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CASE REPORT

Multidisciplinary approach to suspected sudden unexpected infant death caused by milk-aspiration: A case report

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Abstract

BACKGROUND

The term sudden unexpected infant death (SUID) is not always properly invoked. It refers to a broad range of conditions that sometimes defy classification. There is not only a strong emotional impact on the family, but such cases are also quite complex. Underlying causes may be multiple, not always readily apparent, and have potential repercussions, especially in terms of forensics.

CASE SUMMARY

A 5-month-old male baby was pronounced dead following acute lung failure and cardiopulmonary arrest. The parents had immediately rushed their child to the hospital, stating the baby was found prone and not breathing. Total-body postmortem computed tomography (PMCT) was performed, revealing a hypodense material of indeterminate nature within the main airways and areas of ground-glass parenchymal change. At autopsy, the respiratory tract mucosa appeared edematous and was coated with a whitish stringy material. There was widespread airspace reduction due to parenchymal collapse. Alveolar sacs and bronchial openings contained abundant amorphous material admixed with white blood cells. Immunohistochemical studies were performed, targeting CD15, CD68, and alpha-lactalbumin. Ultimately, the focus was on alpha-lactalbumin (milk protein), which showed marked immunopositivity within alveolar spaces. Cytoplasmic staining of macrophages was also particularly prominent.

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CONCLUSION

Postmortem investigations are thus essential to identify causes of death and surrounding circumstances. PMCT is a useful tool in this setting, given the frequent dearth of autopsy findings and ambiguity as to cause of death in SUID cases. These findings, later confirmed by immunohistochemical investigations, were indicative of active pneumonia due to aspirated milk. The present account illustrates the importance a broad diagnostic approach to SUID in cases of forensic concern. PMCT is a very valuable aid in cases of forensic interest, as it can provide useful information in all those situations in which the cause of death is uncertain or there are no suggestive dynamics or lesions.

Key Words: Sudden unexpected infant death; Aspiration pneumonia; Postmortem computed tomography; Case report; Diagnosis; Immunohistochemistry

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Core Tip: The most frequent causes of pulmonary aspiration were caused by milk (31.8%). Predisposing factors include any condition that alters the state of consciousness or creates dysfunction of deglutition. In general, Gastric contents are related to aspiration pneumonia and present in the lungs of 30% to 40% of infants whose deaths are attributed to sudden infant death. The postmortem diagnosis of milk aspiration is a challenge for clinician and pathologist. In case of sudden unexpected infant death from milk aspiration a broad diagnostic approach is necessary for an identification of the cause of death. Postmortem computed tomography is a very valuable aid in cases of forensic interest, as it can provide useful information in all those situations in which the cause of death is uncertain or there are no suggestive dynamics or lesions.

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INTRODUCTION

Sudden unexpected infant death (SUID) by definition encompasses all categories of such events. These cases are emotionally devastating to families and often are highly complex, involving multiple and frequently elusive causes with serious repercussions, especially the forensic ramifications. Although incorrectly invoked at times, a broad spectrum of conditions that are difficult to classify qualify as SUID^[1].

In guidelines published by confidential enquiry into stillbirths and deaths in infancy (CESDI)^[2], the criteria for SUID are as follows: (1) Unexpected death at autopsy; (2) Death during an acute not life-threatening illness; (3) Death within 24 h after acute illness in a previously healthy infant; (4) Death from occult conditions; or (5) Death due to external factors (e.g., trauma or poisoning).

Based on the certainty of a named cause of death, SUID is categorized as I-III, where III indicates an established cause and IA denotes unexplained death, despite postmortem studies^[3]. However, comprehensive postmortem investigations (i.e., death scene inspection, autopsy and pertinent biomedical diagnostics) are crucial in narrowing the field of inquiry substantially.

The scenario depicted herein illustrates how postmortem computed tomography (PMCT) and immunohistochemical (IHC) staining helped link an occurrence of SUID to aspiration pneumonia.

In particular, PMCT is a very valuable aid in cases of forensic interest, as it can provide useful information in all those situations in which the cause of death is uncertain or there are no suggestive dynamics or lesions.

CASE PRESENTATION

Chief complaints

A 5-month-old male baby was reportedly found prone and not breathing by the parents, who immediately rushed the child to the hospital.

History of present illness

On arrival, the infant was pronounced dead as a result of acute lung failure and cardiopulmonary arrest.

History of past illness

No previous disease to report in anamnesis.

Physical examination

Cardiopulmonary resuscitation had not been attempted.

Laboratory examinations

Post-mortem examination: Four days after death, the autopsy took place. The baby measured 60 cm in length and weighed 8 kg. No gross external abnormalities were detected. Internally, all major organs were normally placed and well developed. The Letulle technique was used, removing bodily contents en masse. Gross examination of the respiratory tract proceeded along posterior median axis, exposing edematous mucosal linings coated with whitish stringy material (Figure 1). The lungs were purplish in colour. After en bloc fixation, they appeared dense and congested.

Histological examination: Thoracic and abdominal organs were sampled for routine processing and haematoxylin-eosin (HE) staining. Sections of lung tissue showed marked congestion of alveolar septal capillaries, which were also engorged with white blood cells, and widespread loss of airspace was conspicuous due to parenchymal collapse. In macrophages, there was copious cytoplasmic retention of amorphous material. The same substance, admixed with white blood cells, resided in alveolar spaces and bronchial openings. All other organs were histologically intact. Ultimately, sections of lung were subjected to IHC staining, targeting CD15, CD68, and alphalactalbumin. Intense CD15 positivity of alveolar content and septal capillaries was observed, whereas strong CD68 positivity was visible throughout lung parenchyma. Marked alpha-lactalbumin positivity of the intra-alveolar substance was also evident, and cytoplasmic staining of macrophages was especially prominent (Figure 2).

Imaging examination

Total-body PMCT was subsequently performed. In the lungs, a hypodense material of indeterminate nature occupied the main airways bilaterally, from oropharynx to subsegmental bronchi; and ground-glass parenchymal changes were noted in areas (Figure 3).

FINAL DIAGNOSIS

Aspiration pneumonia due to milk aspiration.

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TREATMENT

Unfortunately, physicians were unable to intervene even with resuscitation maneuvers as the death of patient was declared at the time of hospitalization.

OUTCOME AND FOLLOW UP

As previously discussed, the infant was declared dead upon admission to the hospital following a aspiration pneumonia from milk ingestion; final diagnosis was based on instrumental and immunohistochemical studies.

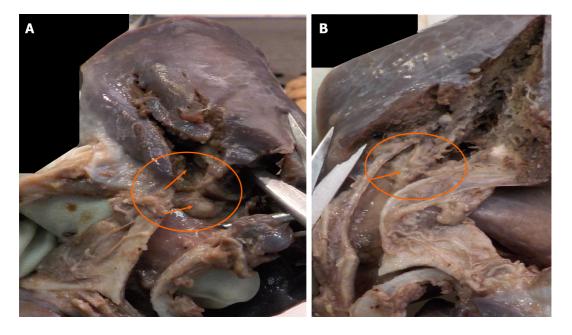


Figure 1 Gross examination of the respiratory tract: main bronchus (A, B) exposing edematous mucosal linings coated with whitish stringy material (orange arrows).

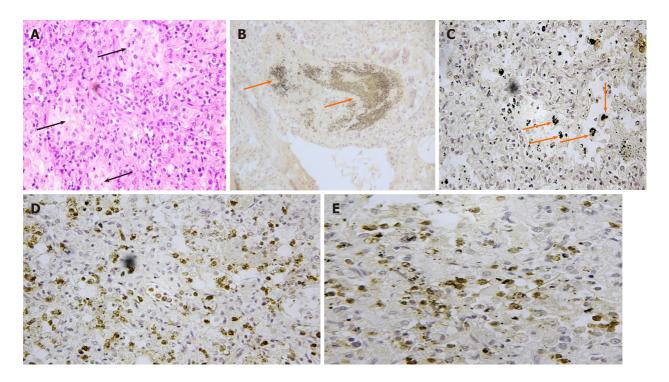


Figure 2 Results of histological examination. A: Lung tissue, marked congestion of alveolar septal capillaries, which were also engorged with white blood cells, and endo-alveolar incongruous material (black arrows) (haematoxylin-eosin, × 60); B: A positive CD15 mantle of cells (orange arrows) was immersed in endobronchial incongruous material; C: Strong CD68 positivity was visible throughout lung parenchyma (orange arrows); D: Marked alpha-lactalbumin positivity of the intra-alveolar substance was also evident; E: Cytoplasmic staining of macrophages was especially prominent.

DISCUSSION

Aspiration pneumonia is incited by foreign materials, often of oral or gastric origin (saliva, food), that enter the bronchial tree^[4]. In general, Gastric contents is related to aspiration pneumonia and present in the lungs of 30% to 40% of infants whose deaths are attributed to sudden infant death^[5,6].

Predisposing factors include any condition that alters the state of consciousness or creates dysfunction of deglutition. Typically, sudden respiratory difficulties (acute dyspnea) and cough develop in conjunction with solid or liquid food intake or

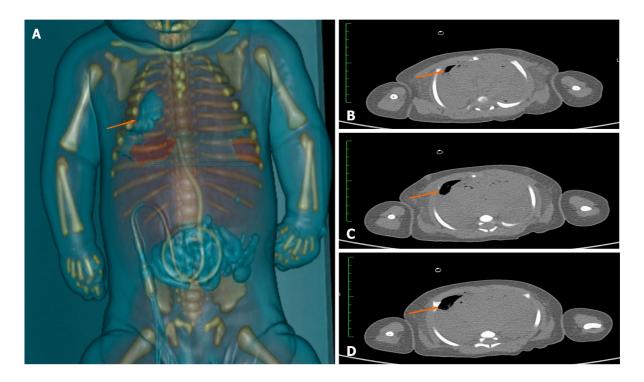


Figure 3 Results of imaging examination. A: Total-body Postmortem Computed Tomography: hypodense material of indeterminate nature occupied the main airways bilaterally, especially the right lung from oropharynx to subsegmental bronchi; B, C and D: The lungs had collapsed and only a part of the right lung (orange arrow) was expanded and ventilated (orange arrows).

regurgitation of gastric contents. The severity of symptoms depends on the nature and quantity of aspirated material. In some cases, cough is accompanied by pinkish and foamy or purulent sputum production. Tachycardia, high respiratory rate, fever, fatigue, myalgia, weight loss, and general malaise, may also ensue. Other consequences are diffuse end-expiratory wheezing, cyanosis, hypoxemia, pleuritic chest pain, bronchoconstriction, and acute pulmonary edema^[7,8].

In a study of Karim $et \, al^{[9]}$, on 107 children with pulmonary aspiration, the most frequent causes of pulmonary aspiration were caused by milk (31.8%) and oral secretions (19.6%). Neurological disorders were present in 29% of children, 5.6% had asphyxiation at birth and 10% were premature.

To establish the diagnosis, details of a patient's clinical history (and risk factors) are essential and biomedical diagnostics are pivotal. Chest radiographs readily disclose parenchymal infiltrates, reflecting bodily positions at times of aspiration. In cases of suspected SUID, no distinctive histopathologic changes are encountered, only agonal phenomena, such as pulmonary edema. A comprehensive postmortem investigation is therefore mandatory, which in this instance called for assessing the death scene and its circumstances, tomographic imaging (PMCT) and IHC techniques[10,11].

Because SUID events are often unwitnessed and lack autopsy evidence to explain cause of death, PMCT studies may be immensely productive. Computed tomography is likewise considered useful in the screening of unnatural death[12,13]. Recently, the association between post-mortem magnetic resonance, post-mortem examination and related histological study of the foetus or newborn could help reduce the percentage of cases in which the cause of death remains unexplained. Lastly, it may allow a selective sampling of the organ in order to target histological investigations^[14].

Milk is a common gastric component of newborns, but its triggering of aspiration pneumonia is much debated. Many authors view the presence of milk in the lungs as a postmortem artifact, secondary to cardiopulmonary resuscitation[15]. At autopsy, gastric content limited to distal lung segments (upper airways still clear) would indeed support their contention^[16]. Immunohistochemistry for milk components helps to demonstrate aspirated milk in lung sections.

The postmortem diagnosis of milk aspiration is a challenge for the forensic pathologist, as Moran et al[17] outlined in 1953. To date, few post-mortem studies that evaluate the diagnostic usefulness of specific immunohistochemical assays in the diagnosis of milk aspiration as a cause of death have been published.

In 1986 Boulloche et al[18], have studied of serum IgE assay in milk aspiration and the sudden infant death syndrome. In this study only the infants with a history of milk aspiration had significantly raised global and specific IgE. Iwadate et al[19-21], in three studies they examined 105 cases of aspiration pneumonia by immunostaining with anti-human α-lactalbumin antibody; milk aspiration was detected with immunohistochemical study in 40 cases. In other case reports, the need to carry out immunohistochemical assessments in case of histological examinations show a lot of amorphous material, suspect of aspirated milk^[22]. Experimental studies using a murine model have shown that the detection of aspirated milk in other organs except the lung would be clear evidence of intravital milk aspiration[23,24].

This result indicates that some degree of milk aspiration is not rare in infant death cases and the need for immunohistochemical examinations for the diagnosis of death due to milk aspiration.

In our case infant succumbed to acute pulmonary insufficiency, prompting totalbody PMCT. In the lungs, the main airways contained hypodense material and ground-glass parenchymal changes were present. No alterations were identified elsewhere, implicating the lungs solely as cause of death. The autopsy itself corroborated what was detected by PMCT. Airways of the infant displayed mucosal edema and contained whitish stringy material. IHC staining of CD15, CD68, and alpha-lactalbumin in samples of lung tissue also confirmed the suspicion of aspiration pneumonia. Both CD15 (neutrophil) and CD68 (macrophage) markers were strongly positive within alveoli and throughout lung parenchyma. These features were decisive, underscoring an active inflammatory process prior to death. We also targeted alpha-lactalbumin (milk protein), which proved markedly positive within alveolar and macrophage reservoirs, linking the pneumonia to aspiration of milk. Owing to combined use of PMCT and immunohistochemistry, a cause of death was conclusively determined in this case of SUID[25].

CONCLUSION

Autopsies requested for SUID tend to be unproductive. In those cases where death can be attributable to numerous causes, PMCT may direct the clinician and the pathologist towards a specific etiology. In deaths from aspiration asphyxia, IHC staining is an essential step, helping to clarify the nature of aspirated material and confirm its presence within cellular infiltrates.

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