SUDDEN INFANT DEATH SYNDROME - THE CAUSE OF DEATH

Burulianova I., V. Konstantinova*, V. Dokov*

Department of Forensic Medicine, Department of General and Clinical Pathology, Varna Medical University

Reviewed by: Assoc. Prof. D. Radoinova, MD, PhD

ABSTRACT

Studies on the potential role of agents in SIDS have been published over the years in a variety of journals and involved specific micro-organisms, sleeping position, dysfunction of the central nervous system, damaged arousal reflex cigarette smoking, lower socioeconomic way of life, specific age. Although, there aren't criteria to established specific risk factors. SIDS still remains unexplained in spite of thorough case investigation, including complete autopsy, examination of the death scene and review of the clinical history.

Our humble contribution to this problem included 12 sudden death cases in babies from 20 days to 1 year. We may place our cases in the group of unexpected explained death, because the main cause of death in most babies is pneumonia. The histological changes in lungs were microhaemorrhages in alveoles and interstitium, congestion, oedema, pulmonary emphysema, atelectases, haemosiderin-laden macrophages, bronchitis and catharral-desquamating pneumonia or catharrhalhaemorragic pneumonia, but in two cases there were a purulent pneumonia.

In conclusion most authors consider no laboratory or pathological tests to establish a diagnosis of SIDS and no lesions are found at autopsy in most cases. However, as recent reports pointed out, the affected infant would not be perfectly well before death. Most authors pointed the histopathological changes in lungs that we established and pointed above.

INTRODUCTION

Studies on the role of agents in SIDS have been published in a variety of journals. The articles in this issue examine evidence for the involvement of specific micro-organisms, sleeping position, dysfunction of the central nervous system, histopathological changes in lungs, heart, damaged arousal reflex, cigarette smoking, lower socioeconomic way of life, specific age. Although, there aren't criteria to establish specific risk factors and morphological characteristics. SIDS still remains unexplained in spite of thorough case investigation, including complete autopsy, examination of the death scene and review of the clinical history.

Definition and risk factors

Sudden infant death syndrome /SIDS/ is a postmortem medical diagnosis which stands on a "negative autopsy". The relative large concentration of deaths in the perinatal period and infancy and the need to provide explanation for parents might suggest that clinicians frequently turn to pathologists for information of postmortem examination (5).

Sudden death in babies was first reported in London - 1913 year, but the term SIDS was defined in 1969 at the Second International Conference as "the sudden death of any infant or young child, which is unexplained by history, and the thorough post-mortem examination fails to demonstrate an adequate cause of death"(3). After 1992 year SIDS is on the second or third place among leading death causes in babies between one month and one year. The peak is between 2 and 4 months. There is a seasonal distribution (in January). Prof. Zekov's investigation revealed that the most babies died after midnight, particularly in the morning about 4-5 a.m.(1). The upper age limit was defined one year (23). There are more than 120 different theories on the possible causes of SIDS. Bed sharing is a very interesting issue. US study established 64 death cases in babies between a month and 2 years when they sleep with their mother and father. Some researchers think that there is any survival advantage to a baby sleeping with his/her mother. There is an incredible amount of interactions between two - more arousals (waking up during the night) of both mother and baby when they sleep together. Arousal may be an important mechanism to rescue babies from potentially dangerous situations during sleep. Dr Fleming believes that it is usually the baby who wakes the mother not back to front. However, there are not scientific studies to confirm bed sharing. Some investigations revealed damaged arousal reflex and the babies wasn't...
able to wake up when arose the problems in breathing, heart rate, blood pressure and temperature. Matturi L. at al revealed changes of the neuronal population of medullary arcuate nucleus in SIDS victims. (16). Severe hypoplasia were established in 30% of the babies morphometrically in this nucleus. Concerning interleukins, IL-1 may cause sudden infant death by depressing brainstem neurons important for the control of ventilation. In a Norwegian study, cerebrospinal fluid levels of IL-6 were higher in infants dying of SIDS than in infants dying violently, but lower than in infants dying of infectious diseases.

Disfunction of the central nervous system, cardiorespiratory insufficiency due to infections including atypical immune reactions, and cardiac dysregulation have been discussed during the previous decade. Some authors investigated 387 SIDS cases and established disturbances of the heart after inflammatory diseases of the respiratory tract (70 cases out of 387) (2). Concerning conduction system, Matturi et al. carried out a systematic investigation of this system in 69 SIDS cases and found no significant differences except for the presence of resorptive degeneration (in 97% of SIDS cases compared to 75% of the controls) (17). Dettmeyer's study revealed enteroviruses in 22.5%, adenoviruses in 3.2%, Epstein-Barr viruses in 4.8% and parvovirus B19 in 11.2% SIDS cases (all SIDS cases were 62). Control group samples were completely virus negative. Applying a comprehensive combination of molecular and immunohistochemical techniques, their results demonstrate a clearly higher prevalence of viral myocardial affections in SIDS (9).

There are many articles which have reported about relationship between SIDS and sleeping position. The recent drastic decrease in the number of SIDS cases has been associated with infant sleeping supine instead of prone (15). The prone position are related with increased risk of SIDS (10,11,13). In public health review from Sweden epidemiological research has shown that prone sleeping is major risk factor for sudden infant death syndrome (12). Since 1992 the American Academy of Pediatrics has recommended that infant has to be placed on his back in order to reduce the risk of sudden infant death syndrome. Since then, the frequency of prone sleeping has decreased from about 70% to approximately 20% of US infants and SIDS-rate - by more than 40%. The reason of death is unknown, but the mechanism is similar like suffocation in soft materials (cot death).

There are several potentially risk factors - maternal smoking, low socioeconomic position, more black babies and male sex, the importance of soft bedding and covered airways. Some researchers from New Zealand also found in their epidemiological studies that bed sharing and cigarette smoking is associated with a marked increased risk for SIDS. Cigarette smoking induces nitric oxide production and retards hypothalamic development by augmented apoptosis. Fetal haemoglobin induces hypoxia which is a stimulator of the immune response, while vasodilator gases (CO and NO) reduce hypothalamic function. Hypothalamic failure elevates blood pirogens, induces toxic shock - a feature of SIDS (19).

Infection is not a new idea, but in 2002 (Emma Ross in the European congress of Clinical microbiology and infectious diseases in Milan) is the first time that E.coli was found in the blood of all SIDS babies. There were significant correlation between endotoxin levels in blood and the various organs particularly in SIDS cases and child controls and blood endotoxin levels in SIDS cases were higher in those infants where there was histological evidence of mild to moderate inflammation (6). If bacterial toxins are involved in precipitating SIDS, the possibility of passive immunisation or earlier immunisation of infants with low levels of antibodies to the toxins might reduce further the numbers of these deaths (4). There is a considerable evidence suggesting that respiratory viral infection is involved in the genesis of the sudden infant death syndrome with rates of about 20% of SIDS victims compared to about 13% of controls. Most of the viruses were obtained from children between 3 weeks and 4 months of age (21). Neonatal immaturity of both the acute febrile response and hypotalamus promote neonatal protection from SIDS.

Reid (18) pointed out that SIDS are associated with serious pathological changes - elevated hepatic iron, bone marrow hyperplasia, hypomyelinated respiratory control centres, elevated lung immunoglobulins, cerebral hyperperfusion resembling lesions induces by chronic hypoxaemia, ischemia, congenital heart disease and congenital myocardopathy. Nitric oxide and adenosine are additive as dilators of coronary blood vessels. Blood pressure collapses. NO binds to cytochrome oxidase inhibiting respiration. When NO reaches dangerous levels, the cell turns on production of heme oxygenase. Heme is broken down to iron, carbon monoxide and bile pigments. NO has a huge affinity for hemoglobin which catalyses NO degradation to nitrate. Furthermore, NO is a product of smoke and SIDS incidence is higher in smoking mothers. The mixture of exhaled air and the fresh air during sleep (state with carbon dioxide contamination) can be associated with hypoxia and apnoea and this apnoea can provide an explanation for some cases of SIDS(6).

Our results

Our humble contribution to this problem included 12 sudden death cases in babies from 20 days to 1 year. We may place our cases in the group of unexpected explained death, because the main cause of death in most babies is pneumonia. Only in one of them we have found compound reason of death - bronchiolitis, pneumonia and meningitis and in one baby- only meningitis purulenta. The histological changes in lungs were microhaemorrhages in alveoles and interstitium, congestion, oedema, pulmonary emphysema, atelectases, haemosiderin-laden macrophages, bronchitis and catarrhal-desquamating pneumonia or catarrhalhaemorrhagic pneumonia, but in two cases there were a purulent pneumonia with the areas of abscedent pneumonia in one of them. We found these changes also in the baby with meningitis. Thymic gland has shown a cystic transformation, diminished number of Hassall's corpuscles and in one case - a lot of Hassall's corpuscles, but with cys-
tic degeneration and associated phagocytosis by macrophages ("starry-sky" spaces) - these features are the marks for acute or accidental involution. In one baby there was a third type of thymic hyperplasia with prominent cortical zone (this type is a common feature for sudden respiratory death. In one case we established cytomegalovirus infection. We didn't observed seasonal variation.

DISCUSSION

Most authors consider no laboratory or pathological tests are available to establish a diagnosis of SIDS and no lesions are found at autopsy in most cases. However, as recent reports pointed out, the affected infant would not be perfectly well before death(23). Some authors (22) insisted that hemosiderin-containing macrophages in SIDS cases would be a hallmark of repeated "near-miss" episode that produced pleural petechiae. They pointed out that the age of death of the babies with pulmonary hemosiderin-laden macrophages but no evidence of pulmonary inflammation was predominantly between 1 and 3 months. The increase of the alveolar macrophages could be merely a result of small, but frequent episodes of aspiration. More late investigation revealed that higher macrophage counts observed in non-SIDS cases and those with SIDS - average or below average macrophage count (8). Other insisted that the siderophages are not increased in SIDS and unexplained pulmonary siderophages can be a marker for trauma or repeated hypoxia/asphyxia (20). Severity of pneumonia is one of the most worrisome problem to make a diagnosis of sudden death. It would be somewhat subjective and there is no pathological standart to classify whether the lesion is morbid enough to be a cause of death. Some authors revealed that proximal and distal tracheal chronic inflammation was less severe in the SIDS cases than in the control cases and are neither a cause of SIDS, nor a specific marker for lethal respiratory infection in infants (24). Clinical experience indicates that interstitial pneumonitis or bronchiolitis sufficiently severe to cause death is preceded by clinical illness with signs of lethargy, tachypnea, respiratory distress, feeding difficulties and/or apnea (14). Most authors pointed the following histopathological changes in SIDS: pulmonary congestion, oedema, microhaemorrhages, increase of alveolar macrophages, atelecasis, emphysema, bronchitis and pneumonia. These findings are the most often features in almost all our babies. In Shi's work (21) the majority of the cases of SIDS (60%) died in the autumn and winter months. The same in Valdes-Depena's work (23)-in January are the most death cases. Decrease in the number of SIDS cases has been associated with infant sleeping supine instead of prone.

CONCLUSION

Based on author's experimental, epidemiological, pathological and pathophysiological, we may conclude that SIDS include combination of factors:

1. Unique death distribution with the majority occurring between 2 and 5 months of age (1week to 1year).
2. Excessive number of deaths during the winter months.
3. Higher death rates among blacks and male infants.
4. Mother who usually are of a lower socioeconomic status, predominantly young and with limited education, sometimes unmarried.
5. Frequently they used legal - tobacco and alcohol before, during and after pregnancy and illegal drugs.
6. Most authors pointed the following histopathological changes in SIDS: pulmonary congestion, oedema, microhaemorrhages, increase of alveolar macrophages, atelecasis, emphysema, bronchitis and pneumonia.

REFERENCES

1. Zekov, G - Sudden death in infant and early childhood, Sofia, 1980, Centrum for scientific information in medicine with central medical library
7. Crawley, B.A.and al - Endotoxin in blood and tissue in the sudden infant death syndrome, FEMS Immunology and Medical Microbiology 25 (1999) 131-135
10. Funayama, M, Azumi, J. and Murai N - Sudden unexpected death of infants and prone position. Autopsy cases of infants during 1 year in Tokio Medical Examiner Office - JIFS, 97, 1190 - 1198, 1993
14. Krous, F. et al - A comparison of respiratory symptoms and inflammation in SIDS and in accidental or inflicted infant death