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Original Communication

# Unclassified sudden infant death associated with pulmonary intra-alveolar hemosiderosis and hemorrhage

Homeyra Masoumi MD [a], Amy E. Chadwick BA [a], Elisabeth A. Haas MPH [a], Christina Stanley MD [b], Henry F. Krous MD [a,c,*]

[a] *Department of Pathology, Rady Children's Hospital and Health Center, 3020 Children's Way, MC5007, San Diego, CA 92123, United States*
[b] *Office of the Chief Medical Examiner, County of San Diego, CA, United States*
[c] *Department of Pathology, University of California, San Diego School of Medicine, La Jolla, CA, United States*

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**Abstract**

The significance of severe pulmonary intra-alveolar hemosiderosis in sudden infant death is controversial in forensic pathology. We report a previously healthy 9-month-old female infant who died suddenly and unexpectedly after being placed and then found prone in her crib. Her gestation and delivery were uncomplicated, and she had no history of anemia, hemoptysis, chest trauma, or chronic lung disease. Autopsy revealed diffuse severe pulmonary congestion and severe multifocal intra-alvedar hemorrhage. Metabolic and toxicological screening, microbiologic cultures, and vitreous chemistry were noncontributory. A diagnosis of SIDS had been made by the medical examiner. Subsequent semiquantitative assessment of the severity of pulmonary intra-alveolar hemosiderosis prompted consideration of other disorders, including a heretofore undescribed lethal infantile variant of idiopathic pulmonary hemosiderosis, but none could be confirmed. Therefore, we assigned a study diagnosis of unclassified sudden infant death. We recommend that a diagnosis of SIDS not be made in cases with unexplained large numbers of intra-alveolar PS. We also recommend that quantitative assessment of lung sections stained for iron be undertaken in cases with numerous intra-alveolar macrophages in order to accumulate data that might allow diagnostic correlations with the circumstances of death and autopsy findings.


*Keywords:* Sudden infant death; Idiopathic pulmonary hemosiderosis; Suffocation; SIDS

## 1. Introduction

The significance of pulmonary intra-alveolar siderophages (PS) in cases of sudden infant death is unclear, and has been a matter of some controversy. From a forensic perspective, they have been proposed as a tissue marker that could possibly aid in distinguishing SIDS from "soft" suffocation.[1–7] Indeed, when PS are present in large numbers, some investigators suggest that SIDS is an inappropriate diagnosis.[1,5,8] In our previous study, we found that the number of PS varies widely in cases of sudden infant death caused by SIDS and accidental or inflicted suffocation, and cannot be used as an independent variable to ascertain past attempts at suffocation.[9] However, other less sinister causes must be considered as well. We present a case of sudden unexpected infant death that was found to have large numbers of PS associated with moderately severe hemorrhage, and discuss the possible etiology.

## 2. Case report

A 9-month-old Caucasian female was somewhat fussy with a poor appetite when she was placed alone and prone to sleep in a crib by her day care provider. About 2 h later

* Corresponding author. Address: Department of Pathology, Rady Children's Hospital and Health Center, 3020 Children's Way, MC5007, San Diego, CA 92123, United States. Tel.: +1 858 966 5944; fax: +1 858 966 8087.
*E-mail address:* hkrous@rchsd.org (H.F. Krous).

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she was found prone and unresponsive. Cardiopulmonary resuscitation (CPR) was attempted for 62 min but was unsuccessful.

She was delivered vaginally at 40 weeks gestation following the uncomplicated pregnancy of her mother who had regular prenatal care. Her birth weight was 3060 g (<25th percentile). She was breastfed and received formula supplements. Her immunizations were current at the time of her death. One month prior to her death, she had been successfully treated with antibiotics for otitis media; several days prior to her death signs of "ear pulling" recurred, but in the absence of a fever, a physician was not consulted. There was no history of hemoptysis, apnea, pneumonia, allergies, or chest injuries. Sudden infant or childhood death had not occurred among siblings. The family history was negative for allergies, smoking, drug use, and contact with police or social services. The household was free of fumes, peeling paint, and mold growth.

Autopsy by the San Diego County Office of the Medical Examiner (ME) revealed a normally-developed female infant measuring 70 cms (25th percentile) in length and weighing 7110 g (<5th percentile). The postmortem radiographs revealed no evidence of trauma or underlying disease in the skeleton including the ribs and spine. The bladder was empty. Thymic, epicardial, and pleural petechiae were present. The middle ears were not examined.

The right and left lungs weighed 76 and 68 g, compared with expected weights of 59 and 53 g,[35] respectively; the cut surfaces were medium to dark maroon and oozed bloody fluid. Parenchymal consolidation, thromboembolism, infarction, fibrosis, and vascular thickening were not identified. Postmortem toxicology, microbiologic cultures of blood and CSF, and metabolic screening were negative. Vitreous chemistry was noncontributory. Middle ear and lung cultures were not performed.

The ME identified diffuse severe pulmonary congestion and moderately severe intra-alveolar hemorrhage, but not other significant pathologic findings. Our microscopic examination revealed grade 3 pulmonary intra-alveolar hemorrhage (PH) when assessed semiquantitatively in hematoxylin and eosin (H&E) stained sections of formalin-fixed lung using the following grading system: grade 0 = none; 1 = mild; 2 = moderate, focal; 3 = moderate, multifocal; and 4 = diffuse, severe.[10]

We also identified large numbers of pulmonary intra-alveolar siderophages (PS) in iron-stained tissue from both lungs (Fig. 1). PS were counted in 20 randomly selected but contiguous 400× high-power fields (hpf) in each of the four available lung sections stained by the Prussian blue method, as previously described.[9] PS count (defined here as the average number of PS per 20 hpf per lung section) was 1732 in this case.[9] Eosinophils and mast cells were neither increased nor degranulated when evaluated in appropriately controlled Giemsa stained lung sections. Appropriately controlled Masson trichrome and Verhoff-van Gieson elastic stained lung sections did not reveal evidence of pulmonary fibrosis or hypertensive arteriopathy.

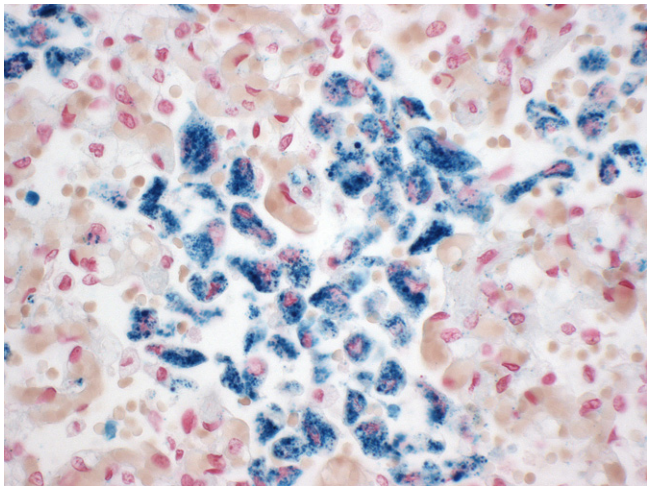

Fig. 1. Lung section in a 9-month-old female, with severe pulmonary hemosiderosis. The average number of pulmonary intra-alveolar siderophages per 20 randomly selected but contiguous fields per section was 1732. Prussian blue stain, 400×.

IgG, IgA, IgM, C3, C1q, properdin, fibrinogen, and albumin were not present in microscopic lung sections that were deparaffinized and reprocessed for immunofloures-cence microscopy (IF). Immunoglobulin controls consisting of plasma cells in tonsil tissue stained appropriately.

## 3. Discussion

We have presented a 9-month-old, term born female infant who died suddenly and was found at postmortem examination to have moderately severe pulmonary hemorrhage. As part of our previous study,[9] we had identified a particularly large number of diffusely distributed PS in this case, prompting us to re-evaluate the cause of death. Since accidental asphyxia and other causes of death were excluded, we considered sudden infant death syndrome (SIDS), inflicted suffocation, and idiopathic pulmonary hemosiderosis (IPH). In fact, her death was initially ascribed to SIDS by the ME (Case 9, Table 5[9]). The most current general definition for SIDS is "the sudden and unexpected death of an infant under one year of age, with onset of the lethal episode apparently occurring during sleep, that remains unexplained after a thorough investigation including performance of a complete autopsy, and review of the circumstances of death and the clinical history".[11] Our case was within the classic SIDS age range and apparently died during sleep; further, she had been placed and found prone in an otherwise safe sleep environment, and at autopsy, had an empty bladder and intrathoracic petechiae. Ancillary autopsy analyses did not explain the death.

In our initial study, we found a wide range of PS in cases of SIDS as well as accidental and inflicted suffocation, indicating that numerous PS can not be used independently to exclude SIDS.[9] However, the PS count in the present case (1732) was exceptionally high; the mean