H177 A Histological Study of Persistent Pulmonary Hypertension of the Newborn (PPHN): A Five-Year Retrospective Analysis of a Fatal Cause in Neonates

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Learning Overview: After attending this presentation, attendees will be aware of the specific histological features of the lung in PPHN and understand their prognostic significance.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by raising awareness of a disease process that may present as unexplained cardiopulmonary arrest in neonates during and after birth hospitalization, giving rise to medical malpractice litigations and lawsuits.

PPHN is a serious condition that occurs in about 1.8–2 per 1,000 newborns (both term and preterm) in the neonatal intensive care unit, and may significantly complicate the clinical course of approximately 10% of neonates with respiratory insufficiency.[1-3] It is associated with an increased risk of an adverse outcome, including neurologic impairment in 15%–25% of neonates with PPHN who survive after hospital discharge.[4] PPHN is defined as a failure to achieve or sustain the physiological decrease in pulmonary vascular resistance at birth associated with the persistence of the typical *in utero* right-to-left shunt. PPHN may eventually lead to life-threatening circulation failure and is one of the main causes of unexpected death of neonates, with a mortality rate of about 10%–20% of the affected patients.[5] PPHN is often associated with structural or functional disorders of the lungs or systemic diseases, such as diaphragmatic hernia, meconium aspiration, pneumonia, and placental insufficiency.

Clinically, PPHN is characterized by tachypnoea, severe cyanosis, acidosis, and rapidly increasing hypoxemia. PPHN diagnosis is confirmed by echocardiographic evidence of increased pressures in the pulmonary artery and right heart chambers in the absence of evidence of congenital heart disease; however, conclusive diagnosis of PPHN-related death currently relies on autopsy examination. Typically, the clinical manifestations are noticeable leading to the antemortem diagnosis of PPHN. Nevertheless, PPHN arising suddenly and early after birth is usually fatal, despite evidence-based treatment. PPHN remains a challenge in therapeutic management because the complex etiopathogenesis is yet to be fully explained. Moreover, prenatal assessment of PPHN is very difficult and not always possible.

The present study comprised a five-year retrospective analysis of data from neonatal autopsies collected in two hospitals in Northwest Italy (i.e., "Ospedale Ginecologico Sant'Anna," Torino, and "Ospedale Pediatrico G. Gaslini," Genova). It entailed thorough identification and analysis of histologic findings in PPHN cases. The aims of the study were to enable better prediction of lung function outcomes in affected neonates and potentially help clarify cases of medical malpractice litigation. From January 2014 to December 2018, the hospital-selected units in Torino and in Genova performed 1,312 and 456 autopsies, respectively, of which 86 and 111 were on neonates. There were 39 autopsies that involved neonates affected by PPHN in life (i.e., 18 in Torino and 21 in Genova). Thus, the average incidence of PPHN as a cause of death among all neonatal autopsies was 19.79% (i.e., 20.93% in Torino and 18.92% in Genova).

Paraffin-embedded tissue sections from the lungs of all 39 autopsy cases were cut in 2-µm slices and stained with different histologic and immunohistochemical stains. Specific histologic parameters (i.e., degree of lung development, morphological features of bronchioles, alveolar veins and capillaries, interstitial septae structure, presence of arteriolar layers thickening, hyaline membranes, intralveolar histocytes, interstitial or endoalveolar inflammation, and therapy-induced pulmonary alteration) were reevaluated on light microscopy.

In accordance with the literature, this study showed PPHN is a severe syndrome frequently encountered in pediatric hospitals. Moreover, it is often responsible for the sudden death of neonates during hospitalization after birth. This presentation offers attendees an insight into the importance of an in-depth knowledge of histologic criteria in PPHN that may enhance appreciation of the severity of the disease, guide better management, and help predict pulmonary response. This is fundamental to significantly reduce the rate of neonatal mortality and the associated medicolegal implications.

Reference(s):

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