Observational study

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Histopathological Insights into Pulmonary Hemorrhages: Enhancing Forensic Diagnoses

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Abstract

Pulmonary hemorrhage is a pathological condition characterized by bleeding within the lung parenchyma, ranging from localized microbleeds to extensive hemorrhagic events that significantly compromise respiratory function. The etiology of pulmonary hemorrhage encompasses multiple clinical and forensic contexts. For forensic pathologists, the most significant pulmonary hemorrhages occur in cases involving traumatic incidents, asphyxiation, narcotic substance use and resuscitation procedures. This study aims to analyze the histopathological features of pulmonary hemorrhages in a forensic context, highlighting the specific histopathological characteristics. The authors analyzed cases of pulmonary hemorrhages taken from sectoral case studies from the Forensic Department of Legal Medicine at the University of Foggia, spanning from 2019 to 2024. In all these cases the histological investigation was important for identifying the cause of death and for characterizing the lung damage, even in the absence of macroscopic contusions. In cases of asphyxia, ingestion of narcotic substances, and post-resuscitation, the edematous component prevails over the hemorrhagic component. The hemorrhagic component is evident in cases of trauma to the lung and airways, such as in chest compression or lung injury. These histopathological distinctions are pivotal for forensic pathologists as they provide concrete evidence that supports differential diagnoses, helping to clarify the cause of death in complex cases where circumstantial and autopsy data alone may not be conclusive.***Clin Ter 2025; 176 Suppl. 1(2):53-58 doi: 10.7417/CT.2025.5188***

Keywords: *Pulmonary hemorrhage, histopathology, forensic contexts.*

Introduction

Pulmonary hemorrhage is a pathological condition characterized by bleeding within the lung parenchyma, ranging from localized microbleeds to extensive hemorrhagic events that significantly compromise respiratory function. The etiology of pulmonary hemorrhage encompasses multiple clinical and forensic contexts. Indeed, forensic literature has documented pulmonary hemorrhage in multiple death scenarios, including mechanical asphyxia, barotrauma, substance abuse-related deaths, traumatic incidents, Sudden Infant Death Syndrome (SIDS) and complications from medical procedures (intubation).

Pulmonary hemorrhage can be categorized into two main groups: diffuse pulmonary hemorrhage (DPH), which includes diffuse alveolar hemorrhage (DAH), and localized pulmonary hemorrhage.

DAH occurs when bleeding spreads directly into the alveolar spaces and severely impairs gas exchange. Causative factors include pulmonary vasculitis, ANCA-associated pulmonary vasculitis, microscopic polyangiitis, Churg-Strauss vasculitis, Goodpasture syndrome, Systemic Lupus Erythematosus, coagulation disorders, exposure to exogenous substances (e.g. isocyanates, cocaine, crack), mitral stenosis or insufficiency, pulmonary veno-occlusive disease, pulmonary hemosiderosis, drug reactions (e.g. amiodarone, infliximab, methotrexate) and antiphospholipid antibody syndrome (1). These conditions can damage the blood vessels in the lungs, leading to widespread bleeding into the alveoli. Histologically, DAH presents with a blood accumulation in the alveoli, damage to small-caliber pulmonary vessels, pulmonary capillaries inflammation, and

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infiltrates of cells such as neutrophils and macrophages in the lung tissues. These cellular infiltrates indicate an active inflammatory response, which can further aggravate tissue damage.

Conversely, localized pulmonary hemorrhage involves a specific region of the lung. Potential causes include pulmonary vasculitis, secondary aspiration of blood due to chronic bronchitis, bronchiectasis, infections, tumors, pulmonary infarction, tuberculosis, vascular invasion of a lung tumor, pulmonary trauma, pulmonary arteriovenous malformations and iatrogenic maneuvers (e.g. thoracic biopsy) (2, 3).

Pulmonary hemorrhage has been found in various forensic contexts, including deaths from intubation, barotrauma, deaths from mechanical asphyxia, deaths from trauma, SIDS, and substance abuse-related deaths.

Literature analysis shows the presence of pulmonary congestion and edema on histological examinations. For example, regarding deaths from substances of abuse, the presence of pulmonary congestion has been reported in the lungs of those who died from opioid abuse has been reported (4). Drug use can cause pulmonary and aspiration inflammation, cardiogenic pulmonary edema, acute lung damage, pulmonary hemorrhage, barotrauma, and septic embolism. Drugs that can cause thoracic pathologies include cocaine, heroin, opiates, and derivatives of amphetamine substances. The authors of an Italian study reported a case of alveolar hemorrhage in an occasional crack user analyzed with conventional radiological investigation and HRCT, accompanied by clinical laboratory findings and broncho-alveolar lavage (BAL) to confirm the diagnosis based on the morphological data detected (5).

Conversely, pulmonary barotrauma can occur during any dive or hyperbaric exposure, however brief or mild. Meanwhile, decompression illness (DCI) is usually associated with more profound and prolonged episodes of compression. Pulmonary barotrauma manifests clinically during or immediately after decompression, whereas DCI can often appear much later. Lung compression is possible during freediving at depths greater than 30 meters of seawater; however, chest wall compliance may allow deeper dives, although tension within the lungs may lead to intrapulmonary hemorrhage (6).

Regarding traumatic deaths, a Polish study showed histopathological changes in the lungs of victims of mountain snow avalanches. Lung sections stained by the AZAN method revealed the presence of intraalveolar hemorrhages in all cases. However, the accurate diagnosis of these hemorrhages was difficult because the hemolyzed erythrocytes were visible only as pale cell shadows (7).

Furthermore, another study demonstrated the presence of pulmonary hemorrhage in SIDS cases. Pulmonary hemorrhage is also found in newborns who die from SIDS, accidental or inflicted suffocation. However, pulmonary hemorrhage cannot be used as an independent indicator to determine the manner of sudden and unexpected death in a newborn. Rather, pulmonary hemorrhage must be interpreted in the context of the victim's medical history, circumstances of death, and autopsy findings (8). Pulmonary congestion has also been reported in cases of death from positional asphyxia (9). These cases provide valuable information to reconstruct the events that led to the individual's death.

This study aims to analyze the histopathological features of pulmonary hemorrhages in a forensic context, highlighting the specific histopathological characteristics. A detailed analysis of lung lesions can reveal distinctive patterns indicative of specific causes of death, such as the presence of particular types of inflammatory cells or the distribution of bleeding within the lung tissue. This approach aims to provide pivotal information to the forensic pathologist, thus contributing to a better understanding and interpretation of cases. Indeed, pulmonary hemorrhage cannot be interpreted in isolation. Forensic pathologists must evaluate medical history, analyze death circumstances and conduct a comprehensive autopsy examination (10).

Materials and methods

The authors analyzed sectoral case studies from the Forensic Department of Legal Medicine at the University of Foggia, spanning from 2019 to 2024. From an analysis of 467 autopsies, they selected five cases characterized by pulmonary hemorrhages.

For each case, the forensic pathologist compiled a comprehensive autopsy report, including histological and toxicological tests, to identify the cause and manner of death. In this article, we present the findings from the pulmonary histological investigations. All slides were stained using hematoxylin-eosin and studied under a light microscope at 10x and 20x magnification.

The first case concerns a 69-year-old individual who died from positional mechanical asphyxia. During the judicial inspection, the body was found kneeling, with the trunk flexed inward and rotated to the right, and the neck hyperextended. Toxicology tests revealed a blood alcohol level of 2.51 g/L. At autopsy, no macroscopic traumatic lesions were observed. However, histological examination revealed multiple areas of interalveolar hemorrhage with leukocyte infiltration, and a minor presence of hemorrhagic pulmonary edema (Fig. 1, 2). Congestion of the septal microcirculation was also evident. Therefore, the anomalous position of the body prevented proper respiratory dynamics, exacerbated by alcohol intoxication, which further hindered the individual's ability to restore a correct posture.

In the second case, a 75-year-old man was working in his countryside on an extensive excavation project. During the work, he was buried up to his neck by a pile of soil that detached from the excavation walls. The autopsy revealed the presence of several rib fractures but no macroscopic pulmonary contusions. Histological examination revealed abundant hemorrhagic edema in all the sampled fields (Fig. 3). Death was determined to be due to confinement asphyxiation.

The third case concerns a 39-year-old individual who died following chest trauma resulting from a fall from a low height (about 1 meter). The man had taken a dose of cocaine (confirmed by toxicological examination) shortly before the fall. At autopsy, there were small areas of pulmonary contusion and four right rib fractures. Histological examination revealed massive intraalveolar hemorrhages and some areas of pulmonary edema in the right lung (Fig. 4), while the left lung was free of lesions. Identifying the cause of death was

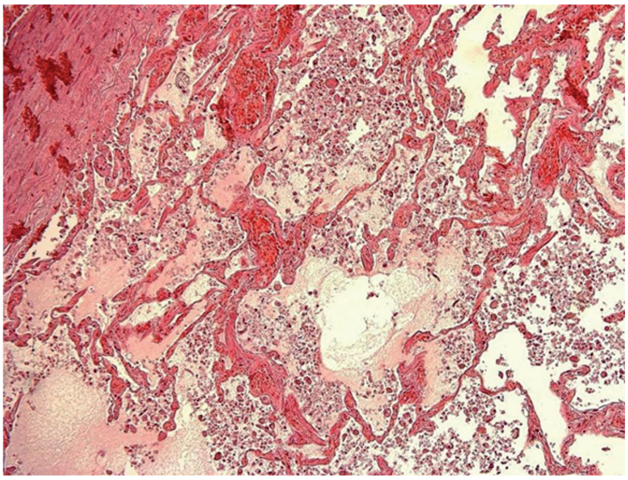

Fig 1

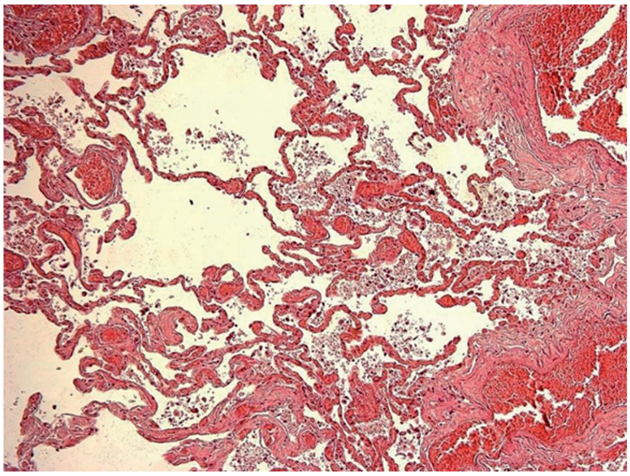

Fig 2

Fig.1 - Fig. 2 - Multiple areas of interalveolar hemorrhage with leukocyte infiltration, with less area of edema, and congestion of the septal microcirculation.

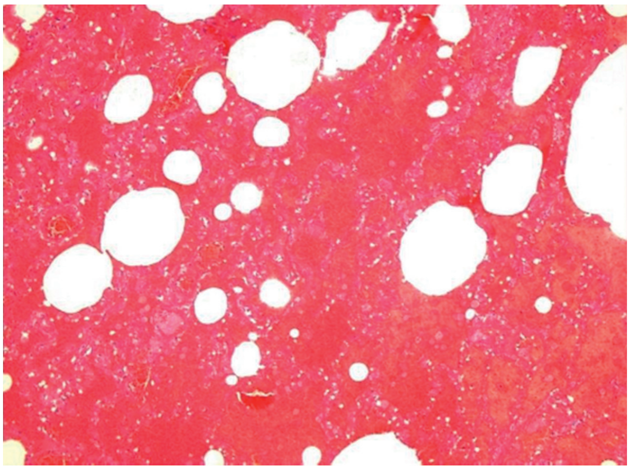

Fig.3. Abundant hemorrhagic edema with signs of putrefaction.

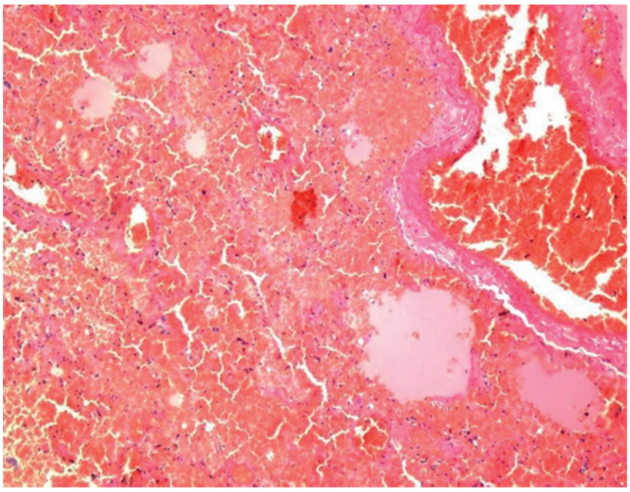

Fig. 4. Massive intraalveolar hemorrhages with less areas of pulmonary edema.

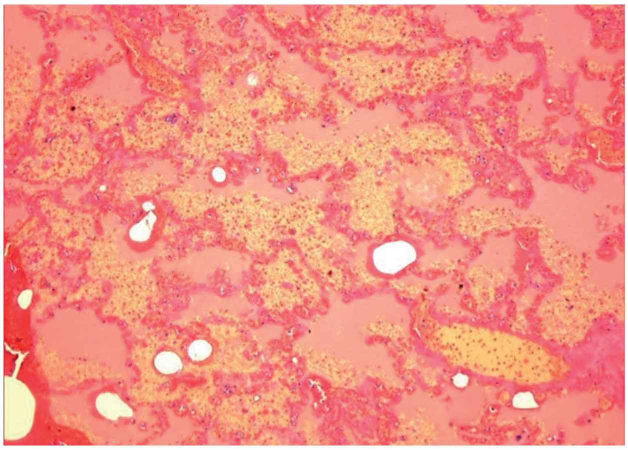

Fig. 5. Hemorrhagic pulmonary edema with septal congestion. The hemorrhagic component is less expressed than the edematous component.

not straightforward in this case because both mechanisms (cocaine ingestion and chest trauma) could potentially cause death. The analysis of the type of pulmonary hemorrhage was pivotal in making the diagnosis, as the presence of less pulmonary edema and more significant hemorrhage indicated thoracic trauma rather than cocaine intake.

The fourth case concerns the death of a young individual following acute cocaine intoxication, confirmed by toxicological examination. Histological examination revealed frank hemorrhagic pulmonary edema with clear identification of the alveolar architecture, also characterized by septal congestion (Fig. 5).

The fifth case concerns a 70-year-old man who underwent surgery for femoral artery stenosis under local anesthesia. During the surgery, he experienced an episode of desaturation and subsequently went into cardiac arrest. The anesthesiologists promptly intubated him and connected him to ECMO (extracorporeal membrane oxygenation). After a day on ECMO, the man died. The autoptic exami-

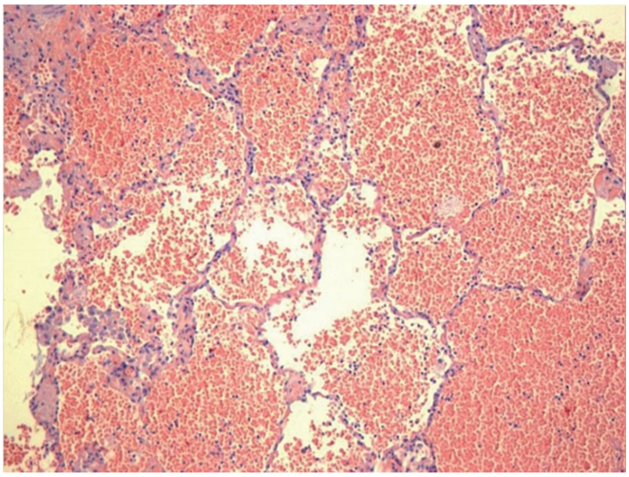

Fig 6

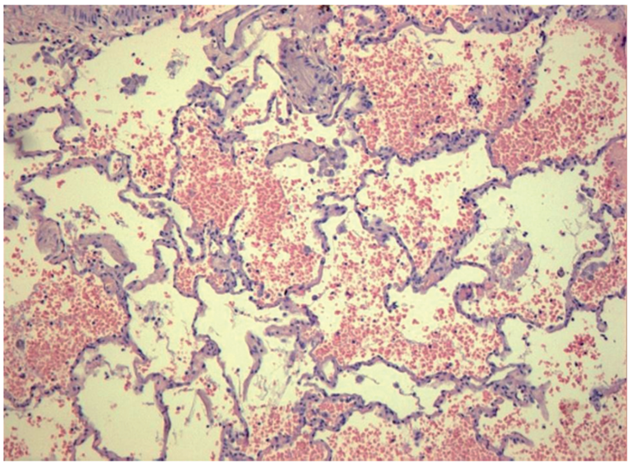

Fig 7

Fig. 6, Fig. 7. Erythrocytes extravasated into the alveoli, in the absence of edema.

nation revealed that the deceased had developed ischemia-reperfusion damage in the lungs, with hemorrhages in the alveoli (Fig. 6, 7).

Discussion

Pulmonary hemorrhages represent a critical area of investigation in forensic pathology; diagnosis is often possible through histological study, even in the absence of macroscopic contusions. Indeed, histological examination often reveals diagnostic insights that may not be apparent through macroscopic observation, making microscopic analysis an essential tool for forensic pathologists. For forensic pathologists, the most significant pulmonary hemorrhages occur in cases involving traumatic incidents, asphyxiation, narcotic substance use and resuscitation procedures. Histopathology plays a pivotal role in differentiating the various causes of pulmonary hemorrhages, providing detailed insights that are not always visible through macroscopic examination alone.

The authors have reported a series of noteworthy cases to forensic pathologists, describing the microscopic findings, summarized in Table 1.

In cases of asphyxia, erythrocytes spill into the alveoli, accompanied by significant pulmonary edema. Macrophages activation is also observed. Another characteristic finding is the presence of microcirculation congestion. These findings indicate mechanical airflow obstruction, providing critical evidence of asphyxiation-related death.

In cases of chest compression, the hemorrhage and pulmonary edema become much more intense, resulting in frank hemorrhagic edema. The severity of the hemorrhagic edema in such cases helps differentiate chest compression from other forms of trauma, where the pattern and intensity of bleeding can vary significantly.

In cases of barotrauma, interalveolar pulmonary edema is characterized by numerous macrophages with granular cytoplasm, leading to a true inflammatory reaction. This distinctive inflammatory response, marked by macrophages with granular cytoplasm, helps identify barotrauma as a cause of death, distinguishing it from other conditions where such cellular reactions are absent or less pronounced.

In cases of lung trauma (e.g., falls, gunshots, road accidents), the hemorrhage is much more evident than the edema, as there is a laceration of the lung parenchyma with extravasation of blood. The presence of lung parenchyma lacerations and the associated hemorrhage are critical histopathological markers that point directly to traumatic injuries, enabling forensic pathologists to accurately attribute the cause of death to physical trauma.

In cases of ingestion of abused substances, especially cocaine, hemorrhagic pulmonary edema is widespread. The preservation of lung structures is essential. The widespread nature of hemorrhagic pulmonary edema in substance abuse cases, coupled with well-preserved lung structures, helps distinguish these deaths from other causes where lung structure may be compromised.

Finally, even in patients undergoing extracorporeal circulation, hemorrhagic extravasations form within the alveoli, with good visualization of the septa, which in some fields appear broken due to the initial ischemia-reperfusion damage. The presence of hemorrhagic extravasations and ischemia-reperfusion damage in these patients provides clear histopathological evidence linking the death to complications arising from medical procedures.

All the cases presented have their peculiarities. Therefore, in cases of asphyxia, ingestion of narcotic substances, and post-resuscitation, the edematous component prevails over the hemorrhagic component. The hemorrhagic component is evident in cases of trauma to the lung and airways, such as in chest compression or lung injury. These histopathological distinctions are pivotal for forensic pathologists as they provide concrete evidence that supports differential diagnoses, helping to clarify the cause of death in complex cases where circumstantial and autopsy data alone may not be conclusive.

These findings can assist forensic pathologists in analyzing cases where circumstantial and autopsy data are not conclusive, such as in the case analyzed by the authors,

Table 1. Main characteristics of pulmonary hemorrhages divided according to the cause of death

Cause of death	Key features	Histopathology	Microcircolatory congestion	Macrophage activation	Pulmonary edema	Laceration of the lung parenchyma	Ischaemia-Reperfusion injury
Asphyxia	Erythrocytes in alveoli, significant pulmonary edema	Microcirculatory congestion, macrophage activation, significant pulmonary edema.	Present	Present	Present	Not present	Not present
Chest compression	Intense hemorrhage and pulmonary edema, frank hemorrhagic edema	Intense pulmonary hemorrhage and edema.	Present	Not present	Present	Not present	Not present
Barotrauma	Interalveolar pulmonary edema, numerous macrophages with granular cytoplasm	Interalveolar pulmonary edema, granular macrophages, inflammatory reaction.	Not present	Present	Present	Not present	Not present
Lung Trauma	Evident hemorrhage compared to edema, laceration of lung parenchyma	Evident hemorrhage, laceration of the lung parenchyma with blood extravasation.	Not present	Not present	Not present	Present	Not present
Ingestion of Abused Substances	Widespread hemorrhagic pulmonary edema, preservation of lung structures	Diffuse hemorrhagic pulmonary edema, preservation of lung structures.	Not present	Not present	Present	Not present	Not present
Patients undergoing extracorporeal Circulation	Hemorrhagic extravasations in alveoli, good visualization of septa	Hemorrhagic extravasations in the alveoli, visualization of septa, ischaemia-reperfusion injury.	Not present	Not present	Present	Not present	Present

where there was doubt whether the cause of death was attributable to trauma from falling or the ingestion of cocaine. By integrating histopathological examination, forensic pathologists can accurately identify the underlying cause of death, ensuring a comprehensive understanding of the events leading to an individual's death (11).

Conclusion

Pulmonary hemorrhages represent a significant challenge in forensic pathology, necessitating a comprehensive histopathological examination to accurately determine the cause of death. The identification of specific histopathological features (e.g. alveolar hemorrhage, edema, macrophage activation, the presence of inflammation) aids forensic pathologists in forming accurate differential diagnoses (12-16). For instance, the presence of alveolar hemorrhage and pulmonary edema may indicate asphyxia, while the activation of macrophages and the presence of congestion in the microcirculation can provide further evidence supporting this diagnosis (17-20).

Overall, the detailed histopathological analysis of pulmonary hemorrhages enhances the forensic pathologist's ability to differentiate between various causes of death, thus contributing to the accuracy and reliability of forensic diagnoses (21-23). This approach is pivotal for clarifying the cause of death in complex cases where circumstantial and autopsy data alone may not provide definitive answers. By integrating histopathological findings with other investigative data, forensic pathologists can formulate more precise conclusions regarding the cause of death, thereby contributing significantly to the administration of justice (24-26).

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