Post-Trauma Combined Pulmonary Fat and Bone Embolism: Literature Review with Case Presentation

Sara Sablone 1,*, Gerardo Cazzato 2, Lorenzo Spagnolo 1, Caterina Berterame 1, Federica Mele 1, Francesco Introna 1 and Aldo Di Fazio 3

1 Section of Legal Medicine, Department of Interdisciplinary Medicine, Bari Policlinico Hospital, University of Bari, 70124 Bari, Italy; lorenzospagnolo90@gmail.com (L.S.); caterina.berterame@asl.taranto.it (C.B.); f.mele17@studenti.uniba.it (F.M.); francesco.introna@uniiba.it (F.I.)
2 Section of Pathology, Department of Emergency and Organ Transplantation, Bari Policlinico Hospital, University of Bari, 70124 Bari, Italy; gerardo.cazzato@uniba.it
3 Regional Complex Intercompany Institute of Legal Medicine, 85100 Potenza, Italy; aldo.difazio@ospedalesancarlo.it

* Correspondence: sara.sablone@policlinico.ba.it; Tel.: +39-338-9057823

Abstract: Following an accident in the workplace, a man received deep wounds in his left groin and left lower limb caused by plow blades. An external examination was carried out showing multiple, large, and deep slash injuries of the scrotal region, the left groin, and the left thigh. A complete autopsy was performed. The gross examination of the lungs showed edema and congestion, with some areas of parenchymal contusion and wide emphysema. The left femur showed complete, comminuted, displaced, and exposed fracture of its diaphyseal tract. Histopathological analysis was then carried out, showing unusual abnormalities in both lungs, with numerous endovascular drop-shaped fat globules with surrounding hematopoietic marrow that were mixed with small bone particles. The other organs did not show any signs that could explain the death. Given macroscopic and histopathological elements, the cause of death was ultimately identified as a traumatic shock with a high hemorrhagic component combined with pulmonary bone marrow and bone embolism. This paper aims to outline a rare case of post-trauma combined bone and bone marrow embolism. This occurrence is scantily described in the literature and should be considered in major trauma deaths. Therefore, in such cases, an accurate histopathological analysis should be mandatory to identify the correct cause of death and evaluate a possible medical liability.

Keywords: non-thrombotic pulmonary embolism; bone embolism; fat embolism; trauma; forensic autopsy

1. Introduction

Non-thrombotic pulmonary embolism is defined as embolization of the pulmonary circulation that can be caused by a wide range of non-thrombotic embolic agents. These can include cells (e.g., adipocytes, hematopoietic, amniotic, trophoblastic, and tumor cells), bone, infective agents, and a variety of foreign materials and gases.

Bone embolism is a very rare event, and only a few reports are available in the medical literature [1–7]. In this paper, a rare case of post-traumatic pulmonary embolism caused by bone fragments and fat globules with surrounding hematopoietic marrow is described and a comprehensive literature review is carried out. The detection of simultaneous bone and fat/bone marrow embolism in the lung microcirculation through histological assessment is an important forensic sign of vitality that could provide relevant information on survival after the injury.

2. Materials and Methods

We conducted a literature review using PubMed and Web of Science (WOS) search engines, entering the words “non-thrombotic pulmonary embolism” or “bone embolism”
or “fat embolism” and/or “post-trauma pulmonary embolism” to retrieve descriptions referring to this entity. Together with the review, we report a case of combined post-trauma pulmonary embolism undergone judicial autopic analyses at our Institute of Legal Medicine.

Case History

During working agricultural activity in an open field, a 58-year-old man was accidentally hit by a plow pulled by a moving tractor. The other workers immediately called the emergency health service and provided first aid to the injured man who had deep and bleeding wounds in his left groin and left lower limb. After about fifteen minutes from the call, an air ambulance arrived at the scene of the accident and transferred the man to the nearest emergency unit. However, right after the arrival, the patient had a cardiocirculatory arrest and died notwithstanding ALS measures. Considering the relevant traumatic lesions, the doctors attributed the death to severe polytrauma, mainly involving the abdomen and left lower limb. However, to accurately assess the mechanism of death, a complete autopsy was ordered 2 days after by the judicial authorities.

3. Results
3.1. External Examination

Firstly, a careful external examination was performed. The body was 156 cm in length and weighed 70 kg. Post-mortem hypostases were at the back and very slight, probably due to post-traumatic hemorrhage. The left lower limb was shortened and extra-rotated. The corpse showed multiple, large, and deep injuries to the scrotal region, the left groin, and the left thigh and leg, with typical morphological and dimensional characteristics of slash injuries. Indeed, the edges of the wounds were well defined and bruised, and underlying muscles and organs were widely exposed or sharply cut (Figure 1). The following relevant wounds were found: an extensive skin lesion of $22 \times 10$ cm in the inguinal/scrotal region; a lesion of $7 \times 5$ cm on the medial surface of the thigh from which emerged the distal stump of the fractured femur; a lesion of $18 \times 7$ cm in the posterior face of the thigh and left leg. Finally, multiple irregular excoriations, abrasions, and contusions were evident on the upper and lower extremities, with greater concentration for the left hemisome.

Figure 1. Multiple, large, and deep injuries of the penis, the scrotal region, the left groin, the left thigh, and the left leg with an exposed femoral fracture.
3.2. Autopsy Findings

A complete autopsy was performed using the Virchow technique (one by one), comprising dissection of all three body cavities. Following dissection, sampling of relevant organs was carried out for the subsequent histopathological assessment.

No fractures or deformations were found in the skull. The brain was edematous without relevant focal or diffuse hemorrhages and weighed 1230 g.

The dissection of the thorax revealed multiple rib fractures of the left hemithorax. Pneumothorax was ruled out. The left pleural cavity contained 45 mL of blood, deriving from the laceration of the intercostal vessels near to the rib fractures. The right pleural cavity was normal. The lungs were edematous and congested, with some areas of parenchymal contusion and wide emphysema (Figure 2). The left lung weighed 970 g, heavier than the right lung weighing 756 g, probably because of the contusions with pulmonary subpleural hemorrhage, more evident on the left side than on the right. Before removing the heart, the main pulmonary artery was opened “in situ” by making an incision with a pointed scissor and cutting towards the infundibulum and the bifurcation. At the opening, the lumen was free from clots or other solid material. The heart did not show any relevant lesion, was normal in shape and weight, and presented patent coronary arteries.

The dissection of the abdominal cavity revealed a retroperitoneal hematoma surrounding the left kidney and confined within the renal capsule. The left kidney weighed 110 g and showed multiple parenchymal lacerations. The right kidney weighed 100 g and did not show any pathological signs.

The dissection of the left inferior limb showed a complete, comminuted, displaced and exposed fracture of the femur at its diaphyseal tract without the involvement of the main veins and arteries.

The autopsy was completed for all other anatomical districts, but none of these showed any further pathological findings.

3.3. Histopathological Findings

The organ samples were fixed in alcohol and formol and, after washing and dehydration, were embedded in paraffin. Thin sections (2.5 µm) were obtained by sled microtome and underwent staining with hematoxylin and eosin.

Microscopy examination showed unexpected abnormalities in both lungs. Sections of tissue from the upper lung fields revealed numerous endovascular drop-shaped fat globules with surrounding hematopoietic marrow that were mixed with small bone particles in every field of view (Figures 3 and 4).
Figure 3. Histological images of pulmonary bone marrow embolism: (A) Fat globules with surrounding hematopoietic marrow (arrows) in the precapillary arterioles, without any signs of perivascular reaction; (B) Fat globules with surrounding hematopoietic marrow (arrows) in alveolar capillaries, without any signs of perivascular reaction (Hematoxylin and eosin staining. (A): original magnifications ×20. (B): original magnifications ×10; inset, original magnifications ×40).

Figure 4. Histological images of pulmonary bone embolism. Dark/purple-staining of particles of bone (arrows) in small lung arteries (Hematoxylin and eosin staining. Original magnifications ×10; inset, original magnifications ×40).

Bone fragments ranged in diameter from 3 μm to 15 μm and were stained black/purple. Most of the particles were in the precapillary arterioles and alveolar capillaries, without signs of perivascular reaction. The absence of leukocytes, interstitial and intra-alveolar edema, and hemorrhage around the embolized vessels suggested that the survival time from the trauma was not long enough to allow changes in lung microcirculation and lung tissue. The remaining lung parenchyma revealed either edema and congestion or atelectasis and emphysema, with signs of modest lymphocytic inflammatory infiltration in interstitial and subpleural spaces.

Apart from the left kidney, which was affected by pericapsular and intraparenchymal hemorrhagic infiltration, the histological examination of the other organs did not show any other pathological signs.

4. Discussion
4.1. Fat Embolism

Fat embolism was first observed and described by Zenker in 1861 [8]. The term fat embolism (FE) denotes the presence of fat particles within the blood; this can cause occlusion of small vessels, which occurs mainly in the lung microcirculation. FE is generally a self-limiting pulmonary complication of fracture of the long bones or major trauma. In these cases, fat emboli originate from bone marrow or adipose tissue and enter the
circulation via ruptured vascular sinusoids or venules [9]. Instead, the term fat embolism syndrome (FES) was first clinically diagnosed by von Bergmann in 1873 [10] as a clinical entity that is characterized by the systemic manifestation of fat emboli within the blood, with dysfunction of several organs, including the lungs and the brain [11].

Postmortem studies following major trauma have shown a relatively high incidence of FE (52–96%), while its clinical manifestation in the form of FES appears to be a much rarer event, with an incidence of 19% in patients presenting with major trauma [12]. Thus, embolization of fat is almost universal in patients who sustain major trauma and for those who undergo endomedullary nailing of fractures, or placement of knee or hip prosthesis [13]. It is most commonly associated with fractures of long bones and the pelvis (i.e., marrow-containing bones) and more frequently in closed rather than open fractures, where the incidence increases with the number of fractures involved [14,15]. Thus, patients with a single long-bone fracture have a 1% to 3% chance of developing FES, although it has been reported in up to 33% of patients with bilateral femoral fractures [16,17].

FE is also associated with burns, barotraumas, soft-tissue injury, osteomyelitis, diabetes, surgical operations on fatty tissue, sepsis, steroid therapy, acute pancreatitis, viral hepatitis, and alcoholic fatty liver [18,19]. Many other conditions have been reported to involve FE, such as transplanted lungs from a trauma donor [20], sickle-cell disease [21], and blast injuries [22].

However, the pathogenesis of FE remains poorly understood. In the 1920s, two theories were developed: the mechanical theory of Gauss and the biochemical theory of Lehman and Moore. Gauss [23] held the opinion that injury to adipose tissue, rupture of veins within a zone of injury, and “some mechanism that will cause the passage of free fat into the open ends of blood vessels” would cause FE. Lehman and Moore [24] proposed that plasma mediators would mobilize fat from body stores, which would lead to droplet formation. Wenda et al. [25] observed that, in patients with fractured femurs, there was an elevation of their intramedullary pressure, which ranges from 140 mmHg to 830 mmHg. Other studies have found evidence of a shunt mechanism between the arterial and venous systems in bone and have suggested that a rise in intramedullary pressure might affect the precarious balance between the arterial and venous systems and result in embolization of fat particles [26]. More recently, Mudd et al. [27] suggested that soft-tissue injury, rather than fractures, is the primary cause of FE.

4.2. Bone Marrow Embolism

Bone marrow embolism represents a particular form of FE. It has been reported in 6% of patients with trauma [28] and 7% of 620 unselected autopsies [29]. Moreover, bone fragments have been observed in approximately 12% of patients with bone marrow embolism [1]. However, in general, bone fragment embolism is a rare event [7]. Only one case was observed in a series of 9000 autopsies [4], while 12 cases have been reported after bone-marrow transplantation [3], and one case after vertebral body-marrow infusion for tolerance induction [30].

4.3. Casuistry

A silent embolism of lamellar bone chips was documented following implantation of hip endoprostheses in two patients, who died 3 months and 2 years after their operations, respectively [2]. Bras and Veraart [2] suggested that during total hip replacement, the milling of the acetabulum with special reamers can cause a rise in temperature, which will result in vasodilatation and blood vessel damage. The pressure between the reamer and the acetabular surface also exceeds the intravenous pressure, which will thus allow some of the bone fragments produced during the acetabulum milling to pass into the venous vessels, and then get to the right side of the heart and into the pulmonary circulation.

During posterior spinal surgery, pulmonary embolism with bone fragments can occur because of the use of many devices, such as the Husting’s frame, which is designed to obtain an abdomen free of restrictions and to decrease lordosis. These devices increase
the gravitational gradient between the right atrium and the vertebrae by reducing both caval pressure and perivertebral venous pressure. Consequently, the patients are at risk of venous embolism [31].

Bone embolism has also been reported as a consequence of osteomyelitis. Inflammation is not necessarily a prerequisite for bone embolism, although it might trigger it by breaking up the bone structure [5].

4.4. Case Study and Interpretation

The present study demonstrates that trauma can induce combined pulmonary fat, bone marrow, and bone embolism, that this particle’s mobilization is rapid, and that it is a vital reaction to trauma. In this case, according to the main theories from the 1920s, the force of the trauma would have pushed bone marrow droplets from the edges of the lesions into the injured venous channels, together with bone fragments. These particles are then likely to have been transported by the circulation during the agonal period of survival, toward the lungs.

Pulmonary fat/bone marrow and bone embolism can be an immediate cause of death or at least a contributory factor. However, only severe pulmonary combined embolism is considered to cause death without concomitant factors. In a polytrauma patient, minor pulmonary fat and bone embolism can act together with other injuries (e.g., blood loss, fractures, possible intracranial injury) and thus contribute to death. As bone chips do not usually occlude the blood vessel lumen, they do not cause severe disorders in the pulmonary blood circulation. Thus, fat and bone embolism alone are not normally followed by death. Nevertheless, the relatively high number of bone fragments found in the pulmonary vessels in the present case suggests that these pathological findings were at least a contributing factor to the death mechanism. Moreover, combined fat/bone marrow and bone embolism should be assumed as a sign of an extensive degree of injured bone fragmentation and the presence for a significant time of valid hemodynamics. The survival time in the present case was, therefore, long enough to allow, on the one hand, the endovascular transport of bone fragments and bone marrow particles and, on the other hand, the formation of pulmonary edema. Considering all the elements coming from both the macroscopic examination and the histopathological assessment, the cause of death was ultimately identified as a traumatic shock with a high hemorrhagic component combined with pulmonary bone marrow and bone embolism.

5. Conclusions

Combined bone and bone marrow embolism is a very rare occurrence in the case of major trauma-related deaths and could be considered at least a contributing factor together with the hemorrhagic component. Embolic pulmonary involvement should always be sought as it provides relevant information about the extent of bone fragmentation and the period of survival, even in cases where death is not directly related to the embolism. Therefore, in such cases, an accurate histopathological analysis should be mandatory in order to identify the correct cause of death and to evaluate a possible medical liability.

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