# Fat embolism syndrome with prevalence of neurological symptoms

Diego A. Rangel Rivera, Stiven Fuentes Abreu,
Julian Guerrero Caballero, Juan C. Rodríguez Durán

*Department of Internal Medicine, Hospital Regional de San Gil, Santander, Colombia*

*Received on February 18th, 2016; accepted after evaluation on February 23rd, 2016* • DIEGO A. RANGEL RIVERA, MD • dar_2333@hotmail.com

## Abstract

Fat embolism syndrome (FES) makes reference to a set of symptoms and signs secondary to the release of fat into the bloodstream. It occurs in approximately 1% of patients with femur fracture. The FES classical triad includes respiratory distress with hypoxemia, neurological changes and petechial rush. In spite of the isolated descriptions that document improvement in symptoms after corticosteroids administration, there is no clear evidence of these drugs usefulness—therefore, current management is based on cardiovascular and respiratory support. We present a young adult patient with FES and minimal respiratory manifestations following a traumatic fracture in his femur.

**Key words:** Fat embolism syndrome; femur fracture; acute cognitive condition
**Level of evidence:** IV

**Síndrome de embolismo graso con predominio de síntomas neurológicos**

## Resumen

El síndrome de embolismo graso hace referencia a un conjunto de signos y síntomas secundarios a la liberación de lípidos dentro de la circulación sanguínea. Ocurre en alrededor del 1% de los pacientes con fracturas de fémur. La tríada clásica de este síndrome incluye dificultad respiratoria con hipoxemia, alteración neurológica y exantema petequial. Pese a las descripciones aisladas que documentan la mejoría de los síntomas después de administrar corticoides, no existe clara evidencia de la utilidad de estos fármacos, por lo que el manejo actual consiste en soporte cardiovascular y respiratorio. Se presenta un paciente adulto joven con síndrome de embolismo graso y manifestaciones respiratorias mínimas tras una fractura traumática de fémur.

**Palabras clave:** Síndrome de embolismo graso; fractura de fémur; trastorno cognitivo agudo.
**Nivel de Evidencia:** IV

## Introduction

In 1873, Bergmann described in a series of patients with fracture of long bones a number of symptoms (dyspnea, mental confusion and petechiae) he grouped in a specific syndrome that he called fat embolism syndrome (FES).[1] Ever since there have been publications with case reports and retrospective and prospective studies that document important variations in the presentation of this syndrome, even without respiratory manifestations.[2-5]

Conflict of interests: The authors have reported none.

In 1970, Gurd and Wilson published a series of medical criteria which are necessary to diagnose the FES.[6] Apart from the classical triad described by Bergman, they added other symptoms and signs less frequent: focal neurological deficit, fever, retinopathy, hemoptisis, jaundice and low platelet count.[6] These criteria are the medical pillar to sustain this diagnosis and, although there are other authors' criteria, the Gurd and Wilson classification is the most accepted one so far.[5]

According to epidemiological studies, the FES frequency is 0.1-3.5% in patients that suffer isolated or multiple fractures.[7,8] However, this number increases if specific risk factors are considered, such as multiple fracture, diabetes mellitus and delayed surgery, and rates can be as high as 10%. With respect to prognosis in patients with this syndrome, mortality rates are considered to oscillate between 5 and 10%.[9]

We present the case of a young patient with FES with no medical signs of respiratory distress following a closed fracture in his right femur.

## Case

An eighteen years old male patient with no relevant medical background is taken to the ED following an accident in which his motorcycle crashes a sedan car.

Upon arrival, his vital signs are within normal ranges, with no signs of neurological involvement; cardio-respiratory and abdominal evaluation is normal.

As positive findings we detect multiple abrasive injuries and bruises in upper and lower limbs, misalignment in the middle third of his right thigh associated with severe pain, edema and right lower limb functional impairment. Femur X-ray confirms displaced diaphyseal fracture in his right femoral middle third, with transverse fracture line classified as 32-A3 by the AO Foundation (Figure 1).

We splint the patient with extended dorsal cast for immobilization and prescribe analgesic management, hydration and open treatment. Due to the administrative procedures necessary to get the osteosynthesis material, we carry out surgery 22 hours after the accident. Under spinal anesthesia we perform open reduction and osteosynthesis with locking nail in the right femur, with a proximally locked 11x420 mm intramedullary nail and no complications.

Five hours after the surgery, the patient shows intermittent periods of altered level of consciousness, reported as drowsiness, which are progressively accompanied by mutism followed by aphasia, spatial and temporal disorientation, emotional lability and motor agitation.

Neurological complications stemming from cranioencephalic trauma are considered for ruling out; however, simple cranial CT scan is normal (Figure 2). Lab tests results show anemia (hemoglobin= 9.2 mg/dl) and low platelet count (127,000/mm·). Ionogram, kidney function and coagulation tests are normal. When evaluated again, the patient shows bilateral thorax, abdomen and armpit petechial injuries (Figure 3). The respiratory pattern and oxygen saturation levels (94% with 21% FiO2) are not altered. Based on these findings, the patient is considered to suffer FES, given full anticoagulation, i.v. corticosteroids (methylprednisolone 10 mg, unique dose) and taken to the ICU.

Upon arrival at the ICU, the patient's neurological changes remain, but he shows neither dyspnea nor altered vital signs. Arterial gases values are: pH= 7.39; pCO2= 38mmHg; pO2=59.5 mmHg; bicarbonate= 27.1 mEq/l, with 3 l/m supplementary oxygen by nasal cannula (approximate 32% FiO2). Taking into account the patient's context and the arterial gases results, it is decided to administer noninvasive ventilation.

CT scan with protocol for pulmonary thromboembolism is prescribed, and a mild area of low blood perfusion in pulmonary bases with no other relevant findings is documented. On second ICU day, the patient shows normal blood oxygen levels with stable neurological status and no agitation. On the same day the patient starts assisted oral feeding with adequate tolerance. On ICU day five, the patient is alert, oriented, with no respiratory deficit, hemodynamically stable, and with no requirement of vasopressor drugs; noninvasive ventilation is definitely taken off after gradual withdrawal. He is discharged from the ICU.

The patient is taken to the General Ward, where he receives the same management as he did at the ICU, including anticoagulation and i.v. fluids. He stays two more days in hospital and is discharged in good general conditions, and satisfactorily recovered from the neurological point of view. As a sequel, the patient reports bilateral scotoma at follow-up consultation three months after the accident.

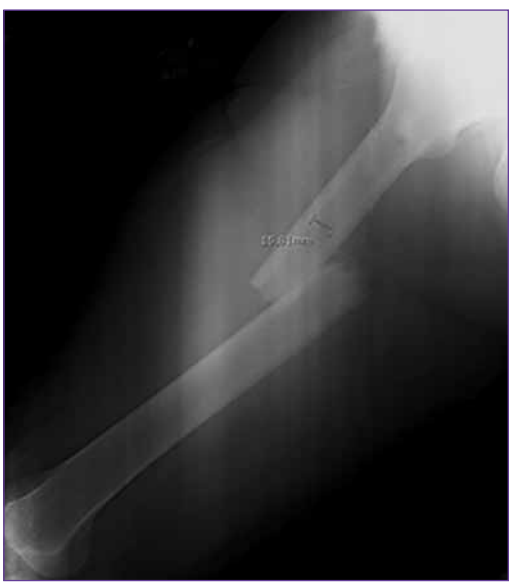

**Figure 1.** Fracture in the middle third of the right femoral diaphysis.

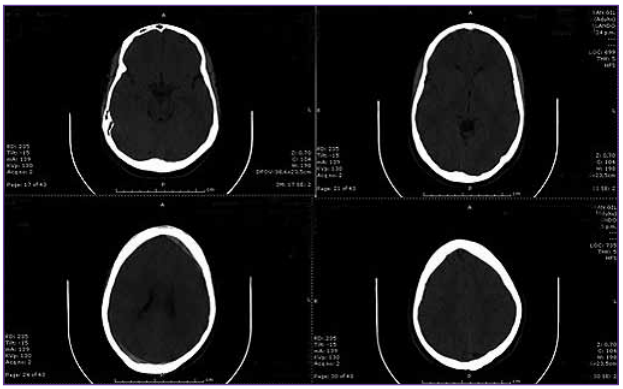

**Figure 2.** Simple brain CT scan with no evidence of hemorrhage, middle line deviation or bone injuries.

**Figure 3.** Petechial injuries widespread in the thorax-abdomen area.

## Discussion

In medical literature, the term "fat embolism" is used for two conditions alike—although related to each other, these two conditions represent different concepts whose meaning is important to differentiate. In 1861, Zenker verified that in capillary vases in corpse lung tissue from persons who had suffered accidents with thorax-abdominal impact, in general there were fatty micelles which were called fat embolism.[10] Further findings showed that these phenomena also occurred in peripheral bloodstream.

Fat embolism as an isolated phenomenon does not necessarily produces symptoms. This characteristic makes it different from the FES, which is considered a physipathological consequence of fat embolism,[11] with established diagnosis criteria (Table)[6] and associated with specific risk factors, such as long bone fracture, multiple fracture, closed fracture, conservative treatment, and intramedullary reaming.[12]

The FES physiopathology is not a hundred percent understood. However, there have theories trying to explain the different phenomena associated with this syndrome. The two more accepted theories are the biochemical one and the mechanical one.[9,13] However, these hypothesis do not exclude one another, and, on the contrary, they should be considered as complementary to try to explain this complex syndrome. In fact, some authors refer to them as different phases of the same event.[13]

The mechanical theory sustains that the fatty tissue enters systemic bloodstream through the venous drainage system when pressure in this vascular bed is outdone by bone marrow pressure.[13] Upon entering bloodstream, the little fatty drops get the different capillary vessels where their pro-coagulant properties or the accumulation of several fragments of considerable size produce mechanic obstruction to blood flow.[13] Likewise, this theory explains the presence of petechia in the thoracic and conjunctival areas caused by red blood cells extravasations in small capillary vessels, favored by endothelium, platelet and coagulation factors injury caused by free fatty acids.[10]

The authors that set out the biochemical theory sustain that the fatty tissue in systemic bloodstream coming from the bone marrow is metabolized by the lipase enzyme and originates free fatty acids which, upon adding to the fat tissue at capillary vessel level, can trigger endothelial dysfunction.[9] Therefore, there are different degrees of dysfunction in the affected organ. In the lungs, for instance, vascular involvement leads to inflammatory factors release, with accompanying edema and alveolar

**Table.** Diagnostic criteria in the fat embolism syndrome

| Diagnostic clinic criteria | |
|---|---|
| **Major criteria** | **Minor criteria** |
| Respiratory failure (PaO2 <60 mmHg, FiO2 <0.4)<br>Acute manifestations in the central nervous system<br>Armpit or subconjunctival petechia | Tachycardia >120 b/min<br>Fever >38°C<br>Unexplained anemia<br>Low platelet count<br>Increase in ESR<br>Characteristic retina changes (fat or petechia)<br>*Fat macroglobulinemia*<br>Fat particles in sputum<br>Fat particles in urine |

*For the FES diagnosis it is necessary to detect the presence of either two major criteria, or one major criterion together with, at least, four minor criteria.

hemorrhage that can trigger diverse degrees of respiratory distress.[9] Moreover, there are reports on heart contractility changes caused by free fatty acids.[10] The importance of this theory lies on the fact that it explains the delay in medical findings in some patients (24-72 hours), time in which the free fatty acids involved are produced.

The case that we present has a particular trait— the minimal respiratory manifestations only shown in arterial gases and with no respiratory distress. This type of FES has already been described in several cases, what shows that, although respiratory manifestations represent the commonest early findings in this syndrome, in some patients what may prevail is neurological symptoms, as in the case that we report.[4,5,14-16]

It is sustained that the neurological findings in the patients with FES ask for embolism to spread throughout bloodstream up to the central nervous system. The presence of a permeable oval foramen, intra-pulmonary arterial-venous shunts, re-opening of a closed oval foramen (for acute increase in pulmonary blood pressure) or micro-embolism (≤7 μ-diameter fatty fragments) that can go through lung bloodstream represent different pathways that embolism particles can take in order to get the target organ—in this case, the brain.[12,17] However, there is one study that affirms that a permeable oval foramen does not increase the incidence of systemic (kidney) embolism as compared to pulmonary embolism; therefore, extra-pulmonary manifestations may be preferably linked to intra-pulmonary shunt, anastomosis or micro-embolism.[18]

There is no evidence of an effective treatment to counteract the effects of fat embolism. Once the diagnosis is made, it is essential to stabilize the patient from the cardiovascular, respiratory, hematological and neurological points of view as a pillar condition for the management of the FES. Anticoagulants have been described as treatment for the FES, but there is no sound evidence about their use since they do not improve mortality rates.[9,19] Moreover, they should be used with precaution given the patient's traumatic context, and the hematologic changes that can accompany this syndrome.

There is no availability of convincing published evidence concerning the use of corticosteroids in patients with confirmed diagnosis of FES.[9] However, there are isolated studies that suggest favorable results, such as improvement of respiratory symptoms and hypoxemia following the administration of high doses of corticosteroids. In one case report in which the patient was administered an initial dose of 1500 mg methylprednisolone, there was improvement in hypoxemia and in lung X-ray findings 12 hours after corticosteroids administration. Afterwards, the patient was given a new dose of 1000 mg with evident medical improvement.[20] However, doses, frequency and duration of treatment have not been established. Likewise, it has not been possible to show improvement in mortality rates.[19]

In this context, the FES approach should be oriented to prevent its onset, something diagnosis is not necessary for, because this is all about hygienic measures in patients with risks factors for the development of this syndrome. Among the preventive measures that literature describes there is early fracture immobilization, which decreases remarkably the onset of the FES.[21] Moreover, there are reports on risk decrease when the patient is given open surgical correction instead of conservative treatment in fractures which could trigger this syndrome.

An intra-operative recommendation to control FES risk in orthopedic procedures that has got favorable results is limitation to the increase of intra-bone pressure. This measure decreases the access of bone marrow fat to the bloodstream and, this way, it theoretically minimizes the risk of developing this syndrome.[22] There is a clinical trial in which during the procedure the patient was given a "ventilation foramen", so as to drain the bone marrow cavity in the hip replacement surgery the patient was undergoing and, this way, to control increase in intra-bone pressure. The study concluded that the number of fat embolism episodes decreased significantly in the group that was given such procedure as compared to the control group (20% and 85% respectively).[23]

In a meta-analysis of seven small clinical trials with 389 patients, prophylactic administration of corticosteroids to patients with long bones fracture decreased 78% the risk of FES and 61% that of low blood oxygen levels.[24] On the other hand, there were no differences in patients' mortality or infection rates. However, some authors put this study results into question given its uneven diagnostic criteria, differences in the trauma severity among the diverse groups being compared, and the lack of long-term results.[25]

## Conclusion

This case report shows an infrequent presentation of the FES, in which there are neurological impairment and petechia and in which, although hypoxemia was documented in medical records, it did not show as respiratory symptoms. As it has already been mentioned, this type of manifestations in patients with FES asks for the access of embolic particles to the systemic bloostream. In our patient, it was not possible to prove the presence of a permeable oval foramen; therefore, medical manifestations could be associated with microembolism or intra-pulmonary shunts. It is necessary to continue this line of research so as to define the specific management of this condition, because current evidence is limited.

## Bibliography


1. Talbot M, Schemitsch EH. Fat embolism syndrome: history, definition, epidemiology. *Injury* 2006;37(Suppl 4):S3-7.
2. Jacobson DM, Terrence CF, Reinmuth OM. The neurologic manifestations of fat embolism. *Neurology* 1986;36(6):847-51.
3. Kotan D, Ayas ZO, Sayan S, Inanmaz ME, Acar BA.Cerebral fat embolism diagnosed by cognitive disorder. *Eurasian J Med* 2014;46(2):135-7.
4. Kamano M, Honda Y, Kitaguchi M, Kazuki K. Cerebral fat embolism after a nondisplaced tibial fracture: case report. *Clin Orthop Relat Res* 2001;(389):206-9.
5. García-Estévez DA, Castro-Menéndez M, Canal-Perez MG. [Fat embolism syndrome in the brain: a clinical case triggered after fracture of the humerus and without any associated respiratory distress]. *Rev Neurol* 2015;60(1):45-6.
6. Gurd AR. Fat embolism: an aid to diagnosis. *J Bone Joint Surg Br* 1970;52(4):732-7.
7. Stein PD, Yaekoub AY, Matta F, Kleerekoper M. Fat embolism syndrome. *Am J Med Sci* 2008;336(6):472-7.
8. Campo-López C, Flors-Villaverde P, Calabuig-Alborch JR. Síndrome de embolia grasa tras fractura ósea. *Rev Clin Esp* 2012; 212:482-7.
9. Kosova E, Bergmark B, Piazza G. Fat embolism syndrome. *Circulation* 2015;131(3):317-20.
10. Saigal R, Mittal M, Kansal A, Singh Y, Kolar PR, Jain S. Fat embolism syndrome. *J Assoc Physicians India* 2008;56:245-9.
11. Mellor A, Soni N. Fat embolism. *Anaesthesia* 2001;56(2):145-54.
12. George J, George R, Dixit R, Gupta RC, Gupta N. Fat embolism syndrome. *Lung India* 2013;30(1):47-53.
13. Filomeno L, Carelli C, Silva C, Filho T, Amatuzzi M. Fat embolism: a review for current orthopaedic practice. *Acta Ortopedica Brasileira* 2005;13:196-208.
14. Lee J. Gradient-echo MRI in defining the severity of cerebral fat embolism. *J Clin Neurol* 2008;4(4):164-6.
15. Finlay ME, Benson MD. Case report: magnetic resonance imaging in cerebral fat embolism. *Clin Radiol* 1996;51(6):445-6.
16. Bardana D, Rudan J, Cervenko F, Smith R. Fat embolism syndrome in a patient demonstrating only neurologic symptoms. *Can J Surg* 1998;41(5):398-402.
17. Dhar D. Fat embolism syndrome. *J Coll Physicians Surg Pak* 2012;22(12):800-2.
18. Nikolic S, Zivkovic V, Babic D, Djonic D, Djuric M. Systemic fat embolism and the patent foramen ovale--a prospective autopsy study. *Injury* 2012;43(5):608-12.
19. Habashi NM, Andrews PL, Scalea TM. Therapeutic aspects of fat embolism syndrome. *Injury* 2006;37(Suppl 4):S68-73.
20. Kubota T, Ebina T, Tonosaki M, Ishihara H, Matsuki A. Rapid improvement of respiratory symptoms associated with fat embolism by high-dose methylprednisolone: a case report. *J Anesth* 2003;17(3):186-9.
21. Riska EB, Myllynen P. Fat embolism in patients with multiple injuries. *J Trauma* 1982;22(11):891-4.
22. Pitto RP, Hamer H, Fabiani R, Radespiel-Troeger M, Koessler M. Prophylaxis against fat and bone-marrow embolism during total hip arthroplasty reduces the incidence of postoperative deep-vein thrombosis: a controlled, randomized clinical trial. *J Bone Joint Surg Am* 2002;84(1):39-48.
23. Pitto RP, Schramm M, Hohmann D, Kossler M. Relevance of the drainage along the linea aspera for the reduction of fat embolism during cemented total hip arthroplasty. A prospective, randomized clinical trial. *Arch Orthop Trauma Surg* 1999; 119(3-4):146-50.
24. Bederman SS, Bhandari M, McKee MD, Schemitsch EH. Do corticosteroids reduce the risk of fat embolism syndrome in patients with long-bone fractures? A meta-analysis. *Can J Surg* 2009;52(5):386-93.
25. Akoh CC, Schick C, Otero J, Karam M. Fat embolism syndrome after femur fracture fixation: a case report. *Iowa Orthop J* 2014;34:55-62.