. The patient was then referred to the Transplant Center in St. Marina University Hospital in Varna, where he underwent an allogeneic stem cell transplant (ASCT) from a fully human leukocyte antigen (HLA)-compatible related donor—brother. A complete donor chimerism (CDH) with cleared blast cell population was achieved and retained. During the 12 months of the posttransplant observation period, the patient was diagnosed with extensive chronic graft-versus-host disease (GVHD) according to the National Institutes of Health (NIH) criteria (skin, eyes, liver, lungs). The initial corticosteroid treatment did not improve GVHD symptoms, and the treatment was switched to second-line treatment with a JAK 1/2 inhibitor—ruxolitinib.

CONCLUSION: The presented case highlights the clinical challenges associated with a rare variant of BP CML, which exhibits resistance to conventional chemotherapy and tyrosine kinase inhibitors. The achievement of CDH and the subsequent clearance of blast cells after successful application of ASCT emphasize the potential of ASCT to induce remission in refractory cases.

Keywords: *case report, chronic myeloid leukemia, blast phase, allogeneic stem cell transplant, chronic graft-versus-host disease*

CHRONIC STRESS AS A RISK FACTOR FOR DEVELOPING STOMACH CARCINOMA

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ABSTRACT

INTRODUCTION: Chronic stress is increasingly prevalent in modern society due to persistent stressors such as long-term illness, trauma, and lifestyle factors. This condition is linked to adverse health outcomes, including disruptions in sleep, fatigue, hypertension, and gastrointestinal symptoms. Additionally, chronic stress may contribute to the risk of developing stomach cancer (SC), alongside established risk factors like genetics, alcohol use, smoking, and Helicobacter pylori infection.

AIM: This study aims to investigate and describe the mechanisms underlying stress-induced gastric mucosal ulceration and its progression to malignant metaplasia, potentially leading to stomach carcinoma.

METHODS AND MATERIALS: A comprehensive review of relevant literature from the last 20 years, including scientific publications in databases such as PubMed, Google Scholar, and Scopus, and gastroenterology and pathophysiology textbooks, was conducted to understand the relationship between chronic stress and gastric malignancy.

RESULTS: The data indicate that chronic stress results in recurrent sympathetic nervous system (SNS) activation, which reduces gastric mucus production and elevates gastrin levels, contributing to chronic inflammation. This inflammation facilitates the onset of conditions like gastritis due to weakened immunity, thereby increasing the risk for malignancy. Sympathetic nervous system activation also diminishes mucosal blood flow, leading to ischemia, ulcer formation, and potential malignancy.

Furthermore, chronic stress elevates epinephrine, activating β2-adrenergic receptors and modulating tumor suppressor genes, such as p53, while stimulating proinflammatory macrophage activity and IL-6 production. The hypothalamic-pituitary-adrenal (HPA) axis is similarly activated, producing angiotensin II, which reduces mucosal blood flow, impairs energy metabolism, and promotes reactive oxygen species (ROS) production, thereby encouraging DNA damage and tumorigenesis.

CONCLUSION: Chronic stress may be a significant risk factor for stomach carcinoma by contributing to gastric mucosal damage, chronic inflammation, and cellular changes favoring malignancy. Ongoing clinical trials should examine the role of chronic stress in the development of gastric cancer to further substantiate these findings. Recognizing chronic stress as a modifiable risk factor could lead to preventive strategies and improve patient outcomes.

Keywords: *stomach, carcinoma, chronic stress, epinephrine, malignancy*

DUAL MALIGNANCIES—DUCTAL PAROTID CARCINOMA IN A 70-YEAR-OLD WOMAN WITH A HISTORY OF CHILDHOOD NASOPHARYNGEAL CARCINOMA: A CASE REPORT

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ABSTRACT

INTRODUCTION: Ductal parotid carcinoma is a rare and aggressive malignancy arising from ductal epithelial cells of the salivary glands. This case is notable due to the patient's history of nasopharyngeal carcinoma during childhood, treated with surgery and radiotherapy, raising the possibility of a radiotherapy-induced tumor. Secondary malignancies in the parotid gland post-radiation, though uncommon, have been documented. The aim of this report is to detail the diagnostic complexities and treatment approach for a rare case of ductal parotid carcinoma, providing insights into managing malignancies potentially related to prior radiation therapy.

CASE PRESENTATION: A 70-year-old female patient, previously treated for nasopharyngeal carcinoma at age 13, presented with a firm, non-mobile, and non-tender mass in the left parotid region. The lesion was adherent to the underlying tissues, raising concerns for malignancy. Magnetic resonance imaging (MRI) revealed a heterogeneous enhancing lesion consistent with mucoepidermoid carcinoma. The left parotid gland measured 26 x 21 mm. Additionally, an enlarged lymph node in the left submandibular region measuring 17 x 12 mm was noted.

A biopsy revealed a heterogeneous tumor with both low and high-grade malignancy features, including a basaloid-type adenocarcinoma component alongside invasive ductal carcinoma. Following the results, the oncological committee recommended surgical resection followed by adjuvant radiotherapy. Total sialoadenectomy was performed, and histological analysis confirmed high-grade invasive ductal carcinoma, with basaloid-type adenocarcinoma comprising less than 10% of the tumor. Extraparenchymal diffusion, perineural, and lymphovascular invasion were observed, with metastasis in five regional lymph nodes.

Post-surgery, the patient opted against adjuvant radiotherapy. A follow-up positron emission tomography (PET) scan showed no significant findings, indicating the absence of metabolically active lesions or recurrence.

CONCLUSION: This case underscores the rare incidence of ductal parotid carcinoma in a patient with a history of childhood nasopharyngeal carcinoma. The coexistence of high-grade invasive ductal carcinoma and basaloid-type adenocarcinoma components highlights the potential for secondary malignancies following prior radiation treatment. While surgical intervention successfully removed the tumor and affected lymph nodes, the decision regarding adjuvant radiotherapy remains critical and should be guided by ongoing assessment of the patient's condition. This case emphasizes the importance of individualized treatment planning and vigilant follow-up to monitor for any signs of recurrence.

Keywords: *ductal carcinoma, radiotherapy-induced, secondary malignancy*

APLASIA CUTIS CONGENITA WITH ASSOCIATED FETUS PAPYRACEUS. A CASE REPORT FROM THE GENERAL PRACTICE

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ABSTRACT

INTRODUCTION: Aplasia cutis congenita (ACC) is a rare congenital disorder characterized by the absence of skin layers in localized or widespread areas at birth. The lesions can vary, often involving the scalp, but also affecting the trunk and limbs in some cases. Aplasia cutis congenita has been associated with genetic factors, trauma, vascular disruptions, and teratogens. In 1986, Frieden proposed a classification system outlining 9 clinical subtypes, which are based on factors such as location, number of lesions, and inheritance patterns. One particular subtype—type V—is associated with multiple gestation and fetal demise, leading to fetus papyraceus (FP), or the mummification of one twin. This subtype is extremely rare and poses unique diagnostic and management challenges. This report aims to present a case of ACC associated with FP, characterized by stellate lesions symmetrically distributed over the trunk and extremities, differing from the more common presentation of scalp involvement in ACC.

CASE PRESENTATION: A case of a male newborn who was delivered at term (40 weeks of gestation) following a monochorionic diamniotic (MCDA) twin pregnancy is presented. This was the mother's third natural childbirth. An ultrasound in the first trimester confirmed MCDA twins; however, at 12 weeks, one twin was found to have died in utero. At birth, the surviving twin weighed 3170 grams, was eutrophic, and displayed no dysmorphic features. He was well-adapted and tolerated feeding. However, the newborn exhibited multiple skin aplastic defects, including symmetric, stellate, well-demarcated lesions on both hips, and an erythematous band-like lesion surrounding the stump of the umbilical cord. This presentation suggests that the surviving twin experienced acute hypovolemia due to the demise of the co-twin, leading to impaired blood flow and subsequent underdevelopment of normal skin layers.

CONCLUSION: This case represents a rare diagnosis of ACC associated with FP, a condition that has been reported in only around 60 cases worldwide. Given the increasing use of assisted reproductive technologies and the consequent rise in multiple pregnancies, clinicians should be aware of the potential for this rare complication. Early recognition and appropriate management, including careful wound care and monitoring for associated anomalies, are crucial for optimal outcomes in such cases.

Keywords: *aplasia cutis congenita, ACC, twin pregnancy, skin abnormalities*

A DIAGNOSTIC CHALLENGE: DRUG-INDUCED PEMPHIGUS HERPETIFORMIS

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ABSTRACT

INTRODUCTION: Drug-induced allergic dermatoses refer to a range of skin reactions caused by immune-mediated hypersensitivity to medications. These dermatological reactions vary widely in presentation, ranging from mild rashes to severe, life-threatening conditions like Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Accurate diagnosis and management of drug-induced skin reactions are challenging due to their diverse clinical manifestations and the difficulty in identifying the offending drug.

CASE PRESENTATION: A 2-year-old was admitted to the Paediatrics Emergency Department with fever (up to 39°C), periorbital edema, pruritic papules, erosive and erythemathous skin lesions distributed across the entire capillitium, neck, pubic and inguinal region, upper and lower limbs as well as the sacral area. History revealed that the patient was treated with multiple antibiotics including ampicillin, sulbactam, amikacin, and cefotaxime a few days prior to the onset of the symptoms. In the course of hospitalization, a number of differential diagnoses were considered some of which—drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, Job's syndrome, baboon syndrome, bullous pemphigoid, pellagra, and toxic epidermal necrolysis (TEN). A skin biopsy and immunofluorescence testing ultimately confirmed the diagnosis of drug-induced pemphigus herpetiformis (PH).

CONCLUSION: This case highlights the diagnostic challenges in drug-induced allergic dermatoses, demonstrating how drug-induced pemphigus herpetiformis (PH) can closely mimic other autoimmune blistering disorders, such as dermatitis herpetiformis and bullous pemphigoid. The overlap in clinical presentation complicates accurate diagnosis, underscoring the importance of thorough evaluation and the need for histopathological confirmation to differentiate between these conditions.

Keywords: *drug-induced pemphigus herpetiformis, diagnosis, allergic dermatosis*

DISCOID LUPUS ERYTHEMATOSUS MIMICKING SKIN INFECTION

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ABSTRACT

INTRODUCTION: Cutaneous lupus erythematosus (CLE) is an autoimmune inflammatory disease affecting the skin, characterized by various types of lesions, including butterfly rash, discoid rash, psoriasiform or ring-shaped lesions with polycyclic patterns, and alopecia. Based on clinical morphology, histopathological changes, and the duration of skin lesions, CLE is classified into three categories: chronic (CCLE), subacute (SCLE), and acute (ACLE). Discoid lupus erythematosus (DLE), the most common form of chronic CLE, primarily affects sun-exposed areas such as the face, ears, neck, and scalp. The typical lesions start as erythematous macules or papules that progress to scaly, discoid plaques. Left untreated, these lesions may result in scarring, alopecia, and poikilodermatous appearance. Diagnosis of DLE is usually based on clinical presentation, but in cases of uncertainty, a skin biopsy is recommended, which reveals characteristic changes such as hyperkeratosis, inflammatory infiltration, and alterations in the basement membrane. The primary treatment involves sun protection and the use of topical corticosteroids. In severe cases, systemic therapy with antimalarials and corticosteroids may be required.

CASE PRESENTATION: We present a clinical case of discoid lupus erythematosus with an unusual manifestation—confluent lesions with extremely indurated edges, numerous pustules suggestive of a skin infection, and post-lesional hypertrichosis instead of the classic lupus-associated alopecia. In the diagnosis of the case, a number of differential diagnoses were proposed, some of which—mycotic infection, bacterial infection, demodecosis, and skin tuberculosis, which were successively rejected after a number of clinical and laboratory tests. The 38-year-old female patient was serologically and histologically diagnosed with discoid lupus erythematosus.

CONCLUSION: During the course of immunosuppressive therapy, the patient's condition progressively worsened, ultimately leading to a confirmed diagnosis of pulmonary tuberculosis.

Keywords: *discoid lupus erythematosus, immunosuppression, tuberculosis*

A PATIENT WITH PRADER-WILLI SYNDROME AND SEIZURES, FOLLOWED UP AT A SINGLE EXPERT CENTER FOR RARE ENDOCRINE DISEASES. A CASE REPORT

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ABSTRACT

INTRODUCTION: Prader-Willi syndrome (PWS) is a complex genetic disorder, affecting approximately 1:15000 births. It is characterized by pre- and postnatal growth retardation, neonatal hypotonia, hyperphagia and early development of obesity, hypogonadism, learning and cognitive deficits, and temper outbursts. Patients with this rare condition sometimes present with peculiar complaints and highly specialized care for a proper follow-up is needed.

CASE PRESENTATION: A case of 6-year-old-boy with genetically confirmed PWS (deletion 15q) at 3 months of age is presented. At that time, an increase in the head circumference size was noted. Computer tomography evidence of dilated lateral ventricles was found. Our patient developed non-occlusive hydrocephalus in the following months. A ventriculoperitoneal shunt was placed at the age of 9 months. The patient presented to our Expert Center for Rare Endocrine Diseases for the first time at the age of 10 months. Complaints of staring spells started at the age of 1. Electroencephalography was performed. The result was abnormal and the patient started treatment with valproic acid, with regular follow-up and good control of the epilepsy up to this moment.

DISCUSSION: This syndrome is a connecting point between neurological disorders such as epilepsy and the predisposition of these deletion genotype patients for developing structural changes in the brain, the most common of which is ventriculomegaly. Ventriculoperitoneal shunt systems are the mainstay therapy for patients with hydrocephalus, but several authors have reported an increased risk of epileptic seizures after shunt-treated hydrocephalus, especially in children. Clinical studies also show a correlation between Prader-Willi syndrome and the manifestation of epilepsy, with staring spells being the predominant type of seizures among the tested individuals. Our patient is an example of a complicated case in which the etiology of the seizures remains unclear. This indicates the need for a careful reassessment of neurosurgical intervention in patients with similar complaints in the future.

CONCLUSION: This case highlights the importance of a multidisciplinary approach when treating patients with PWS. The complexity of this rare syndrome necessitates referral to expert centers for rare endocrine diseases, because these patients need very specialized care and proper follow-up in order to maintain a better quality of life.

Keywords: *Prader-Willi syndrome, epilepsy, multidisciplinary team, rare disease*

A CASE REPORT HIGHLIGHTING THE CHALLENGES OF DIAGNOSING BACLOFEN WITHDRAWAL SYNDROME IN BULGARIA

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ABSTRACT

INTRODUCTION: Inflation of the global baclofen market since 2004 has facilitated increased baclofen misuse, but does incognizance ultimately lead to clinical challenges? Baclofen, a GABAb receptor agonist, typically acts as a myorelaxant, however, high doses mirror anxiolytic, sedative, and psychostimulant effects. A study in the Journal of Clinical Psychiatry suggests withdrawal can occur after doses as low as 20 mg/day, while abrupt cessation may result in life-threatening complications with diverse somatic, neurological, and psychiatric manifestations.

CASE PRESENTATION: A 22-year-old Bulgarian male with a history of long-term polysubstance abuse, including baclofen, pregabalin, and ephedrine is presented. Upon admission to psychiatry, he presented with an acute psychotic state, exhibiting psychomotor agitation, disorganisation, delirium and multimodal hallucinations. Subsequently, his condition rapidly deteriorated to fever, tachycardia, hypertension, and grand-mal seizures, succumbing to a sopor state with meningoradicular irritation. The patient was transferred to neurology for intensive care. Laboratory tests indicated multi-organ dysfunction and coagulation abnormalities. A lumbar puncture with polymerase chain reaction (PCR) for 15 antigens and virology yielded negative results. Magnetic resonance imaging (MRI) showed nonspecific fluid-attenuated inversion recovery (FLAIR) hyperintensities. Despite treatment with antipsychotics and anticonvulsants, the patient worsened. After excluding baclofen intoxication, neuroleptic malignant syndrome, rhabdomyolysis, autoimmune, and viral encephalitis, baclofen withdrawal was identified as the issue. His treatment regimen included reintroduction of baclofen at 10 mg/day, increasing to 20 mg/day by the third day, which led to full recovery. The patient was discharged on 10 mg/day for three weeks. Gradual tapering under psychiatric supervision is planned as ongoing therapy.

CONCLUSION: An integrated multidisciplinary approach was essential for this patient's recovery. Currently, due to a scarcity of reported cases, there is a limited framework to support baclofen dependency. This case underscores the challenges of identifying the rare complications of substance abuse, calling for increased awareness and research to better understand clinical implications and improve management strategies.

Keywords: *baclofen, dependency, withdrawal*

PYOGENIC SPONDYLODISCITIS IN A PATIENT WITH MULTIPLE SCLEROSIS. A CASE REPOST

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ABSTRACT

INTRODUCTION: Multiple sclerosis (MS) is a chronic immune-mediated inflammatory disease that attacks myelinated axons in the central nervous system, destroying the myelin and the axon in variable degrees and producing significant physical disability. It is a common cause of atraumatic neurological disability in young adults. Spondylodiscitis is an inflammatory disease that can be defined as a primary infection of the intervertebral disc, with secondary infections of the vertebrae (spondylitis) and accounts for 2% to 7% of all infections of the musculoskeletal system with an incidence estimated to be around 1/100,000 people per year, with a male prevalence which is double that of females (2:1). Staphylococcus aureus is the most frequently encountered bacteria (40–80%), causing the infection.

CASE PRESENTATION: We report the case of a 55-year-old woman admitted to the First Neurology Clinic at St. Marina University Hospital in Varna, Bulgaria, in July 2019. The patient presented with lower limb weakness, unstable gait, vertigo, and difficulty climbing stairs. She had been diagnosed with the cerebrospinal form of MS earlier that year, confirmed by magnetic resonance imaging (MRI). Her medical history included type 2 diabetes and coxarthrosis. Neurological examination showed moderate lower spastic paraparesis, positive bilateral Babinski signs, and mild urinary incontinence. MRI confirmed active MS lesions, meeting the European Multicenter Research Network criteria, and corticosteroid treatment was initiated, leading to symptom improvement. On the fifth day of hospitalization, the patient developed new severe chest and lumbar pain along with fever. Magnetic resonance imaging of the lumbar spine revealed an inflammatory purulent collection compressing the dural sac, cauda equina, and conus medullaris, as well as spondylodiscitis at L4–L5 and an abscess in the left psoas muscle. Drainage of the abscess was performed, and microbiological analysis confirmed Staphylococcus aureus infection. Antibiotic therapy led to significant improvement, and the patient was discharged with stable vital signs after rehabilitation.

CONCLUSION: This case highlights the importance of closely monitoring patients receiving high-dose corticosteroid therapy, as immunosuppression can result in opportunistic infections that may complicate their clinical course and require prompt intervention.

Keywords: *multiple sclerosis, spondylodiscitis, corticosteroid therapy*

STEINERT MYOTONIC DYSTROPHY. A CASE REPORT FROM THE NEUROLOGY CLINIC

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ABSTRACT

INTRODUCTION: Steinert disease (myotonic dystrophy type 1, DM1) is an inherited multisystem disorder presenting with muscle-related symptoms (muscle weakness, muscle atrophy, and myotonia) and systemic manifestations (cardiac, endocrine, cerebral, gastrointestinal, skin, uterine, and immunologic involvement). Clinical signs vary depending on the age of onset. There are three phenotypes correlated with the disease—mild, classic, and congenital. Myotonic dystrophy type 1 is caused by the expansion of a CTG trinucleotide (cytosine-thymine-guanine) repeat in the noncoding region of DM1 protein kinase gene (DMPK).

AIM: Our aim is to present a case of a neurological disease, affecting multiple members of an affected family, each with symptoms of different severity.

CASE PRESENTATION: Several cases of a family with an affected daughter, mother, aunt, several uncles and cousins, seeking hospitalization, regarding neurological symptoms over the course of ten years are presented. The most severe presentation is observed in the daughter with mental retardation, muscle weakness in all four extremities, leg cramps, and weakness of the masticatory muscles. Her mother, aunt, and one of the uncles presented with muscle weakness, more expressed in the lower extremities, lumbar pain, radiculopathy, difficulty in swallowing, change in phonation, cataracts, and missing tendon and periosteal reflexes. More pronounced weakness in the upper extremities and myopathic gait are seen in one of the uncles.

DISCUSSION: As an autosomal dominant inherited disease, this case series of DM1 highlights the importance of molecular genetic testing for early diagnosis of relatives at risk. It allows better monitoring and treatment of systemic manifestations.

Keywords: *neurological disease, genetic testing, muscle weakness*

UNCOMMON NEUROLOGICAL COMORBIDITY: PATIENT WITH MYASTHENIA GRAVIS AND EPILEPSY. A CASE REPORT

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ABSTRACT

INTRODUCTION: Myasthenia Gravis (MG) is an autoimmune disorder caused by an antibody-mediated blockade of neuromuscular transmission resulting in skeletal muscle weakness and rapid muscle fatigue. It is a relatively rare acquired, autoimmune disorder. Epilepsy is a neurological condition that causes unprovoked, recurrent seizures, and rarely coexists with MG. However, recent research indicates that patients with autoimmune diseases, including MG, are at a higher risk of developing epileptic seizures. Studies show that up to 3% of MG patients may have epilepsy, with a risk nearly five times higher than that of the general population. This potential comorbidity may be linked to autoimmune factors or long-term anticonvulsant therapy. The recognition of epilepsy in MG patients has significant clinical implications, as it may require careful neurological evaluation and treatment adjustments.

CASE PRESENTATION: We present the case of a 73-year-old woman diagnosed with MG in 2018, who was initially treated with Kalyimin® (pyridostigmine). Over the course of one year, the patient experienced three nocturnal episodes of loss of consciousness, tongue biting, bladder incontinence, and postictal confusion, each lasting 15–20 minutes. Her last episode occurred one week prior to hospitalization. She had a history of ischemic stroke in 2018. On neurological examination, she exhibited bilateral ptosis, increased limb fatigue, and dysphagia. Electromyography (EMG) confirmed postsynaptic neuromuscular damage consistent with MG. Electroencephalography (EEG) revealed epileptiform activity in the right frontotemporal region, supporting a diagnosis of epilepsy. A computed tomography (CT) scan ruled out a thymoma but identified a nodule in the thyroid gland.

CONCLUSION: This case highlights the rare but important association between MG and epilepsy. While epilepsy in MG patients has traditionally been attributed to long-term anticonvulsant therapy, recent studies suggest a possible autoimmune link. In this patient, the coexistence of both conditions underscores the need for comprehensive neurological evaluation in MG patients presenting with seizure-like symptoms. Clinicians should remain vigilant to avoid misdiagnosis, as appropriate treatment for epilepsy may be required. Further research is needed on autoimmune comorbidities in neurological disorders.

Keywords: *myasthenia gravis, epilepsy, autoimmune disorders, rare comorbidity, case report*

VAGUS NERVE STIMULATION AS A TREATMENT FOR DEPRESSION

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ABSTRACT

INTRODUCTION: Vagus nerve stimulation (VNS), an established form of neuromodulation, by increasing amygdala-dorsolateral prefrontal cortex connection and linking to the microbiome-brain-gut axis, which is related to lessening inflammation, has shown promise in the treatment of depression.

Aim: The objective of this study is to evaluate the benefits of VNS, which is one of the advanced methods for diagnosis and treatment of depression.

MATERIALS AND METHODS: The analysis in this paper consists of a literature review conducted in the international database of Google Scholar and PubMed. Afterwards, the information gathered was discussed with Dr. Sonya Maneva, a psychiatry resident with interests in general and specialized psychiatry.

Results: The results indicate that VNS is an innovative approach to treating depression, providing new hope for patients who do not respond to traditional therapies.

CONCLUSION: Clinical trials focused on the application of VNS for lowering seizure frequency in epileptic patients revealed its effects on mood. Consequently, VNS has been FDA-approved for depression. The area of VNS is evolving, and with the swift advancement of non-invasive VNS, it is crucial to consider historical insights to guide the creation of upcoming brain stimulation treatments.

Keywords: *VNS, depression, epileptic patients, treatment*

ACUTE RESPIRATORY DISTRESS SYNDROME ASSOCIATED WITH LENNOX-GASTAUT SYNDROME IN A 5-YEAR-OLD PATIENT: A CASE REPORT

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ABSTRACT

INTRODUCTION: Lennox-Gastaut syndrome is a rare form of epilepsy, characterised by multiple types of seizures. That makes it a possible risk factor for the development of aspiration pneumonia and potentially acute respiratory distress syndrome.

CASE PRESENTATION: A 5-year-old male patient previously diagnosed with Lennox-Gastaut syndrome and a history of daily seizures presented with fever and coughing. After a short unsuccessful outpatient treatment, a chest X-ray revealed findings consistent with bilateral bronchopneumonia, leading to hospitalisation. Despite oxygen therapy, the patient developed cyanosis and tachypnea. He was transferred to a Pediatric Intensive Care Unit (PICU). Over the next two days, the patient remained febrile and developed bradycardia, which led to cardiopulmonary resuscitation and intubation. The clinical and paraclinical features were consistent with acute respiratory distress syndrome. The patient experienced a slight remission of symptoms, however, the respiratory failure symptoms persisted. Twelve days after admission to the PICU, an attempt at tracheostomy was made, which was unsuccessful, due to the patient developing severe cyanosis, bradycardia and tachypnea in the operating room. Resuscitative measures were able to temporarily stabilise him but the patient was pronounced deceased later that evening. No pathogens were isolated over the course of the evaluation.

CONCLUSION: This case illustrates a possible connection between the various types of seizures caused by Lennox-Gastaut syndrome and acute respiratory distress syndrome. Although impossible to confirm the causation of the primary diagnosis, the patient did have an impaired swallowing reflex, which stemmed from the developmental delay from the syndrome, and a history of daily seizures. This combination creates a predisposition for frequent aspirations, leading to the development of aspiration pneumonia, associated with acute lung injury. This case highlights the need for heightened vigilance for respiratory complications, when treating patients with Lennox-Gastaut syndrome.

Keywords: *Lennox-Gastaut syndrome, acute respiratory distress syndrome, aspiration pneumonia*

A CASE REPORT OF POTENTIAL SUBCLAVIAN STEAL PHENOMENON/SYNDROME—IS IT CRUCIAL TO BE CRITICAL TO "USUAL" CT ISCHEMIC STROKE FINDINGS?

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ABSTRACT

INTRODUCTION: Bilateral carotid artery stenosis, in combination with possible subclavian steal phenomenon/syndrome (SSS), is a rare condition. Reported findings could be presented as transient ischemic attack (TIA) or as ischemic stroke. Multiple vascular ischemic lesions should always be evaluated carefully and the possible etiology factors should be precisely estimated.

CASE PRESENTATION: A 65-year-old male patient was admitted to the hospital due to symptoms of neurological deficit after an examination performed by a neurologist in outpatient settings. Only two hours after the admission, he underwent a non-enhanced computed tomography (CT) examination of the brain and the surrounding cranial structures. There were imaging findings in the left insular region for acute ischemic stroke with associated hyperdense MCA (M2/M3 segments) and chronic parietal infarction zone on the left—ASPECTS 9 (-1). Two days later, the acute insular finding presented as subacute and we distinguished three new subacute hypodense lesions—one on the left, in the temporal lobe, and two frontal lesions on the right. After 5 days, a CT angiography of the cerebral arteries showed occlusion of both the internal carotid artery (ICA) and the left subclavian artery. Due to severe atherosclerosis, SSS is presented as vertebrobasilar insufficiency and is the cause of the ischemic accidents.

CONCLUSION: Stroke is the second most common cause of morbidity worldwide and it could affect different vascular territories. Patients present with a wide range of exact neurological deficits and clinical symptoms. In case of ischemic stroke, there are some simple and useful classifications (TOAST and ASCOD), which refer to the most popular examples of etiology and also give information about the possible risk factors. One of the mentioned etiology factors is the clinically relevant stenosis of ICA, resulting in TIA episodes and ischemic stroke accidents. But if there is critical stenosis of one of the subclavian arteries (relatively rare—2–4% of the general population) we should consider the steno-occlusive disease as a main reason for the ischemic pattern and presence of potential SSS. At the same time, we cannot exclude any other reason for the multiple lesions involving multiple arterial territories, but present atherosclerotic plaques are the most common reason.

Keywords: *subclavian steal syndrome, bilateral carotid artery stenosis, multiple vascular ischemic lesions, radiology, stroke*

SURGERY

AN INNOVATION IN ORTHOPEDICS: TRABECULAR METAL ACETABULAR REVISION SYSTEM

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ABSTRACT

INTRODUCTION: Acetabular revision surgery is particularly challenging due to the higher occurrence of severe defects and the compromised quality of the remaining bone. Addressing bone deficiencies in the acetabulum is one of the most difficult aspects of hip surgery.

AIM: Trabecular metal system is an implant made from tantalum that demonstrates similar structural and functional properties as the bone matrix. It is a porous structure that can easily fixate and initiate enough amount of perfusion for the bone, allowing the proliferation of cells and formation of new more stable tissue through the pores. By using the acetabular system as an implant during operations, healthcare providers can increase the process of vascularization and healing, while also lowering the chances of infections and prevent complications.

MATERIALS AND METHODS: A systematic literature review was conducted, including scholarly magazines, research papers, and websites. The search included research papers and information about orthopedic fractures and trabecular augmentation. An overviewing debrief was held with a representative from the department of Anatomy and Cell Biology in Medical University of Varna.

RESULTS: The result of our research showed that numerous articles sustain the thesis that there are beneficial properties such as speeding up of the healing process following bone fractures.

CONCLUSION: The number of cases where the trabecular metal acetabular revision system is used is tending to grow. By reducing the surgical time and providing an antiadhesive and antibacterial surface, which can more easily be accepted by the human cells, the newly implemented revision system shows as an innovative method in the field of post-operative healthcare.

Keywords: *trabecular metal, acetabulum, porous, orthopedics, deformation, innovation*

AN INNOVATIVE APPROACH IN POSTSURGICAL HEALTHCARE: FRACTURE MONITOR

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ABSTRACT

INTRODUCTION: Delayed healing of fractured bones still presents as a main challenge within the orthopedic trauma surgery field. Information about the postsurgical healing process has been hard to gather due to the inaccessibility of the confined region and limited diagnostic methods.

AIM: A recent development by ARI suggests a novel approach to continuously measuring both fracture healing and patient activity. The Fracture Monitor is a biofeedback sensor system that consistently and objectively monitors the healing progression. It is composed of an implantable data logger attached to a standard bone plate and a wirelessly connected smartphone app, which provides the needed information.

MATERIALS AND METHODS: A systematic literature review was conducted including scholarly magazines, research papers, and websites. Using the method of analysis, we summed up the characteristics, main goals, and applications of the revolutionary device in the postsurgical healing period. After that, an interview with a representative of the Department of Anatomy and Cell Biology at Medical University of Varna was conducted and a discussion was held.

RESULTS: The results from the search show that numerous articles mention the benefits of the use of the Fracture Monitor in the surgical and postsurgical period. As this sensor is currently monitoring the healing process of a fractured bone in a 61-year-old patient, implanted with the system in 2023, we can continuously observe fracture healing over time: how the space between the bone plates differs, if both are consolidating the right way or are in need an adjustment.

CONCLUSION: The revolutionary system will allow surgeons and patients to detect and react to healing disturbances before a second surgery is necessary. Waiting for an X-ray or computed tomography (CT) can be just the time needed to avoid further unwanted procedures. Therefore, the Fracture Monitor can prevent unnecessary complications, reduce hospital visits, and save time for the doctors, allowing them access to information via their smartphones.

Keywords: *fracture, monitoring, sensor system, healing progression*

A CASE OF AMYAND'S HERNIA IN RECURRENT RIGHT INGUINAL HERNIA

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ABSTRACT

INTRODUCTION: A hernia involves the protrusion of an organ or tissue through its containing cavity wall and may be congenital or acquired. Inguinal hernias represent roughly 70% of abdominal wall hernias, with a 90% male predominance and an incarceration rate of 5–15%. Only about 1% of inguinal hernias contain the appendix, first documented by Claudius Amyand in 1735. The appendix within these hernias may be unaffected or present with inflammation or perforation. The incidence of acute appendicitis within an inguinal hernia is rare, reported to be between 0.07% and 0.13%.

CASE PRESENTATION: A 62-year-old woman presented with right-sided abdominal pain, nausea, vomiting, and fever (38.3°C), persisting for 3–4 days. Her history included surgery for an incarcerated right inguinal hernia via lower median laparotomy. On examination, the abdomen was distended with localized tenderness in the right lower quadrant, and a palpable 7–8 cm mass was observed. Blood tests indicated leukocytosis (12.25 x10^9/L) and elevated C-reactive protein (CRP) (411.58 mg/L). Computed tomography (CT) findings suggested a right inguinal hernia involving the cecum, appendix, and a periappendicular abscess. Emergency surgery revealed a phlegmonous appendix and cecum segment within the incarcerated hernia sac. The procedure involved abscess drainage, appendectomy with primary cecal sutures, and hernia repair with own tissues following Lawson-Taid's method. The postoperative course was uneventful, and histology confirmed phlegmonous appendicitis with local peritonitis. Microbial culture identified E. coli and Serratia marcescens.

CONCLUSION: Amyand's hernia is a rare but critical diagnostic consideration in cases of incarcerated inguinal hernias with an inflammatory component. Ultrasound and CT imaging are essential for diagnosis. Surgical intervention is necessary, with the decision to use mesh depending on the presence of appendiceal inflammation.

Keywords: *Amyand's hernia, appendix in hernia, incarceration, inguinal hernia*

A CASE OF HARTMANN'S PROCEDURE WITH LEFT HEMICOLECTOMY

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ABSTRACT

INTRODUCTION: A tumor is an abnormal mass of cells that can spread through the bloodstream and lymphatic system. There are two types: benign and malignant. Benign tumors usually do not affect nearby tissues or develop into cancer, so they rarely require treatment, though they can cause complications by pressing on adjacent tissues. Malignant tumors, however, can spread and affect other organs, with metastases indicating their progression.

CASE PRESENTATION: A 46-year-old male presented at the emergency room with constant pain in the upper abdominal region that radiated to his left hypochondrium. Other symptoms reported were constipation, bloating, and absence of flatus with a wasting syndrome of 15 kg. Imaging studies: roentgenography and computed tomography (CT) of the abdomen revealed a tumorous formation in the distal part of transverse colon that caused obstruction and consequential proximal dilatation of the colon. The mass formation lay on the anterior abdominal wall with a possibility of infiltration. The surgery started with a medial laparotomy and exploration of the abdominal cavity that showed a progressed tumor in the area of lienal flexure with size of 10/8 cm. There was an infiltration of the greater curvature of the stomach and the tail of the pancreas. The procedure consisted of left hemicolectomy and removal of the sigmoid colon with the usage of flat stapler. A resection of the infiltrated part of the stomach was performed. Two drainages were placed in the left lateral canal and another one on the right side. At the end of the operation, a transverse colostomy was performed, along with layered laparoscopic synthesis and the application of a sterile dressing.

CONCLUSION: This kind of surgery is life-saving but leaves a permanent change in the patient's life. After 6–12 months in which the colon has had the chance to heal, the patient's condition should be reevaluated. If there are no complications, a surgery of rejoining the colon to the rectum is done along with closing the colostomy.

Keywords: *Hartmann's procedure, hemicolectomy, tumor, case report*

CYSTIC ECHINOCOCCOSIS— TO OPERATE OR NOT TO OPERATE?

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ABSTRACT

INTRODUCTION: Cystic echinococcosis (CE) is a zoonotic helminthiasis caused by *Echinococcus granulosus*, which affects the liver, lungs, and other internal organs. Although surgery has traditionally been the mainstay of treatment, non-surgical options have become increasingly effective.

AIM: This review compares the recommended algorithms for decision upon surgical versus non-surgical treatments for CE, considering the organ localization, cyst's numbers, size, stage, and patient characteristics.

MATERIALS AND METHODS: A systematic search in the scientific databases was performed using the keywords "cystic echinococcosis", "*Echinococcus granulosus*", "treatment", "surgery", "PAIR", "watch and wait", and their synonyms and combinations. Only studies investigating surgical interventions, percutaneous treatments, pharmaceutical management, and the watch-and-wait strategy with regard to the treatment selection, efficacy, and risk-of-recurrence were included in the review.

RESULTS: Surgery remains essential for echinococcal cysts with a high risk of complications or relapse. It is the only treatment option for complete cyst removal, but it carries risks of intraoperative complications and recurrence due to spillage of cyst contents. Non-surgical approaches, such as continuous albendazole therapy combined with praziquantel, have shown efficacy in reducing relapses and improving outcomes for uncomplicated cysts. Percutaneous treatment options can be enhanced by using innovative nanoparticle scolicidal agents, such as selenium and silver. Despite advancements, inappropriate surgical interventions are still common, particularly for inactive cysts, which could be managed with a watch-and-wait approach.

CONCLUSION: While surgery remains vital for complex cases, non-surgical treatments and pharmacological management provide effective alternatives for uncomplicated CE or in cases when operation is contraindicated. Adopting stage-specific decisions, as recommended by the WHO, or furthermore, patient-specific or individualized management, is vital to improve patient outcomes and reduce the risk of relapses or complications.

Keywords: *cystic echinococcosis, Echinococcus granulosus, surgery, PAIR, albendazole, nanoparticles*

ECTOPIC PANCREAS IN MECKEL'S DIVERTICULUM: A CASE REPORT

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ABSTRACT

INTRODUCTION: Ectopic pancreas, also referred to as heterotopic or aberrant pancreas, is characterized by the presence of pancreatic tissue outside its typical anatomical and vascular connections. This ectopic tissue, when found alongside other gastrointestinal malformations, may indicate a shared embryonic origin. Meckel's diverticulum, the most frequently occurring omphalomesenteric anomaly, is observed in 2–3% of the population. While generally asymptomatic, complications develop in only about 2% of cases, primarily within the early years of life, with a predominance in children under the age of two.

CASE PRESENTATION: A 79-year-old female presented urgently to the Second Clinic of Surgery at St. Marina University Hospital in Varna with primary complaints of abdominal pain, nausea, and recurrent vomiting. On examination, the patient appeared to be in a severely affected state, with marked tenderness in the hypogastric region, noticeable abdominal distension, and significantly reduced or absent peristalsis. Laboratory evaluations indicated leukocytosis (13.1), along with elevated urea (29.7) and creatinine (455.0) levels, with other parameters such as blood glucose, transaminases, and alpha-amylase remaining within normal limits.

An abdominal ultrasound showed multiple dilated small bowel loops with pendulous peristalsis up to 25 mm. Bilateral nephrosclerosis was more pronounced on the left side. Abdominal X-rays confirmed hydroaerial levels in the small intestine, while computed tomography (CT) provided further clarity by revealing small bowel obstruction due to internal incarceration of the distal ileum and confirming the presence of Meckel's diverticulum.

Surgical exploration identified significant dilatation of the ileum approximately 30–40 cm proximal to the ileocecal valve, with evidence of necrosis in the entrapped segment. Additionally, Meckel's diverticulum was identified in the proximal jejunum. Surgical intervention included resection of the affected intestinal segment, ileal anastomosis, and wedge resection of Meckel's diverticulum. Pathological examination of the resected Meckel's diverticulum demonstrated ectopic pancreatic tissue, involving the submucosa, muscularis propria, and subserosal layers. The tissue was organized into lobules containing acini, with small ducts embedded in fibrous stroma, and included Langerhans islets dispersed among the acini.

CONCLUSION: Following surgery, the patient was monitored in the intensive care unit (ICU) due to underlying cardiac pathology, specifically atrial fibrillation. After stabilization, her postoperative course was uneventful, with the restoration of bowel function and no complications at the surgical site. She was discharged in stable condition, with no reported symptoms at follow-up evaluations.

Keywords: *ectopic pancreas, Meckel's diverticulum, case report*

LIVER ECHINOCOCCOSIS IN AN ADOLESCENT: A CASE REPORT

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ABSTRACT

INTRODUCTION: Echinococcosis is a parasitic infection commonly affecting the liver and lungs. It poses a diagnostic challenge, especially in young patients, due to its often asymptomatic nature until complications arise. This clinical case highlights the importance of considering hepatic echinococcosis in the differential diagnosis of abdominal pain and liver cysts, particularly in endemic regions.

CASE PRESENTATION: A 17-year-old female presented with abdominal pain and was initially diagnosed with acute appendicitis. After undergoing laparoscopic appendectomy, persistent abdominal pain and laboratory investigations demonstrating elevated leukocyte and eosinophil levels raised suspicion of a parasitic infection. Further evaluation through ultrasound and computed tomography (CT) imaging revealed multiple cystic lesions in the liver, particularly in segments VI and VIII near the diaphragm. Subsequent serology confirmed echinococcus granulosus infection. The patient underwent laparoscopic echinococcectomy during which 400 mL of cystic fluid was drained and the cyst walls were removed. Post-operatively, she was treated with albendazole and had an uneventful recovery, with follow-up ultrasound imaging after a month showing no recurrence of cysts.

CONCLUSION: This case underscores the necessity of prompt recognition and management of hepatic echinococcosis, even when initially asymptomatic or presenting with non-specific symptoms. Early intervention with surgery and antiparasitic therapy can lead to favorable outcomes.

Keywords: *echinococcosis, liver, infection*

ADJACENT LEVEL FRACTURE FOLLOWING VERTEBROPLASTY IN AN OSTEOPOROTIC PATIENT: A CASE REPORT AND REVIEW OF RISK FACTORS

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ABSTRACT

INTRODUCTION: Vertebroplasty is a widely used treatment for osteoporotic vertebral fractures, offering immediate pain relief and improved mobility. However, one potential complication is the occurrence of adjacent level fractures, particularly in osteoporotic patients. We present a case of a 67-year-old female who developed an adjacent level fracture following vertebroplasty for a TH11 fracture. The aim of this case report is to highlight the risk of adjacent level fractures after vertebroplasty and emphasize the importance of careful post-operative monitoring in osteoporotic patients.

CASE PRESENTATION: We present the case of a 67-year-old female who was admitted to the neurosurgery ward of Dobrich Multidisciplinary Hospital for Active Treatment with lower back pain, persisting for two weeks following a fall. Magnetic resonance imaging (MRI) revealed spinal stenosis at the L4-L5 segment and a fracture of the TH11 vertebra. Under general anesthesia, she underwent spinal canal decompression via microsurgical technique and vertebroplasty at TH11. Despite being mobilized the day after surgery, her pain persisted. A follow-up MRI revealed an adjacent level fracture at TH12. Vertebroplasty of TH12 was performed under general anesthesia, resulting in significant pain relief, with no further surgery-related complications.

CONCLUSION: Adjacent level fractures after vertebroplasty are a recognized risk, particularly in osteoporotic patients. This case report highlights the potential for increased mechanical stress on adjacent vertebrae due to the stabilization effects of cement augmentation. We underscore the need for careful patient selection and monitoring to detect early complications. Potential contributing factors include altered biomechanics post-procedure and weakened bone quality. Although the second vertebroplasty resolved the patient's pain, prevention strategies, such as optimizing bone health, may reduce the incidence of adjacent level fractures.

Keywords: *case report, vertebroplasty, adjacent fracture, complication, osteoporosis*

BERTOLOTTI SYNDROME— AN UNUSAL CASE PRESENTATION

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ABSTRACT

INTRODUCTION: Congenital spinal abnormalities that include sacralization of the lowest lumbar vertebra or lumbarization of the first sacral vertebra (also known as the lumbosacral transitional vertebra, or LSTV), causing pain, are known as Bertolotti syndrome (BS). The spinal morphology for these abnormalities ranges from a full fusion to a widened transverse process (TP). In addition to a patient's medical history, physical examination, diagnostic imaging, and injections can be used to diagnose BS. In this case report, we present an unusual early presentation of BS, characterized by dull pain in the lumbosacral region and complications of sciatica and scoliosis, which differs from the normal age range of onset, which typically begins at around 30 years of age.

CASE PRESENTATION: An active 18-year-old female presents with constant, dull, unilateral lumbar pain. The pain is not associated with physical activity during the day. Over the course of 4 years, the condition has been misdiagnosed as piriformis syndrome. After a period of intense physical activity, new symptoms of pain and parasthesia in the left leg appeared. Neurological examination revealed lower back pain (LBP), scoliosis, left L5 radicular pain and L5 dermatome parasthesia. Imaging results showed sacralization of L5 (Castellvi 2a—pseudoarthrosis of the transverse process and sacrum, on the left), paramedian disc bulging at the level of L4-L5 on the left side, and scoliosis. She was successfully treated with non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. Two months later she was feeling well and was leading a physically active life.

CONCLUSION: Bertolotti syndrome must be considered in the differential diagnosis of patients with LBP, including the young adult population. It can be associated with other degenerative or congenital spinal diseases. Non-steroidal anti-inflammatory drugs and conservative management should be the initial treatment strategy in BS. If these fail, local injections and surgery can be discussed.

Keywords: *lower back pain, lumbosacral transitional vertebra, Bertolotti syndrome*

CHALLENGES IN DIAGNOSING VERTEBRAL METASTASES: A COMPLEX CASE OF INITIAL NEGATIVE BIOPSY IN LUNG CANCER PATIENT

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ABSTRACT

INTRODUCTION: Vertebral bone metastases account for 33% of lung cancer incidences, which creates a high-risk, late-stage diagnosis and challenging treatment in such patients. Though biopsy examination is a standard procedure, misinterpretation of the material could lead to a delayed diagnosis.

AIM: The aim of this article is to report a clinical case of a patient with an initial false-negative biopsy for vertebral metastasis and review the diagnostic challenges and treatment methods for stabilisation of the spine.

CASE PRESENTATION: We present the case of a 74-year-old male patient with lung cancer who underwent an L4 vertebroplasty operation with biopsy examination showing a negative result for a malignancy. Later he entered the Neurosurgery Clinic with clinical manifestations with severe pain in the upper and the lower back radiating to the lower limbs with tingling lasting for three months. Computed tomography (CT) revealed a stenosis of the spinal canal at level L4-L5 and a herniated spinal disc, which was handled with a laminectomy and decompression of the spinal canal. The biopsy examination was now positive for cancer. The surgery included tumour extirpation, stabilisation, and metallic osteosynthesis of the L4 vertebra. Postoperatively, the patient had a reduction of the symptoms, and no complications were observed.

CONCLUSION: The false-negative biopsy caused the late-stage diagnosis of the tumour formation and its challenging treatment. The misinterpretation could be the result of a sampling error, tumour heterogeneity, or insufficient biopsy material. The spinal stenosis and the disc herniation are signs of possible malignancy of the vertebrae. A late diagnosis can lead to worsening of the clinical manifestations and other neurological sequelae. The second biopsy examination proved that the lung cancer metastasised to the L4 vertebra. The patient was relieved from the symptoms after the tumour extirpation and stabilisation of the vertebra. The combination of imaging techniques and repeated biopsies prevents the delayed diagnosis of vertebral metastases and impairment of the spinal cord.

Keywords: *vertebral metastases, biopsy, lung cancer*

INCISION AND DRAINAGE VERSUS TONSILLECTOMY AS TREATMENT OPTIONS FOR PERITONSILLAR ABSCESS. ASSESSING RECURRENCE RATE AND HOSPITAL STAY DURATION: A LITERATURE REVIEW

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ABSTRACT

INTRODUCTION: A peritonsillar abscess (PTA) is a localized collection of pus in the peritonsillar space between the tonsillar capsule and superior constrictor muscle. Since PTAs have a high recurrence likelihood, proper treatment options are still debated.

AIM: This literature review aims to compare two of the most commonly used treatment options for PTA management—incision and drainage (I&D) and tonsillectomy, in the following categories: recurrence rate and hospital stay duration.

SEARCH METHODOLOGY: A Google Scholar and PubMed literature review was conducted, using appropriate search terms to identify suitable articles, published after the year 2010. The search yielded 8 pertinent articles, 4 of which were excluded, due to not matching the date of publication criteria.

RESULTS: Two of the studies compared I&D and tonsillectomy as treatment methods for PTA. Both studies showed higher recurrence rate of PTA in patients after I&D; in regard to tonsillectomy, there was 2.8% and 6.7% recurrence rate in the first and second study, respectively. Another study presented a high recurrence rate of PTA among adolescents and young adults, treated with aspiration or incision for drainage in combination with antibiotics. The reviewed literature supported the notion that tonsillectomy as treatment for PTA requires longer hospital stay.

CONCLUSION: Although I&D has a higher recurrence rate than tonsillectomy, the former also requires shorter patient hospital stay. Tonsillectomy is a preferred method of treatment in recurring cases of PTA, especially in adolescents and young adults, where the recurrence rate is higher. The field could benefit from more studies, closely comparing the results of the two treatment options.

Keywords: *incision, drainage, tonsillectomy, peritonsillar abscess, recurrence rate, hospital stay*

SPINAL CORD STIMULATION AS A METHOD FOR TREATMENT OF FAILED BACK SURGERY SYNDROME

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ABSTRACT

INTRODUCTION: Failed back surgery syndrome (FBSS) is defined as lumbar pain of unknown origin that persists despite postoperative manipulation. This condition has different manifestations, but it is commonly associated with chronic pain that may become resistant to pharmacologic therapy. These patients have to take different types of medications in high doses with unsatisfactory effect. This will eventually lead to further deterioration of the patient's quality of life (QoL). Spinal cord stimulation (SCS) is an innovative method for the treatment of drug-resistant chronic pain in which electrodes are implanted in the epidural space and the dorsal column Aβ-fibers are stimulated. This technique can modulate nociception and improve the patient's QoL. In this case, we present the key aspects of SCS treatment, the step-by-step surgical procedure, and the positive outcome in a patient with FBSS.

CASE PRESENTATION: A 59-year-old patient with FBSS was admitted to the Clinic of Neurosurgery, St. Marina University Hospital in Varna due to complaints of back pain aggravated by motion, radiating to the dorsolateral surfaces of both legs. On neurological examination the patient presented with lower back pain, neurogenic claudication, weakened patellar and Achilles reflex on both sides, and the visual analog scale (VAS) score was 8 points. Surgery was performed to place a temporary percutaneous SCS device and electrodes. After a successful trial period, she underwent a second surgery for implantation of a permanent SCS device. Postoperatively, the patient was without additional neurological deficits. There were no complications, and the VAS score was 2 points.

CONCLUSION: Spinal cord stimulation is an innovative, minimally invasive surgical treatment for chronic pain due to FBSS that provides satisfactory results in patients who are refractory to analgesics. It is crucial to understand its risks and limitations, such as surgical complications, patient selection, and others. This method shows good results and will be increasingly used in the near future for various conditions related to chronic pain.

Keywords: *Chronic pain, Spinal cord stimulation, Failed back surgery syndrome*

SURGICAL REMOVAL OF GLOSSOPHARYNGEAL SCHWANNOMA AFTER FAILED RADIOTHERAPY

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ABSTRACT

INTRODUCTION: Schwannomas are nerve sheath tumors formed by Schwann cells, which are often described as slow growing. Vestibular schwannomas, or acoustic neuromas, are the most prevalent type of schwannomas, those of the trigeminal, facial, and lower cranial nerves are the next most common types. Glossopharyngeal schwannomas (GPS) are uncommon tumors and there are not many case reports of them in the literature. The standard treatment is surgical removal of the tumor while preserving nerve function. Radiation therapy is an option for slow-growing small- and medium-sized (<3 cm) schwannomas and for patients who prefer this type of therapy. We present a rare clinical case of a GPS with a good outcome who was operated after failed radiotherapy.

CASE PRESENTATION: A 27-year-old woman with a history of GPS presented with symptoms of headache, dizziness, and hearing loss. She had undergone radiotherapy one year prior, which resulted in hearing loss and worsened her symptoms. Neurologically, she presented with intracranial hypertension, right glossopharyngeal nerve paresis, right side anacusis, and ataxic gait. Head magnetic resonance imaging (MRI) showed tumor growth, compressing the fourth ventricle and 3 mm midline shift. Suboccipital retrosigmoid craniotomy was performed to remove the tumor. Neuroendoscopic total excision of the tumor formation was achieved despite tissue changes and adhesions because of radiotherapy. Postoperative computed tomography confirmed the complete removal of the tumor. A GPS was confirmed histologically. No additional neurological deficits or complications were observed after surgery. Glossopharyngeal nerve function was preserved and hearing and gait improved. Five months postoperatively she is doing well. She has no new complaints.

CONCLUSION: This case highlights the importance of selecting the appropriate treatment strategy for schwannomas, such as those with GPS. After initial radiotherapy, which led to worsening of the symptoms and tumor progression, surgical intervention proved to be effective. Excision of the tumor confirmed the diagnosis and preserved glossopharyngeal nerve function, resulting in a good clinical outcome with no additional neurological deficits. This case supports surgical resection as a viable option for patients with tumor growth or treatment failure following radiotherapy.

Keywords: *glossopharyngeal, schwannoma, cranial nerve tumor*

ARTIFICIAL INTELLIGENCE IN THORACIC SURGERY: A REVIEW

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ABSTRACT

INTRODUCTION: The recent upsurge of artificial intelligence (AI) offers promising perspectives in all fields of everyday life, such as economics, data analysis, and medicine. Even though current usage of AI in the medical field is still fairly limited, major strides have been made in recent years. Studies have shown that AI can not only assist in pre-operative assessment and decision-making in thoracic surgery patients but provide useful insights intra- and postoperatively as well.

AIM: The main goal of this international interdisciplinary review is to examine the present-day situation of AI in thoracic surgery, outline possible future applications, and determine its limitations.

MATERIALS AND METHODS: The PubMed database was screened for relevant articles in the period between 2014 and 2024. Out of 255 total, 10 were deemed sufficiently relevant. References of interest in the selected articles were also reviewed.

RESULTS: Artificial intelligence can quickly and conveniently process enormous amounts of data and respectively reveal statistical relations, make correct predictions, and recognize pathology on medical imaging. Deep learning and artificial neural networks (ANNs) consistently outperform radiologists on low-dose chest computed tomography (CT) in specificity and sensitivity. Computer vision algorithms are used to assess intraoperative blood loss in video-assisted thoracoscopic surgery (VATS). Augmented reality and AI have been shown to be beneficial in operative spatial awareness and tumor tissue recognition. Artificial neural networks offer better pre-operative stratification compared to conventional scales and can predict complications. A pilot study has shown that AI can correctly assess lung ultrasounds, leading to both reduced costs and X-ray exposure. Currently, a small number of AI algorithms are officially approved, including IBM's Watson Oncology treatment generator, IDx-DR, a diabetic retinopathy autonomous diagnostic instrument.

CONCLUSION: This review establishes that AI has an ever-increasing importance in thoracic surgery. Multiple algorithms have been developed, serving various purposes. While small-scale studies have proven successful, large multicenter studies are needed to verify specificity and sensitivity. A myriad of legislative and ethical issues, such as representative samples and sufficient reliability, hinder widespread adoption.

Keywords: *artificial intelligence, thoracic surgery, AI, lung cancer, cardiothoracic surgery*

A CASE OF MINIMALLY INVASIVE DIRECT CORONARY ARTERY BYPASS (MIDCAB) FOR THE TREATMENT OF ISOLATED DISEASE OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY

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ABSTRACT

INTRODUCTION: Minimally invasive direct coronary artery bypass (MIDCAB) is a surgical treatment for isolated disease of the left anterior descending (LAD) coronary artery. It is a less invasive alternative compared to traditional coronary artery bypass graft surgery (CABG), which requires a median sternotomy. In MIDCAB, access to the heart is achieved through a left anterior mini-thoracotomy (a 5-to-7 cm incision between the ribs), resulting in faster recovery times, lower rates of complications, and smaller scars. This case report presents the successful application of MIDCAB in a patient with occlusion (100% stenosis) of the LAD artery.

CASE PRESENTATION: A 64-year-old male with a history of hypertension, hyperuricemia, and hyperlipidemia was referred for myocardial revascularization due to significant coronary artery disease. Selective coronary angiography (SCAG) revealed: LAD—chronic occlusion of the mid-segment (TIMI-0), left circumflex artery (LCx)—borderline stenosis, and right coronary artery (RCA)—50% stenosis in the proximal segment. Given the nature of the disease and the patient's preference for a minimally invasive approach, MIDCAB was chosen as the preferred treatment option. The surgery was performed in the following order: a 7 cm left anterior thoracotomy in the fourth intercostal space, harvesting of the left internal mammary artery (LIMA), incision of the pericardium, arteriotomy of the LAD using an OCTOPUS stabilizer, and terminolateral anastomosis with LIMA, using a continuous suture. Left pleural drain was inserted, followed by closure of the thoracotomy, and application of an ointment dressing. The procedure was completed without intraoperative complications, and the patient experienced an uneventful postoperative recovery. He was discharged on the fifth postoperative day with instructions for regular follow-up.

CONCLUSION: Minimally invasive direct coronary artery bypass is particularly advantageous for patients with isolated LAD disease, as it minimizes the trauma associated with traditional CABG. In this case, the patient benefitted from a shorter hospital stay and a quicker recovery. This case emphasizes the importance of personalized treatment selection in coronary artery disease and demonstrates the effectiveness of MIDCAB for isolated LAD stenosis.

Keywords: *minimally invasive direct coronary artery bypass (MIDCAB), coronary artery disease, LAD stenosis, case report*

VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA AFTER COVID-19 VACCINATION: A CASE REPORT AND REVIEW

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ABSTRACT

INTRODUCTION: COVID-19 is associated with heightened thrombotic risk due to various thrombo-inflammatory pathways. Vaccine-induced immune thrombotic thrombocytopenia (VITT), characterised by post-vaccination thrombosis and thrombocytopenia has emerged as a rare but serious complication, particularly following adenovirus-vectored vaccines.

CASE PRESENTATION: A 34-year-old female presented with severe headaches and visual disturbances two weeks after receiving the ChAdOx1 (Oxford/AstraZeneca) vaccine. Physical examination revealed bilateral papilledema. Computed tomography (CT) imaging showed cerebral venous sinus thrombosis (CVST). Laboratory results indicated thrombocytopenia (platelet count 70,000/μL) and elevated D-dimer levels (1,500 ng/mL). Anti-PF4 antibodies were confirmed, leading to a diagnosis of VITT. The patient was treated with non-heparin anticoagulation and improved significantly.

MATERIALS AND METHODS: A literature review was conducted, analysing data from various studies reporting post-vaccination thrombotic events. Statistical analysis included a comparison of cases reported to the European Medicines Agency (EMA), specifically evaluating the incidence of thrombocytopenia in patients vaccinated with ChAdOx1 and other vaccines.

RESULTS: Among 213 reported CVST cases post-vaccination, 187 were associated with the ChAdOx1 vaccine, with thrombocytopenia present in 107 cases (57%). Comparatively, none of the mRNA vaccine recipients experienced thrombocytopenia. Pre-COVID-19 studies indicated that only 8.4% of patients with CVST had mild thrombocytopenia, suggesting a distinct mechanism in VITT (P values not readily available).

DISCUSSION: This case underscores the need for clinicians to recognize the unique presentation of VITT following COVID-19 vaccination. The presence of anti-PF4 antibodies suggests a mechanism akin to heparin-induced thrombocytopenia, indicating the necessity for heightened awareness in post-vaccination patients presenting with thrombosis. Ongoing studies are essential to enlighten the pathophysiology of this complication, especially given the increasing number of vaccinated individuals.

CONCLUSION: Vaccine-induced immune thrombotic thrombocytopenia represents a rare but critical complication following COVID-19 vaccination. Understanding its mechanisms and clinical presentation is vital for timely diagnosis and management, highlighting the importance of continued surveillance in vaccination programs.

Keywords: *vaccine-induced thrombotic thrombocytopenia, COVID-19 vaccine, thrombosis, case report, statistics*

GENDER REASSIGNMENT SURGERY IN A MALE-TO-FEMALE TRANSSEXUAL PATIENT: A CASE REPORT

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ABSTRACT

INTRODUCTION: Transgender refers to the broad spectrum of individuals whose gender identity is different from their birth-assigned gender. Transgender patients undergo gender affirming surgery (GAS) as an effective treatment for gender dysphoria. It features multiple genital and nongenital surgical procedures. In male-to-female (MtF) transsex patients, GAS include phallectomy, orchidectomy, vaginoplasty, and clitoro-labioplasty. Nongenital procedures, such as breast augmentation, facial feminization surgery and voice surgery can complete the process of surgical gender affirmation.

CASE PRESENTATION: We report the case of a 24-year-old MtF transgender patient who underwent GAS performed by the two senior authors. The patient had been receiving hormonal therapy for five years prior to the surgical procedures, which included estradiol 2 mg, cyproterone 100 mg, and finasteride 5 mg. A complete psychiatric evaluation was undertaken to ensure a correct diagnosis.

Under general anesthesia, a bilateral orchidectomy was done. Afterwards the penis was degloved, with the penile skin creating a tubular flap. A glans flap was raised based on the neurovascular dorsal bundle in order to create the neoclitoris. Both the corporal bodies were resected completely but the urethra was preserved. The vaginal cavity was created by blunt dissection behind the urethra and in front of the rectum. The inverted penile flap was used to cover the neovagina. The urethra was shortened and repositioned. Scrotal flaps were used for the labioplasty. Breast augmentation using anatomical prostheses placed in the prepectoral plane through the inframammary fold approach was done in the same operating time. There were no post-operative complications.

CONCLUSION: It is crucial to have a multidisciplinary approach in the care of transgender patients. Progress in surgical techniques is vital for the effective treatment of transsexual patients. Understanding the new anatomy and the common complications is vital for healthcare providers.

Keywords: *gender dysphoria, vaginoplasty, breast augmentation, plastic surgery, gender affirming surgery*

RECONSTRUCTION OF CHEEKBONE LACERATION USING A ROTATION FLAP: A CASE REPORT

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ABSTRACT

INTRODUCTION: Angle grinder injuries to the facial region often result in complex wounds requiring specialized reconstructive approaches to restore both function and aesthetic integrity. This case highlights an angle grinder injury to the cheekbone area managed with a rotation flap, illustrating the surgical technique and the selection process in facial trauma reconstruction.

CASE PRESENTATION: A 60-year-old male presented to the emergency department after sustaining a severe laceration to the right cheekbone area from a self-made angle grinder. The injury resulted in a 5 cm laceration with significant soft tissue avulsion. Initial imaging via computed tomography (CT) scan excluded a zygomatic arch fracture. The reconstructive approach involved the use of a rotation flap from the adjacent cheek tissue to ensure optimal coverage and healing.

DISCUSSION: Various flap types were considered, including rotation, advancement, and transposition flaps. The rotation flap was chosen for its renowned application in traumatic defects in the malar area, due to the adequate skin laxity and the conformity to the natural skin lines, enhancing the final cosmetic appearance. The technique involves marking a semicircular incision adjacent to the defect, elevating the flap, and gently rotating it into position while maintaining vascular integrity with its blood supply coming from the dermal plexus. In the area near the lower eyelid, the anchoring of the rotation flap to the periosteum of the orbital rim is crucial in order to prevent complications such as a lower eyelid ectropion. Additionally, Burrow's triangle played a crucial role in this case, as it allowed for effective mobilization of the soft tissues. This triangular flap design provided a reliable base for rotation, ensuring adequate perfusion and minimizing tension at the suture line.

The rotation flap technique successfully restored the contour and function of the facial area, emphasizing the importance of individualized reconstructive strategies in managing traumatic injuries.

CONCLUSION: This case illustrates the effectiveness of rotation flaps for midface wounds and the critical role of anatomical principles in optimizing flap design and surgical outcomes.

Keywords: *cheekbone laceration, reconstructive surgery, rotation flap*

SPONTANEOUS PREGNANCY FOLLOWING RECONSTRUCTIVE TUBAL SURGERY AS PART OF THE COMPREHENSIVE TREATMENT OF INFERTILITY. A CASE REPORT

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ABSTRACT

INTRODUCTION: Infertility is defined as the inability to conceive after one year of unsuccessful attempts with regular sexual intercourse without the use of contraceptive methods. According to the World Health Organization, approximately 17.5% of the adult population suffers from infertility. Tubal infertility accounts for about 25–30% of all cases of infertility. Obstructed fallopian tubes can result from conditions such as endometriosis, *Chlamydia trachomatis* infection, salpingitis, peritonitis, ectopic pregnancy, and other infectious conditions. Reconstructive tubal surgery is fundamental to the comprehensive treatment of infertility, helping to eliminate the tubal factor that has led to it. Despite the surgical risks and high postoperative rates of ectopic pregnancy, surgery remains a primary option for patients with obstruction or other types of tubal damage, serving as a last step before in vitro fertilization (IVF). However, studies indicate that in severe cases, salpingectomy improves IVF success rates. *Chlamydia trachomatis* is the causative agent of one of the most common sexually transmitted infections globally. The infectious cycle includes two forms with specific characteristics. Due to the sexually transmitted route, preferred locations remain the epithelial cells of the endocervix and upper vaginal tract in women, which predisposes to the development of pelvic inflammatory disease (PID). It is one of the main causes of ectopic pregnancy and infertility in women.

CASE PRESENTATION: We presented two clinical cases of tubal infertility that were treated through reconstructive tubal surgery, resulting in spontaneous pregnancies.

CONCLUSION: The aim of the presented clinical case is to demonstrate that, despite the advances in assisted reproductive technologies, minimally invasive reconstructive surgeries on the fallopian tubes remain a primary method and first-line treatment in the comprehensive management of infertility, providing patients with the opportunity for natural conception.

Keywords: *infertility, pregnancy, treatment, reconstructive tubal surgery*

PUBLIC HEALTH

ANTIMICROBIAL RESISTANCE AS A PUBLIC HEALTH THREAT. CHALLENGES AND POSSIBLE ONE HEALTH SOLUTIONS IN BULGARIA

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ABSTRACT

INTRODUCTION: Antimicrobial resistance (AMR) represents a significant public health threat, primarily driven by the overuse of antibiotics (ABs). While the European Union has successfully reduced AB consumption since 2009, Bulgaria has experienced an increase in AB use in both communal and hospital settings. According to the 2021 Eurobarometer, Bulgaria's AB consumption rate is double that of Germany, and only 41% of Bulgarians are aware that ABs are ineffective against viruses. Antimicrobial resistance is, therefore, a critical public health issue, underscoring the need for comprehensive interventions through a One Health (OH) approach. The OH strategy integrates human, animal, and environmental health to address the complexities of AMR.

AIM: This study aims to highlight AMR as not merely a clinical issue but a problem with cross-border ramifications. It calls for the involvement of various stakeholders in preserving antibiotic efficacy and promoting sustainable AB use through OH approaches.

MATERIALS AND METHODS: A desk review, based on a search in PubMed using the keywords "One Health," "AMR," and "drug resistance in Bulgaria," was conducted, along with a targeted qualitative content analysis of OH definitions and models.

RESULTS: To tackle AMR in Bulgaria, a coordinated OH strategy is essential. Researchers and educators should introduce AMR and OH concepts by offering training and raising public awareness about responsible antibiotic use. Traditional practices, like phytotherapy, may help reduce unnecessary AB prescriptions. A recently implemented legislative reform—the electronic prescription (eRx)—has proven effective in reducing AB sales. Currently, Bulgaria remains one of the few EU countries without an OH action plan against AMR or an intersectoral framework connecting veterinary, food, and health authorities. Although relatively unfamiliar in Bulgaria, there is political momentum for adopting OH policies, as evidenced by the inclusion of such strategies in the recently adopted National Health Strategy 2030.

CONCLUSION: Immediate action is required to address AMR in Bulgaria. By adopting successful EU strategies and utilizing the OH framework, this analysis paves the way for a regional OH project, funded by the Medical University's Science Fund (No. 22007).

Keywords: *antimicrobial resistance (AMR), Bulgaria, One Health, public health*

PROPHYLACTIC STRATEGIES FOR PREVENTING CYCLOPHOSPHAMIDE-INDUCED HAEMORRHAGIC CYSTITIS: THE ROLE OF UROMITEXAN AND HYDRATION

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ABSTRACT

INTRODUCTION: Cyclophosphamide-induced haemorrhagic cystitis (HC) is a common and serious complication resulting from the urotoxic metabolite acrolein. It often affects patients undergoing high-dose chemotherapy or stem cell transplantation. Effective prophylactic strategies are essential for preventing HC and minimizing the risks associated with cyclophosphamide therapy. Among these strategies, Uromitexan, hydration protocols, and antiviral agents are widely employed.

CASE PRESENTATION: Uromitexan, a uroprotective agent, works by binding to acrolein in the bladder, preventing its direct interaction with the bladder mucosa and thus reducing urotoxicity. Hydration protocols aim to flush acrolein from the system, further minimizing its harmful effects. For patients at risk of BK virus reactivation, antiviral agents provide an additional line of defense by preventing viral-induced damage to the bladder. These combined strategies aim to prevent HC and ensure the safety of patients receiving cyclophosphamide therapy.

DISCUSSION: This study conducts a systematic review of the efficacy of Uromitexan, hydration, and antiviral agents in preventing HC in patients treated with cyclophosphamide. The review explores the mechanisms of each prophylactic strategy and evaluates their clinical outcomes. Despite the routine use of Uromitexan and hydration, there remains some variability in their effectiveness, with certain patient populations showing a higher incidence of HC. Antiviral prophylaxis has been shown to reduce HC incidence in patients at risk for BK virus reactivation, but its role in broader populations remains under investigation. This study highlights the importance of tailored prophylactic strategies for individual patients based on risk factors.

CONCLUSION: This research aims to clarify the most effective prophylactic strategies for preventing cyclophosphamide-induced HC, with a focus on Uromitexan, hydration, and antiviral therapies. By assessing current data and identifying gaps in the literature, this study provides recommendations for improving patient safety and enhancing the effectiveness of prophylaxis in cyclophosphamide therapy.

Keywords: *haemorrhagic cystitis, cyclophosphamide therapy, antiviral approaches, allopurinol, prevention*

APPLICATION OF THE SENSAMOVE METHOD IN SCIENTIFIC RESEARCH WORK

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ABSTRACT

INTRODUCTION: SENSAMOVE is a device, known as a balance disc, which allows investigation of changes in coordination due to stimulation of vestibular system. Technically, this device is a wooden disc with a stabilization pad, which changes its position relative to the horizontal line during measurement. Thus, coordination is reported in real time and the results are recorded by computer software designed to work with the disc.

MATERIALS AND METHODS: The main methods used in the research conducted are proprioception tests and balance exercises with increasing difficulty at different levels. This method is used in the study, assessment, and monitoring of the coordination environments of cadets conducting long-term sailing practices in the open sea, among athletes and volunteers.

RESULTS: The obtained data provide information about the coordination of the examined. It is used as an argument in researches and effect on confirming or rejecting existing hypotheses. SENSAMOVE is widely used in scientific research practice. The device is used in vestibular function tests that measure balance and coordination.

CONCLUSION: SENSAMOVE is a useful instrument in scientific research focused on understanding and improving coordination and balance in different populations.

Keywords: *SENSAMOVE, coordination, vestibular system, exercise*

DEVELOPMENT OF DISASTER PREPAREDNESS IN MÜNSTER AFTER RECENT CRISES: A CASE STUDY

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ABSTRACT

INTRODUCTION: Due to the increasing impact of climate change, natural disasters are expected to occur with greater frequency and intensity. This makes it essential to evaluate the preparedness of German cities and to assess whether they have adapted based on lessons learned from past crises. Particular emphasis must be placed on the resilience of critical infrastructure in the face of future disasters.

AIM: The objective of this essay is to highlight existing vulnerabilities and to draw attention to areas requiring urgent improvement. It aims to evaluate whether the city Münster has effectively responded to past crisis and improved its ability to manage future crisis and whether Münster and other German cities are aware that due to climate change the disaster tend to be worsen.

MATERIALS AND METHODS: An open data program from the city of Münster and a range of statistical data spanning from the past decades were used. The dataset used offered significant insights into the trends of the city's disaster preparedness and demand plan for disaster prevention.

CONCLUSION: To enhance preparedness for future crises, it is essential to utilize the intervals between emergencies to train a skilled workforce and provide them with the necessary resources. This proactive approach ensures that personnel are adequately equipped to safeguard citizens and mitigate the impact of subsequent disasters.

Keywords: *disaster preparedness, response strategy evolution, climate change, critical infrastructure*

THE IMPACT OF CRITICAL INFRASTRUCTURE ON THE SEVERITY OF DISASTERS

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ABSTRACT

INTRODUCTION: This case study analyzes two major seismic events: the 2011 Tōhoku earthquake in Japan and the 2023 earthquake in Turkey. These events exemplify how the quality of critical infrastructure, coupled with the enforcement of building codes, significantly influences disaster severity. Japan's stringent building regulations and comprehensive preparedness measures are contrasted with the structural vulnerabilities and inadequate construction standards observed in Turkey.

AIM: This case study contributes to the growing amount of evidence that proper infrastructure investment, construction planning and safety regulations are essential in terms of disaster mitigation.

MATERIALS AND METHODS: A literature search was conducted using the following literature: *Lessons Learned from the Great East Japan Earthquake Disaster*, as well as *How Turkey's Infrastructure Impacted Earthquake Casualties*.

RESULTS: In 2011, the magnitude 9.0 Tōhoku earthquake triggered a large-scale tsunami; however, Japan's stringent building codes and advanced early warning systems played a crucial role in mitigating the extent of casualties and property damage. In contrast, the 2023 earthquake in Turkey, despite its lower magnitude, resulted in extensive destruction, primarily due to poorly enforced building regulations and the use of substandard construction materials. The widespread structural failures led to the collapse of thousands of buildings, exacerbating the humanitarian crisis, which was further compounded by delays in emergency response caused by damaged infrastructure.

CONCLUSION: In Japan, the strict building codes in combination with early warning systems limited the damage of the Tōhoku earthquake, whereas in contrast the earthquake in Turkey (2023) caused widespread building collapse, due to poor construction of buildings and the usage of substandard materials. This comparison highlights the critical importance of resilient infrastructure and the strict enforcement of construction regulations as fundamental factors in disaster mitigation. Whilst far from perfect, Japan's preparedness proved effective, whilst the challenges of Turkey stress the need for stronger regulations and infrastructure modernization to reduce future risks.

Keywords: *critical infrastructure, disaster mitigation, earthquakes, building codes*

DENTAL MEDICINE

EARLY DETECTION OF CRACKS IN TEETH— THE USE OF NEW TECHNOLOGIES FOR MORE ACCURATE DIAGNOSIS

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ABSTRACT

INTRODUCTION: The early detection of cracks in teeth is crucial for preventing further damage and ensuring effective treatment. Cracks, if left undetected, can lead to structural compromise, bacterial infiltration, and eventual tooth loss. Traditional diagnostic methods may miss microcracks, leading to delayed or inadequate intervention. However, advances in technology, such as high-magnification microscopes, dental microscopes, optical coherence tomography (OCT), cone-beam computed tomography (CBCT), near-infrared transillumination (NIR), and artificial intelligence (AI) and machine learning offer more accurate detection of these issues.

AIM: This review aims to explore the effectiveness of modern technologies in the early and accurate diagnosis of dental cracks, enhancing clinical outcomes and minimizing invasive procedures.

Materials and Methods: Relevant literature and studies on the use of microscopes, OCT, CBCT, NIR, and AI in diagnosing dental cracks were analyzed. Comparative studies, highlighting the diagnostic accuracy, resolution, and clinical benefits of these technologies, were reviewed to understand their role in improving early detection and treatment planning.

RESULTS: Studies demonstrate that these emerging technologies significantly enhance the visibility of small and complex cracks that may not be detected through conventional methods like visual inspection or radiographs. Microscopes provide high magnification for detecting surface-level cracks, while CBCT and NRI offer three-dimensional imaging, and AI and machine learning reveal cracks within the tooth structure.

CONCLUSION: The use of advanced technologies represents a significant improvement in the early detection of cracks in teeth. While no single method can ensure perfect detection in all cases, these tools together improve diagnostic accuracy and allow clinicians to make more informed treatment decisions, potentially reducing tooth loss.

Keywords: *dental cracks, CBCT, microscopes, early diagnosis, dental technology, AI, NRI, machine learning*

ENDODONTIC TREATMENT IN PATIENTS WITH EPILEPSY

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ABSTRACT

INTRODUCTION: Epilepsy is a neurological disorder characterized by convulsions. As a dental care provider, understanding these conditions will help provide better dental care to patients with epilepsy. Patients with epilepsy suffer from poor oral health, tooth loss, periodontal disease, recurrent tooth decay, and more. Elective treatment in these patients usually involves taking an anti-epileptic drug appropriate for the type of seizure (phenytoin, phenobarbital, etc.). However, many of these drugs used to control seizures have implications for oral and dental care.

AIM: Seizures in the dental office are medical emergencies and should be treated with caution. Patients diagnosed with epilepsy are at a higher risk of accidental injury compared to people without neurological conditions, because they are unable to use protective reflexes, especially during a first seizure, which, depending on the site of the convulsion, can result in head and neck injuries, orthopedic trauma, soft tissue injuries, and burns or submersion. Procedures need to be carried out much more quickly to prevent an emergency situation from occurring. It is also necessary to ensure complete peace of mind for the patient during operation, explaining to them every sparing step in performing the manipulation.

MATERIALS AND METHODS: When a tooth becomes infected and painful, dentistry offers two options. However, many people prefer to save the tooth rather than extract it. Endodontics is a careful procedure that removes the infected pulp and periradicular exudate using appropriate instruments and biocompatible chemicals combined with medications to keep the tooth inert.

RESULTS: If the procedure is performed on a healthy individual, focusing on the technical means is enough, but if the tooth needs to be saved in a patient who is undergoing treatment for a systemic disease, it is equally important to avoid possible medical emergencies. Therefore, it is important for the specialist to be aware of the common diseases and medications that play a role in endodontics, as well as the treatment options in such cases.

CONCLUSION: Only by understanding these types of diseases can dentists treat those patients, have a positive psychological impact on patients, and encourage them to maintain good oral hygiene to improve their overall health.

Keywords: *endodontic treatment, epilepsy, patients, oral health*

IMPACT OF ORTHODONTIC TREATMENT MODALITIES ON EXTERNAL APICAL ROOT RESORPTION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF BIOLOGICAL AND GENETIC INFLUENCES

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ABSTRACT

INTRODUCTION: External apical root resorption (EARR) is a frequent and often irreversible complication of orthodontic treatment. It results from mechanical forces that activate cellular processes, compromising the root structure. Risk factors include genetic predisposition, tooth morphology, treatment duration, and applied force. The growing use of aligners as an alternative to fixed braces necessitates comparing EARR incidence across treatment modalities.

AIM: The purpose of this study was to systematically evaluate EARR across orthodontic treatments, examining the influence of appliance type, treatment duration, and individual factors such as dental vitality. Additionally, the study aimed to explore the genetic basis of EARR by reviewing recent findings on associated genetic markers.

MATERIALS AND METHODS: A systematic review and meta-analysis were conducted using data from randomized controlled trials, observational studies, and clinical trials across five databases. Inclusion criteria consisted of full-text studies focusing on EARR in orthodontic patients. Quantitative analyses measured root resorption in millimeters and as a percentage of the original root length, utilizing cone-beam computed tomography (CBCT) and digital subtraction radiography. Factors like appliance type and genetic markers were included.

RESULTS: External apical root resorption was present across all treatment modalities, with similar resorption levels across systems. Fixed appliances with continuous heavy force resulted in higher EARR, especially with prolonged treatment. Clear aligners exhibited a slightly lower incidence, particularly in non-extraction cases. Endodontically treated teeth demonstrated reduced EARR compared to vital teeth. Genetic studies identified three groups of markers associated with EARR based on impact scores: IL1B and IL1A formed the high-impact group, indicating significant genetic predisposition, RANKL TNFRSF11B and VDR comprised the moderate-impact group, while IL6 OPG SPP1 and P2XR7 exhibited lower-impact scores, indicating a comparatively reduced influence on EARR susceptibility.

CONCLUSION: External apical root resorption is influenced by biological and treatment-related factors. Fixed appliances present a higher risk, while aligners may reduce EARR in specific cases. Genetic screening could improve risk assessment in clinical practice. Advances in imaging and genetic analysis promise better early detection and intervention strategies for EARR.

Keywords: *external apical root resorption, orthodontic treatment, genetic polymorphisms, CBCT, case report*

NEW METHODS OF IRRIGANT ACTIVATION

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ABSTRACT

INTRODUCTION: Root canal therapy is fundamentally aimed at regulating infection within the root canal system through the elimination of existing microbial pathogens and the prevention of future reinfection. The anatomical complexities of the root canal system, coupled with the variability of infections, create significant challenges for treatment. These factors limit the efficacy of mechanical instrumentation and irrigation in fully eradicating infections. The effectiveness of conventional irrigation methods is frequently inadequate. Consequently, various instruments have been developed to activate irrigants, thereby enhancing the debridement of complex root canal systems. Additionally, advanced techniques have been devised to augment the physical kinetic energy applied to the irrigant, consequently increasing the shear force on the root canal walls and activating the irrigants to improve the efficacy of chemical disinfection.

AIM: This article aims to review and present current scientific research and literature on the latest methods for root canal irrigation in endodontics. It will explore both innovative and traditional techniques, highlighting advancements in medical science while assessing the effectiveness and safety of various approaches. By integrating new and established methods, the article provides a comprehensive overview of developments in endodontic practice, guiding clinicians in optimizing treatment procedures.

MATERIALS AND METHODS: A comprehensive research study is being undertaken through the systematic review and comparison of peer-reviewed scientific literature to synthesize current knowledge on root canal irrigation techniques. This study aims to evaluate the efficacy, safety, and clinical outcomes associated with various irrigation modalities. The following methods are being analyzed as central techniques within the study:

- **conventional syringe irrigation;**
- **mechanical agitation irrigation;**
- **sonic irrigation;**
- **ultrasonic irrigation;**
- **negative and positive pressure irrigation;**
- **laser-activated irrigation.**

This critical analysis seeks to elucidate the comparative advantages, limitations, and clinical relevance of each method, thereby contributing to an evidence-based approach for optimizing endodontic treatment protocols.

RESULTS: The newly developed methods generate more intense shock waves, inducing vigorous movement of the irrigant within the root canal. This results in enhanced disinfection and improved penetration of the irrigant throughout the canal system.

CONCLUSION: Ongoing research seeks to identify solutions that incorporate as many desirable properties as possible to improve the prognosis of endodontic treatment. Each irrigation method presents distinct advantages and disadvantages, and the selection of the technique may depend on clinical circumstances, the types of devices being used, and the preferences of the dental practitioner.

Keywords: *endodontic, treatment, irrigants, activate, methods, laser, disinfection*

COMPARATIVE ANALYSIS OF WARM AND COLD TECHNIQUES FOR ROOT CANAL OBTURATION. INDICATIONS, ADVANTAGES AND DISADVANTAGES

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ABSTRACT

INTRODUCTION: The success of root canal treatment depends on the complete hermetic obturation of the root canal system. The different obturation methods of a shaped and cleaned root canal system include cold filling methods (single cone, lateral condensation) and warm methods (vertical/lateral compaction, continuous wave compaction technique, thermoplasticized injection techniques, carrier-based gutta-percha).

AIM: The aim of this review is to compare warm and cold techniques for root canal obturations, focusing on their indications, advantages, and disadvantages in terms of clinical performance and outcomes.

MATERIALS AND METHODS: A literature review was conducted, analyzing relevant studies on both warm and cold techniques. The comparison was made based on parameters such as success rates, procedural time, and the complexity of use.

RESULTS: The analysis indicates that warm techniques offer better three-dimensional filling of complex root canal anatomies and more homogeneous material distribution. However, they are more technically sensitive and require specialized equipment.

CONCLUSION: Both warm and cold techniques for root canal obturations have their merits, and the choice of technique should be based on the clinical situation, the complexity of the root canal system, and the practitioner's expertise. Warm techniques are preferable for complex cases, while cold techniques remain reliable for simpler canal structures.

Keywords: *root canal, obturation, warm and cold techniques*

PHARMACY

PHARMACEUTICAL USE IN CHILDREN DURING COVID-19: EVALUATING THE RISK OF OVERMEDICATION

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ABSTRACT

INTRODUCTION: The COVID-19 pandemic caused significant disruptions in children's lives, leading to a marked increase in mental health issues, such as anxiety and depression. In response, there was a rise in prescriptions for pediatric mental health conditions, raising concerns about potential overmedication.

AIM: This study aims to evaluate the extent of pharmaceutical use in pediatric populations during the pandemic and determine whether overmedication occurred as a response to pandemic-related stressors.

MATERIALS AND METHODS: A literature review of epidemiological studies and prescription data from public health databases was conducted. The analysis focuses on prescription trends for pediatric populations during COVID-19 and compares these trends to pre-pandemic data. Non-pharmaceutical interventions, such as counseling and behavioral therapies, were also reviewed to assess their usage alongside medication.

RESULTS: Preliminary findings suggest a significant increase in pharmaceutical interventions, particularly antidepressants and anti-anxiety medications, among children during the pandemic. The data also highlights the underutilization of alternative, non-pharmaceutical therapies for managing mental health issues in this age group.

CONCLUSION: While pharmaceutical interventions were necessary to address rising mental health concerns in children, there is evidence of potential overmedication. Public health strategies must balance medical treatment with non-pharmaceutical options to prevent unnecessary long-term medication use in children.

Keywords: *pediatrics, overmedication, mental health, public health, COVID-19, pharmaceuticals*

THE EFFICACY OF ASHWAGANDHA (WITHANIA SOMNIFERA) IN REDUCING STRESS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

INTRODUCTION: Ashwagandha (Withania somnifera) is a prominent adaptogenic herb that has garnered much appeal especially in recent years. A survey conducted by Statista found that 27% of millennials reported using ashwagandha and this usage is predicted to grow. It is renowned for its potential to enhance resilience to stress and promote mental well-being.

AIM: This systematic review and meta-analysis aims to evaluate the efficacy of ashwagandha in reducing stress levels among adults, in light of the growing interest in herbal interventions for stress management.

MATERIALS AND METHODS: A comprehensive literature search will be performed across databases to identify randomized controlled trials (RCTs) that investigate the effects of ashwagandha on stress. Eligible studies will report stress levels using recognized scales and assess changes in serum cortisol levels. The primary outcomes of interest will include reductions in perceived stress and cortisol concentrations.

RESULTS: Data extraction will encompass study characteristics, sample sizes, intervention specifics, and outcomes. The risk of bias will be evaluated using the Cochrane Risk of Bias tool. A meta-analysis will be conducted using fixed or random effects models, depending on the heterogeneity of the included studies. Subgroup analyses will further explore potential moderators, such as dosage and treatment duration.

CONCLUSION: This review seeks to synthesize the existing evidence on the effectiveness of ashwagandha in managing stress. The anticipated findings will provide insights into the role of ashwagandha in enhancing psychological well-being and may guide clinical practice regarding its use as a complementary treatment for stress. Ultimately, this systematic review and meta-analysis will clarify the potential of ashwagandha as an effective herbal intervention for stress reduction and highlight avenues for future research.

Keywords: *ashwagandha, Withania somnifera, stress management, adaptogens, cortisol reduction*

GUT MICROBIOME AND SLEEP QUALITY

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ABSTRACT

INTRODUCTION: The gut microbiome plays a significant role in overall health, including sleep quality. Research indicates a bidirectional relationship between the gut microbiome and sleep, meaning that each can influence the other.

MATERIALS AND METHODS: A comprehensive review of the literature was conducted using the PubMed database, focusing on articles associated with the interaction between gut microbiome and sleep quality and disorders.

RESULTS: The gut microbiome plays a role in sleep quality by influencing circadian rhythms, neurotransmitter production (GABA, serotonin, melatonin) and the functions of immune system and inflammation. Sleep deprivation can negatively impact the diversity and composition of the gut microbiome. Furthermore, poor sleep quality can lead to metabolic dysregulation, including insulin resistance and weight gain, which in turn can alter the gut microbiome and create a vicious cycle where an unhealthy microbiome further disrupts sleep.

CONCLUSION: Nutrition, rich in probiotics and prebiotics, and probiotic supplementation may help treating sleep disorders by enhancing the community of gut microorganisms.

Keywords: *gut microbiome, sleep quality, gut-brain axis, probiotics*

IN VITRO PREBIOTIC AND ANTI-BIOFILM FORMATION ACTIVITIES OF *BISTORTA MAJOR* S. F. GRAY POLYSACCHARIDES AND THEIR FE(III) COMPLEXES

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ABSTRACT

The study aimed to investigate the structural features and biological activity of polysaccharides (PSs) in *Bistorta major* S.F. Gray, which have not been extensively examined. The bistort dried (fresh) leaves contained 20.6% (7.4%) and the roots 33.4% (19.0% fresh) of total PSs. By a two-step extraction with hot water and hot 5% (w/v) NaOH were obtained 6.4% (fresh basis) (2.3%) and 2.6% (1.5%) water-extractable leaf (BML-WEPS) and root (BMR-WEPS) PSs, and 4.8% (1.7%) and 4.3% (2.5%) alkali-extractable leaf (BML-AEPS) and root (BMR-AEPS) PSs, respectively. The total carbohydrate content in the extracted PSs varied between 74.2 ± 1.3% (BMR-AEPS) and 97.6 ± 0.6% (BML-WEPS). Above 97% of the polyuronides in both raw materials, 19.4% and 95.2% of the PSs in the leaves and roots were extracted. WEPSs were methylesterified and acetylated pectic-type heteropolymers based on colorimetric and GC-MS analyses. Structural 2D NMR analysis revealed that the rhamnogalacturonan type I regions of the root pectins were richer in arabinogalactan side chains, in which 1,3,5-linked arabinans were abundant. The pectins in the leaves had a higher content of the acidic homogalacturonan region (42.7 ± 0.5% uronic content) and higher average molecular weight (M_w = 85.0×10^4 g/mol) than the root ones. Under alkaline conditions, a mixture of acidic arabinogalactans, xylan-containing polymers, and α-glucans were isolated from the leaves and roots. Bistort PSs (20 mg/mL) stimulated the growth and biofilm formation, as a sole carbon source, in pure or mixed cultures of the butyrate producer *Clostridium beijerinckii* 4.3A1 and 6A, and in a combination with *Lactobacillus helveticus* 611. All PSs (20 mg/mL) did not express a potent growth-inhibitory activity against reference pathogenic strains of *Escherichia coli, Staphylococcus aureus, Streptococcus mutans,* and *Pseudomonas aeruginosa*, but some PSs inhibited statistically significantly the biofilm formation by *P. aeruginosa* and *E. coli*. The FTIR and HPSEC-RID analyses confirmed the inclusion of Fe^{3+} in WEPSs. Fe-BML-WEPS and Fe-BMR-WEPS expressed a better prebiotic activity than the initial WEPSs, and they reduced the pathogenic biofilm production. The newly isolated PSs and their iron-containing derivatives can be tested in synbiotic products with application in the functional nutrition and supplementary therapy of socially significant diseases characterized by dysbiosis.

Keywords: *Bistorta major, polysaccharides, prebiotics, NMR, probiotics, pathogens, biofilm*

IN SILICO GENERATION OF THE RNA APTAMERS AGAINST HER2 RECEPTORS IN HER2-POSITIVE BREAST CANCER. THERMODYNAMIC COMPARISON OF TRASTUZUMAB AND APTAMER COMPLEXES

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ABSTRACT

RNA aptamers are oligonucleotides that bind to a target with high specificity and affinity. First discovered by Craig Tuerk and Larry Gold through a process called systematic evolution of ligands by exponential enrichment (SELEX). They represent a highly promising class of drugs, with a mechanism of action similar to that of the traditional antibodies. However, compared to the monoclonal antibody therapies, aptamers present a series of unique advantages due to their size, immunogenic factor, and synthesis methods. The purpose of this work is to present the prospects of RNA aptamers as targeted therapeutics, using various 3D modelling software and trastuzumab therapy as an example.

Random RNA sequence pool of a set size has been generated, and the thermodynamic properties of the sequences have been analysed in the RNAfold and RNAcomposer software. Lowest Gibbs free energy aptamers were docked with the HER2 receptor, as well as the trastuzumab complex. This allowed for the analysis of the non-covalent bonds in the pose, while the ZDOCK software has allowed for detailed thermodynamic analysis.

The lowest Gibbs Free energy sequences were H5 (-7.70 kcal/mol), H9 (-8.12 kcal/mol), and H2 (-8.86 kcal/mol). The lowest ZDOCK scores were those of the aptamers H1, H5, and H6 in the group with the HER2: 3581.74; 4201.90 and 3906,42. The statistical analysis of the results using the two-way ANOVA has yielded the values of $P < 0.001$ and $P = 0.004$.

Aptamers H1, H5, and H6 have shown promising results, with the highest number of non-covalent bonds formed, as well as the highest ZDOCK score averages. According to the ZDOCK score, the trastuzumab and HER2 group had the worst thermodynamic properties. Furthermore, aptamers H6 and H8 have predominantly inhibited the subdomains II and IV of the extracellular domains on the HER2 receptor. The inhibition of those domains produces anti-tumour effect. This work suggests a theoretical possibility of RNA aptamers providing a stronger and more efficient response in breast cancer patients, with less adverse side effects. However, the use of aptamers has its own limitations, such as nuclease degradation, low half-life, off-target effects, and lack of research in that field.

Keywords: *HER2 receptor, RNA aptamers, in silico design, aptamer docking, HER2-targeted therapy, molecular docking analysis, thermodynamic comparison, binding affinity, Binding site analysis, domain IV of HER2*