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REVIEWS

LYMPHADENOPATHY—GENERAL DATA AND ITS SIGNIFICANCE FOR MAXILLOFACIAL SURGERY. A REVIEW ARTICLE

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ABSTRACT

INTRODUCTION: Lymph nodes are distributed throughout the body and play an important role as filters for exogenous and endogenous antigens, as well as in the formation of an immune response through activated lymphocytes and antibodies. In various conditions, such as infections, autoimmune diseases, lymphomas and metastatic carcinomas, their size can increase, a condition called lymphadenopathy (LAP)/adenopathy.

MATERIALS AND METHODS: This article is based on a comprehensive review of 34 contemporary full-text articles in English. The information from them, after detailed examination, was analyzed and systematized in order to obtain a complete full-text publication on the general features of lymphadenopathy.

RESULTS AND DISCUSSION: Lymphadenopathy is a frequent finding in clinical practice and may present as either localized or generalized. In the majority of cases, it is benign in nature and tends to resolve spontaneously. The distinction between a normal and an enlarged lymph node is influenced by both the patient's age and the anatomical region involved. Approximately three-quarters of cases are localized, and more than half involve lymph nodes situated in the head and neck. A thorough medical history combined with a detailed physical examination remains fundamental for proper assessment. Nonetheless, imaging techniques often yield more precise data regarding lymph node size and morphology than clinical evaluation alone. Ultimately, histopathological analysis is regarded as the definitive diagnostic approach.

CONCLUSION: The cervical region, along with the maxillofacial region, are most often affected by LAP in all age groups. Thus, maxillofacial surgeons are faced with an extremely wide differential diagnosis, which requires them to know both the characteristics of LAP in general and the multitude of general and local diseases that can cause it. It is an important part of the interdisciplinary team performing the diagnosis and treatment of lymphadenopathy.

Keywords: *lymph nodes, lymphadenopathy, cancer, maxillofacial surgery, head and neck, cervical region*

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INTRODUCTION

Lymph nodes are distributed throughout the body and play an important role both as filters for exogenous and endogenous antigens and in the formation of an immune response through activated lymphocytes and antibodies. In various conditions, such as infections, autoimmune diseases, lymphomas, and metastatic carcinomas, their size can increase, a con-

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dition called lymphadenopathy (LAP)/adenopathy (1). Histological evaluation plays an important role in the diagnosis, treatment, and prognosis of the majority of these conditions (2). About 1/5 of the lymph nodes in the adult human body are in the region of the head and neck (3). This is precisely why it is necessary to know the cervical lymph nodes in normal and pathological conditions in order to ensure maximum coverage of their diseases and to guarantee adequate treatment of patients with cervical LAP—tasks that are the basis of this review article.

MATERIALS AND METHODS

This article is based on a comprehensive review of 34 contemporary full-text articles in English and Bulgarian. The search for the articles included in it did not use specific keywords and included review articles, original articles, and case reports published until the end of 2023. The information from them, after detailed review, was analyzed and systematized in order to obtain a complete full-text publication on the general features of LAP in the maxillofacial region.

RESULTS AND DISCUSSION

Lymphadenopathy is a frequent clinical finding, usually classified as either localized or generalized, and in most cases, it is associated with benign and self-limiting conditions. The term describes lymph nodes that show abnormal enlargement (typically exceeding 10 mm) and/or changes in consistency (4). Still, what is considered *normal* versus *pathological* in terms of lymph node size is strongly influenced by both anatomical location and the patient's age. For example, in children younger than ten years, the immune system is physiologically hyperactive, and lymph nodes up to 2 cm can occasionally be considered within normal limits, whereas an epitrochlear lymph node larger than 0.5 cm is generally regarded as abnormal (5,6).

The characteristics, distribution, and physical properties of LAP play a central role in establishing a diagnosis. Two principal forms are recognized: generalized and localized. Generalized LAP refers to the involvement of two or more anatomically unrelated nodal regions, while localized LAP is restricted to nodes within related drainage areas. Depending on their cause and stage, the affected nodes can vary considerably in presentation and they may appear firm or soft, tender or non-tender, movable or fixed, and may occur as solitary structures or in clusters (7,8).

In 75% of cases, LAP is localized and more than 50% involve the lymph nodes in the head and neck region. In about 25% of cases, it is generalized and is a sign of an underlying general disease (9). The same etiological factors can lead to localized and generalized LAP in some cases (10–12). In cases of localized LAP, the cervical nodes are most frequently affected compared to other anatomical regions, which broadens the spectrum of possible differential diagnoses. Infections of bacterial or viral origin affecting the face, oropharynx, or nasopharynx represent the leading causes of cervical node enlargement (13). Generalized LAP triggered by pathogens such as Epstein-Barr virus or cytomegalovirus can also manifest with acute, bilateral cervical adenitis (14). Tuberculosis demonstrates a strong predilection for this region, with cervical node involvement reported in 60–90% of patients (15). Beyond infectious etiologies, malignancies are also significant contributors. Cervical LAP is often associated with Hodgkin and non-Hodgkin lymphomas, squamous cell carcinoma of the head and neck, and metastatic tumors (16). Additionally, papillary and follicular thyroid cancers, together with nasopharyngeal carcinoma, have a well-documented tendency to spread to cervical nodes, resulting in pathological adenopathy (17–19).

Supraclavicular lymph node LAP should always be suspected in all ages, especially in children (20,21). Lymph from the mediastinum, lungs, and esophagus drains into the right supraclavicular lymph nodes. Lymph from the digestive and genitourinary systems drains into the left supraclavicular lymph nodes and may be affected by malignancies of these systems (22). Lymphadenopathy in this region is also possible in Hodgkin lymphoma, non-Hodgkin lymphoma, breast cancer, mycobacterial, or fungal infections (11,23-26).

Axillary LAP is most often reactive and nonspecific. In cases of metastatic breast carcinoma, enlargement of the anterior and central axillary lymph nodes may be detectable on palpation, sometimes even preceding clinical recognition of the primary tumor. By contrast, Hodgkin and non-Hodgkin lym-

phomas seldom present with isolated axillary node involvement. Among infectious causes, cat-scratch disease is one of the most frequent etiologies of axillary LAP (27).

Benign reactive enlargement of inguinal nodes is often observed in individuals who walk barefoot outdoors. Localized inguinal LAP is commonly associated with infections transmitted sexually. Primary malignant tumors rarely manifest with exclusive involvement of the inguinal nodes; nevertheless, Hodgkin and non-Hodgkin lymphomas, malignant melanoma, and squamous cell carcinomas of the penis, vulva, or anus may occasionally affect this nodal group (28).

Generalized LAP is an uncommon feature of most solid malignancies but occurs frequently in non-Hodgkin lymphoma, which assists in distinguishing it from Hodgkin lymphoma, where nodal spread tends to be more localized. Clinical B symptoms—such as persistent fever, drenching night sweats, unintended weight loss, along with hepatosplenomegaly—are considered strong indicators of an underlying malignant process (29).

Benign etiologies of generalized LAP often include self-limiting viral illnesses, such as infectious mononucleosis, as well as certain drug reactions. Other notable causes are acute HIV infection, active tuberculosis or atypical mycobacterial disease, cryptococcosis, cytomegalovirus, Kaposi's sarcoma, and autoimmune conditions like systemic lupus erythematosus. In addition, generalized LAP may be encountered in hematologic malignancies, including leukemias and lymphomas, as well as in disseminated metastatic carcinomas (16).

For diagnostic orientation, mnemonic strategies have been developed. The MIAMI acronym is widely used, representing: M—malignancies, I—infections, A—autoimmune disorders, M—miscellaneous or rare causes, and I—iatrogenic conditions (25). Another practical tool is the CHICAGO mnemonic, which stands for: C—cancers, H—hypersensitivity syndromes, I—infections, C—connective tissue disorders, A—atypical lymphoproliferative diseases, G—granulomatous disorders, and O—other etiologies (25).

An important step in the evaluation of adenopathy is a good history and a careful physical examination of the patient. If these indicate a benign, self-limiting disease, the patient can be reassured and followed up. If more information is needed, the next step is to perform laboratory tests, among which a complete blood count is important (26).

Imaging studies can provide more accurate information about the characteristics of the lymph nodes than the physical examination. Ultrasound examination plays an essential role in the evaluation of peripheral lymphadenopathy, as it enables the clinician to assess the number, size, anatomical position, margins, and internal architecture of affected lymph nodes. In contrast, computed tomography (CT) and magnetic resonance imaging (MRI) are particularly valuable for identifying nodal involvement within the thoracic and abdominopelvic regions (27). Doppler ultrasonography adds further diagnostic information by analyzing vascular patterns, displacement of vessels, resistance indices, and pulsatility. These parameters can help distinguish between long-standing inactive LAP and recently developed, active disease (28).

Definitive diagnosis, however, relies on histopathological evaluation, which remains the gold standard in the LAP work-up. Fine-needle aspiration cytology (FNAC) is a safe, minimally invasive, and rapid procedure that can provide reliable diagnostic information in cases of reactive hyperplasia, infectious processes, granulomatous lymphadenitis, lymphomas, and metastatic disease. It is particularly advantageous for detecting recurrence in patients with a history of malignancy and can be performed in both inpatient and outpatient settings with immediate results (29). The integration of complementary techniques, such as immunohistochemistry and flow cytometry, significantly enhances the diagnostic precision of FNAC in lymphoproliferative disorders. Fine-needle aspiration cytology demonstrates especially high sensitivity and specificity in identifying metastatic carcinoma (30).

Targeted aspiration biopsy performed under ultrasound guidance offers greater accuracy than blind procedures, as the needle can be directed toward the most suspicious nodal area (31). Core needle biopsy represents another valuable approach, yielding larger tissue samples compared to FNAC. When combined with advanced imaging modalities, this technique

improves diagnostic accuracy and may help avoid unnecessary excisional biopsy (32). Nevertheless, despite the advantages of less invasive methods, surgical excision of the largest, most abnormal, and easily accessible lymph node continues to be regarded as the definitive diagnostic method and remains the gold standard in clinical practice (33,34).

CONCLUSION

Lymphadenopathy is a common condition in medical practice. An important challenge for the physician is to determine whether it is a benign or malignant disease. The cervical region, along with the maxillofacial region, are most often affected by LAP in all age groups. Thus, the maxillofacial surgeon is faced with an extremely wide differential diagnosis, which requires him to know both the characteristics of LAP in general and the many general and local diseases that can cause it. He is an important part of the interdisciplinary team performing the diagnosis and treatment of LAP.

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