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# Essentials of cerebral fat embolism syndrome. A hidden enemy in trauma

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## ABSTRACT

Fat embolism syndrome typically appears after an asymptomatic period of 24 to 72 hours and is typically manifested by the clinical triad of respiratory failure, neurological manifestations and petechiae, together with analytical alterations such as anaemia and thrombopenia. Respiratory distress is the most common symptom. Cerebral fat embolism is an incomplete form of fat embolism, which does not meet all the diagnostic criteria; in fact, it may appear without the presence of respiratory failure; Therefore, its early diagnosis is a challenge in the trauma patient.

## Keywords

cerebral fat embolism,  
trauma,  
diagnosis,  
narrative review



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## INTRODUCTION

Fat embolism syndrome occurs when fat enters the circulation and may embolize and may or may not present clinical manifestations [1,2]. It is a potentially serious complication of fractures, with a reported incidence of 0.5 to 3.5% in isolated fractures of the long bones and 5 to 10% in patients with polytrauma. [3,4] The mortality rate is 5 to 15% [5]. Due to its association with polytrauma, it is much more frequent in the third and fourth decade of life [5,6]. It has also been associated, but to a lesser extent, with non-traumatic conditions such as orthopedic procedures, bone marrow transplants, extensive burns, closed-chest cardiac massage, acute pancreatitis, liposuction, parenteral lipid infusion, fatty liver, diabetes mellitus, osteomyelitis, rupture of a Tarlov's cyst, and other non-traumatic conditions [5,7,8], or even more rarely, a case was reported after chest surgery in a patient with empyema [9]. This complication can target the vascularization of the brain and generate severe ischemic accidents. Considering the potential of this pathological condition to negatively impact the integrity of the central nervous system, and that it is little known by medical students and primary care physicians, the aim of this review is to present basic concepts about its pathophysiological mechanism, important aspects for its early detection and approach.

## PATHOPHYSIOLOGICAL MECHANISMS OF CEREBRAL FAT EMBOLISM

Cerebral fat embolism is caused by lipid droplets that travel through the bloodstream, subsequently blocking small vessels, especially at bifurcations [1,3,10]. This occurs in patients with long bone fractures, so it implies that there is bone trauma with exposure of the medullary fat, and that fat emboli subsequently enter the venous system [3,6,11,12,13]. They all travel into the pulmonary circulation and in the presence of right-to-left shunts pass into the systemic circulation [14]. There are several hypotheses that attempt to explain the pathophysiological mechanism of this disease.

### Mechanical theory

Approximately 100 years ago, specifically in 1924, an author by the name of Gauss posited that bone marrow adipose cells could access venous sinusoids due to increased intramedullary pressure following trauma [1]. These adipose cells have

proinflammatory and prothrombotic attributes [15]. As the venous system travels back toward the heart, they precipitate platelet adhesion and increased fibrin production, forming an embolus and increasing the risk of embolizing the pulmonary arterial circulation when the vessels form capillaries [16]. Capillary obstruction triggers interstitial bleeding, edema, alveolar collapse and reactive vasoconstriction. Massive fat emboli can also cause macrovascular obstruction and shock. Even in special cases such as in the permanence of a patent foramen ovale, fat cells can enter the arterial circulation [17].

### Biochemical theory

Another hypothesis put forward is biochemical. This supports the fact that the clinical manifestations of fat embolism are caused by a proinflammatory state [1]. Bone marrow adipose cells are broken down by tissue lipases to form glycerol and toxic free fatty acids, which cause injury to pneumocytes and pulmonary endothelium, triggering a cascade of proinflammatory cytokines that lead to respiratory failure [18-20]. This theory helps to explain the cases of non-traumatic fat embolism. Experiments in animal models support this hypothesis [1].

However, these results are derived from general concepts. The toxic properties of free fatty acids were demonstrated around 1950 [1]. Since then, fatty acid infusions have been used in animal models to induce embolism-like changes in the circulation and lung. An example of this is the use of triolein to induce fat embolism syndrome and investigate a "second hit" phenomenon in rat models. Lung damage after injection of another toxin has been found to be worse in rats that had a history of this clinically resolved triolein-induced syndrome than in rats that were exposed to the toxin alone [1].

However, it would be interesting to continue with this type of research to determine the precise degree of severity of pulmonary involvement and, specifically, of brain damage.

## CLINICAL PRESENTATION

As previously mentioned, clinical manifestations are usually delayed from 24 to 72 h, and some authors speak of an onset from 12 to 72 hours [21,22]. However, only one case of hyperacute CGD has been reported, whose clinical signs appeared 2 hours after an automobile accident, where the patient reported

fractures of the right femur, tibia and fibula, in addition to non-specific symptoms during the first hours, the subsequent development of the symptoms was of bad prognosis for the patient, with almost no improvement after a few days [23,24].

Typical symptoms of fat embolism syndrome include respiratory failure, cerebral dysfunction and petechial rash. Respiratory manifestations appear in almost 100% of patients, neurological symptoms are usually transient appearing in 80% and petechial exanthema in 20 to 50% of cases and is the most specific, but the most delayed sign [25,26].

Clinically, the syndrome can be variable from headache to diffuse encephalopathy, lethargy, convulsion, coma, pyramidal symptoms, aphasia, visual and auditory hallucinations, sexual hallucinations, aggressive behavior and pupillary paresis [2,27]. Other manifestations described are renal failure, myocardial depression, jaundice and fever. Patients with pure cerebral fat embolism have no respiratory symptoms and a history of cranioencephalic trauma [2,28].

#### DIAGNOSTIC APPROACH

The clinical evolution of the patient must be considered, i.e., that he/she presents respiratory and neurological alterations and, in some cases, cutaneous petechiae after a fracture of long bones, orthopedic surgeries, or due to non-traumatic causes such as sickle cell anemia, which produces infarcts in the bone tissue. On the other hand, the use of imaging is one of the best methods to confirm the diagnosis, and thus exclude other clinical impressions such as diffuse axonal injury [1,2,29,30].

Magnetic resonance imaging (MRI) is considered the method of choice for diagnosis, because it is able to capture the lesions that occur in the brain. MRI can commonly show a characteristic pattern of microemboli in the gray and white matter or cytotoxic edema, evidencing "lesions" by dots in the gray matter that form an image similar to a star field in T2 and DWI [1,2]. This pattern is true in most cases, varying in time the number of lesions that may appear, i.e., an MRI performed during the first hours of neurological dysfunction may or may not show lesions in white matter, but a star field pattern may be present. Another pattern found in DWI and T2 sequences, and whose significance is associated with a worse prognosis, corresponds to confluent bilateral periventricular and subcortical cytotoxic

edema. Finally, T2/FLAIR sequences may show areas of hyperintensity probably associated with vasogenic edema [1,2,31].

#### THERAPEUTIC APPROACH

Treatment is essentially coadjuvant; when one of these cases occurs, it is common to use heparin, dextran, aspirin, albumin and steroids, which are ineffective in treating the disease. Currently, case reports have opted to include statins in their list, due to their anti-inflammatory mechanism rather than their cholesterol-lowering action; where the use of high doses of the drug had a result considered satisfactory, improving neurological functions. However, there is a lack of studies to support it [1,2].

In the case of patients with cerebral embolism, care of neurological manifestations and complications focuses on frequent neurological observation. These patients may develop cerebral edema which, although manageable, increases the risk of morbidity, mortality and disability [29-31]. Continuous monitoring of intracranial pressure should be performed in these cases. Although clinical diagnosis is still considered the preferred diagnostic method for this syndrome, studies have shown that MRI is useful, in cases where there is no head trauma, to assess the severity of cerebral fat embolism and to predict the functional prognosis. In general, sedation and neuromuscular blockade for trauma patients should be titrated so as to keep the patient comfortable, without affecting their serial neurological examinations and, in addition, allowing them to tolerate mechanical ventilation [1,2,29,31].

#### PROGNOSIS

Usually, almost 80% of patients experience spontaneous resolution of symptoms, however, 3% to 8% die. It has been described that the prognosis could be associated to the promptness with which the symptoms appear, suggesting that when presenting in less than 12 hours, the morbimortality is higher [1-6].

#### CONCLUSIONS

Cerebral fat embolism or fat embolism syndrome is a disorder characterized by the appearance of respiratory, neurological and cutaneous dysfunction symptoms (petechiae) frequently found in people who have suffered long bone and pelvic fractures. This pathology requires an adequate diagnosis and

treatment, in order to reduce the morbimortality associated with it, even though there is no treatment oriented to the cause of it. For the time being, few changes have been described in the literature for this disorder, however, small trials are beginning to make inroads in terms of therapies that may be considered effective in the future.

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