OLGU SUNUMU CASE REPORT

DOI: 10.5336/anesthe.2018-63902

Fat Embolism Syndrome with Cerebral Involvement in a Multitrauma Patient

Bir Multitravma Hastasında Serebral Tutulum Gösteren Yağ Embolisi Sendromu

Ömür İLBAN[a],
Mehmet Ali BAŞ[a],
Jale Bengi ÇELİK[a],
Ateş DUMAN[a]

[a]Department of Anesthesiology and Reanimation,
Selcuk University Faculty of Medicine, Konya, TURKEY

Received: 22.11.2018
Received in revised form: 25.12.2018
Accepted: 08.01.2019
Available online: 28.01.2019

Correspondence:
Mehmet Ali BAŞ
Selcuk University Faculty of Medicine, Department of Anesthesiology and Reanimation, Konya, TURKEY/TÜRKİYE
dr.bas@yahoo.com

ABSTRACT Fat embolism syndrome (FES) is a multisystem disorder and often emerges following long bone fractures. In our report, a 34 year-old male patient diagnosed with FES is being presented. 2 days after admission to ICU, his consciousness and respiration deteriorated, and he needed to be intubated and connected to mechanical ventilator. Any signs consistent with pulmonary infiltrates were absent. Diffusion-weighted cranial magnetic resonance imaging (MRI) manifested millimetric multiple hyperintense lesions, compatible with brain involvement. He was operated for orthopedic fractures on 3rd and 6th days. Control MRI on 8th day demonstrated that the areas of diffusion restriction were regressed. On 9th day, he was extubated following improvement in arterial blood gas analyses and consciousness. It is seen in literature that two theories have been proposed, explaining FES etiology. According to first theory, the released fat droplets from site of the trauma pass through right heart, reach lungs' capillary bed and cause ventilation-perfusion mismatch. Second theory, however, offers a biochemical mechanism. Central nervous system involvement in FES has been rarely reported. We confer in our report that fat globules might transmigrate through pulmonary vasculature, enter systemic circulation and eventually cause neurologic symptoms.

Keywords: Embolism, fat; fractures, bone

ÖZET Yağ emboli sendromu (YES) multisistemik bir hastalıktır ve genellikle uzun kemiklerin kırıklarından sonra ortaya çıkmaktadır. Raporumuzda YES tanısı konulan 34 yaşında bir erkek hasta sunulmaktadır. Yoğun bakım yatışından 2 gün sonra bilinci ve solunumu kötüleşmiş ve entübe edilerek mekanik ventilatöre bağlanmak zorunda kalmıştır. Pulmoner infiltratlarla uyumlu olabilecek herhangi bir bulgu saptanmamıştır. Difüzyon ağırlıklı kranial manyetik rezonans görüntüleme (MRG), beyin tutulumu ile uyumlu milimetrik multipl hiperintens lezyonları ortaya koymuştur. 3. ve 6. günlerde ortopedik kırıkları için ameliyat edilmiştir. 8. günde kontrol MRG, difüzyon kısıtlaması olan alanlarda gerileme olduğunu göstermiştir. 9. günde arteriyel kan gazı analizleri ve bilinci iyileşmiş ve ekstübe edilmiştir. Literatürde FES etiyolojisini açıklayan iki teorinin öne sürüldüğü görülmektedir. Birinci teoriye göre, travma bölgesinden salınan yağ damlacıkları önce sağ kalbe gelmekte, daha sonra akciğerlerin kılcal yatağına ulaşmakta ve ventilasyon-perfüzyon uyumsuzluğuna neden olmaktadır. İkinci teori ise biyokimyasal bir mekanizma sunmaktadır. YES'da merkezi sinir sistemi tutulumu nadir olarak bildirilmiştir. Raporumuzda yağ globüllerinin pulmoner vasküler yataktan geçebileceğini, sistemik dolaşıma ulaşabileceğini ve sonuçta nörolojik semptomların ortaya çıkabileceğini sunmaktayız.

Anahtar Kelimeler: Emboli, yağ; kırıklar, kemik

Fat embolism syndrome (FES) is a serious multisystem disorder. It is a triad consisting of respiratory distress, neurocognitive deficit, and petechiae formation. Fever might also accompany the disease. FES often emerges following long bone fractures at 24th-72nd hours of the trauma. Other conditions which might cause the syndrome include bone marrow

transplantation, liposuction, cardiopulmonary resuscitation, burns, liver damage and sickle cell disease.[1,2] The delay time separates the disease from pulmonary contusion. Like acute respiratory distress syndrome (ARDS), FES is accompanied by noncardiogenic pulmonary edema, intrapulmonary shunting, and reduction in lung compliance. The high pulmonary artery pressure gives rise to the number of intrapulmonary shunts to increase. This facilitates passage of fat droplets into the systemic circulation with resultant symptoms. In autopsy studies, fat globules are seen in various organs, especially in the vessels of lungs and cerebrum.[3,4]

CASE REPORT

A male patient aged 34 years old was admitted to the emergency room following a car accident. His brain computed tomography (CT) was normal; however, thoracoabdominal CT revealed right lung contusion, right sided costal fractures, and grade II lacerations of liver and spleen. Bilateral femur and right patella fractures, and atelectasis in the right lung were also visible on plain x-ray. With stable vital signs and a Glasgow Coma Scale (GCS) score of 15, he was admitted to intensive care unit (ICU) and elective orthopedic surgery was planned. Laboratory results at admission were as follows: WBC: 10.2 K/uL, Hgb: 10.4 g/dL, Hct: 30.1%, Plt: 56.4 K/uL (became 108 on 4th day and later fallowed a normal course), PTsec: 11.6 sn, INR: 1.11, urea: 40.8 mg/dL, creatinine: 0.67 mg/dL, Na: 139 mEq/L, K: 4 mEq/L, Ca: 7.1 mg/dL, albumin: 2.8 g/dL, AST: 67 u/L, ALT: 94 u/L, CRP: 183 mg/L, fibrinogen: 544,9 mg/dL, D-dimer: 2350 ng/mL. On 2nd day, his general condition, consciousness and respiration deteriorated. The GCS score became 6 and he had respiratory failure so he was intubated and connected to mechanical ventilator. No signs consistent with pulmonary infiltrates or ARDS were present. Fever (38°C) and skin petechiae on his neck and trunk were visible. Diffusion-weighted cranial magnetic resonance imaging (MRI) revealed millimetric multiple hyperintense lesions in both cerebral hemispheres, centrum semiovale, corpus callosum, and

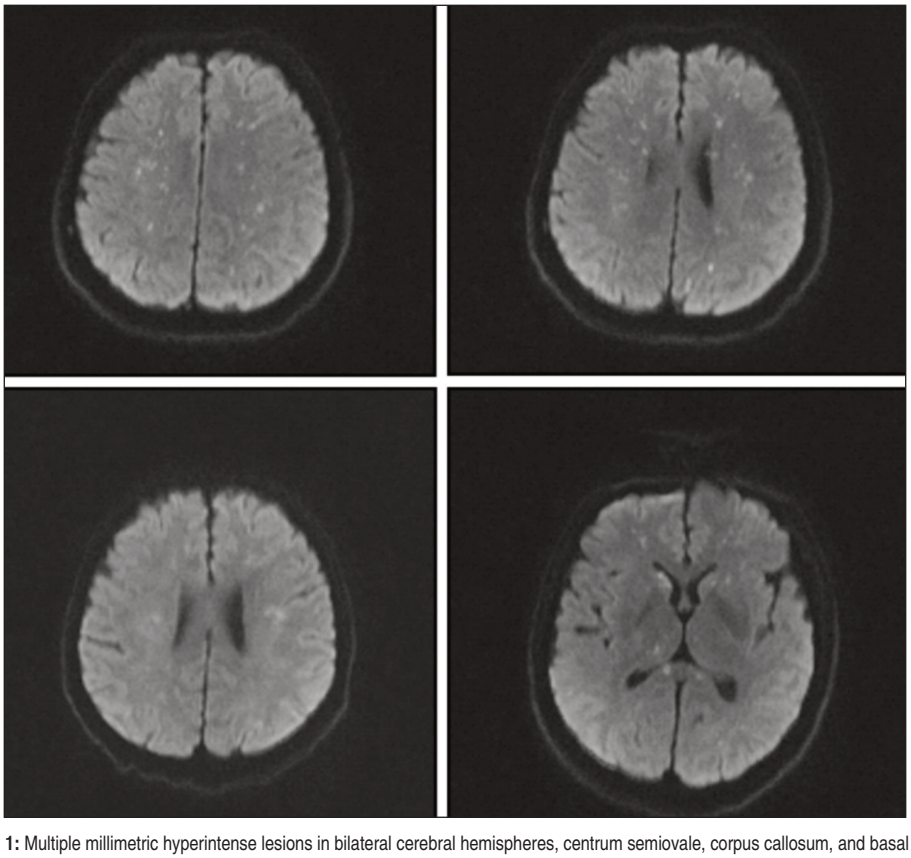

FIGURE 1: Multiple millimetric hyperintense lesions in bilateral cerebral hemispheres, centrum semiovale, corpus callosum, and basal ganglia.

basal ganglia, suggesting acute ischemia (Figure 1). Any intracranial hemorrhage or areas of enhancement were not noticed. Echocardiographic examination was normal and no intracardiac shunt was detected. The patient was operated for the fractures on his right and left lower extremities respectively on the 3rd and 6th days. Because of continuous decline in hemoglobin levels, a total of 18 units of erythrocyte suspensions and 8 units of fresh frozen plasma were transfused in the perioperative period. Thoracoabdominal CT manifested no sign to explain transfusion requirements. At the beginning of transfusion period, some laboratory parameters were measured as follows: WBC: 16.2 K/uL, Hgb: 6.89 g/dL, Hct: 19.3%, Plt: 224 K/uL, PTsec 11.9 sn, INR 1.13, urea: 65 mg/dL, creatinine: 0.56 mg/dL, Na: 142 mEq/L, K: 4.5 mEq/L, Ca: 6.9 mg/dL, albumin: 2.5 g/dL, CRP: 121 mg/L, fibrinogen: 220 mg/dL, D-dimer: 1650 ng/mL, LDH: 735 u/L, amylase: 121 u/L, lipase 152 u/L, direct and indirect bilirubin: 8.24 mg/dL and 3.67 mg/dL. In repeated measurements, AST, ALT, GGT, and ALP levels increased respectively to 90 u/L, 214 u/L, 347 u/L and 209 u/L. In the peripheral smear, polychromasy and schistocytes were observed and reticulocyte count was 5.00%. Urinalysis was as follows: hemoglobin ++, protein +, bilirubin ++, urobilinogen +. In urine microscopy, erythrocyte and leukocyte numbers were measured as 20 and 3 high-power field (HPF). The macroscopic appearance of urine was orange. On the 8th day, control MRI revealed the areas of diffusion restriction were regressed. On 9th day, the patient was extubated following improvement in his arterial blood gas analyses and consciousness. On 12th day, Hgb and Hct values became stable and no additional transfusions were required. He was discharged from ICU with a GCS score of 15 on the 13th day. The report was composed after the informed consent of the patient was received.

DISCUSSION

At least 2 major and 2 minor or a major and 3 minor features are needed to diagnose FES. If hypoxia is to be used as major one, there should not be another reason for it except FES.[1] In our case, three major and four minor features were fulfilled. They included hypoxic respiratory insufficiency, cerebral involvement, petechial rash, pyrexia, jaundice, persistent anemia and transient thrombocytopenia (Table 1). Besides, Schonfeld developed Fat Embolism Index (FEI) to aid diagnosing FES (Table 2). A FEI score of 5 or more reckoned within first 3 days of hospitalization supports the diagnosis.[5] Our patient had a FEI score of 11, which is highly supportive for FES diagnosis.

Approximately 60% of FES patients have petechiae on their axillae, neck, oral mucosa and conjunctivae. The accumulation of fat droplets in the aortic arch and their embolization via subclavian and carotid arteries might explain this peculiar dispersion.[6] The elements contributing to petechiae formation include diminishing of clotting factors and thrombocytes, injury to endothelial cells by

TABLE 1: Major and Minor Diagnostic Criteria for fat embolism syndrome.

Major Criteria
Respiratory insufficiency (96% of cases)
Cerebral involvement (59% of cases)
Petechial rash (33% of cases)
Minor Criteria
Pyrexia (usually <39° C)
Tachycardia (>120 beats/min)
Retinal changes (fat emboli or petechiae)
Jaundice
Renal changes (anuria or oliguria)
Anemia (drop of >20% of the hemoglobin value measured at admission)
Thrombocytopenia (a drop of >50% of the thrombocyte value measured at admission)
High erythrocyte sedimentation rate (>71 mm/hour)
Fat macroglobulinemia

TABLE 2: Schonfeld's Fat Embolism Index (FEI) score.

	Points
Diffuse petechiae	5
Alveolar infiltrates	4
Hypoxemia (< 70 mmHg)	3
Confusion	1
Fever (> 38° C)	1
Tachycardia (> 120 b/m)	1
Tachypnea (> 30 /m)	1

FFAs and consequent rupture of thin-walled capillaries.[7] If extremely severe, alterations in coagulation and fibrinolysis may give rise to disseminated intravascular coagulation (DIC), which is associated with microvascular thrombosis and severe bleeding.[8] In our patient, DIC was not encountered but microangiopathic hemolytic anemia persisted despite improvement in radiological findings and neurological symptoms. Indeed, acute persistent anemia in FES, incompatible with patient's estimated blood loss and resistant to transfusion, is a supporting sign for the diagnosis.

Many researchers have reported that diffusion weighted cranial MRI is a useful adjunct in recognizing cerebral FES.[9-11] In our patient, cranial MRI was consistent with cerebral involvement. He had many scattered small lesions of limited diffusion within both cerebral hemispheres, basal ganglia, centrum semiovale and corpus callosum (Figure 1).

The pathogenesis of FES remains unresolved. However, two main theories have been proposed to explain the etiology. In 1924, Gauss propounded the mechanical theory which is associated with traumatic injury and intramedullary bone pressure. The migration of fat globules from site of trauma to the circulation bears them an access to the right heart and the lungs. Thus, they cause ventilation-perfusion mismatch and consequent respiratory failure.[12-15] The autopsy studies provide additional proof for the theory. Intravascular fat globules in postmortem lungs were evinced to be homologous in composition with bone marrow fat.[16-17] The second mechanism, on the other hand, comes up with a biochemical theory. The inflammation related to trauma results in release of free fatty acids (FFAs), chylomicrons, and very low-density lipoproteins (VLDLs). Various mediators such as catecholamines, C-reactive protein (CRP), protein degradation products and FFAs promote coalescence of chylomicrons (1 μm), VLDLs and FFAs to compose lipid spherules (10 to 40 μm).[18-20] The lipid spherules embolized into the microcirculation of various organs prompt localized hypoxia by sludging of the circulation.[21-23] Thromboplastin release also induces platelets to adhere lipid spherules, resulting in coagulation activation.[21-25] Hence, once lipid spherules exist within various tissues, end organ injury is certain. The biochemical theory ensures an excellent explanation where an intracardiac right-to-left shunt is absent but lipid spherules are spotted in systemic circulation. Thus, microembolic events in our patient might also be explained by the latter theory.

The beneficial effects of steroids on pulmonary capillary membrane stabilization, inhibition of complement activation, preclusion of inflammatory response and prevention of platelet activation are theoretically known. However, treatment duration, dosage and their effect on prognosis are not definite.[26-29] Nevertheless, we preferred to apply 240 mg/day methylprednisolone treatment to our patient in the acute period (during the first 7 days of ICU stay).

Lastly, central nervous system involvement in FES has been rarely reported. We present fat emboli might transmigrate through the pulmonary vasculature and enter into the systemic circulation causing neurologic symptoms.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ömür İlban;* ***Design:*** *Ömür İlban, Mehmet Ali Baş;* ***Control/Supervision:*** *Jale Bengi Çelik, Ateş Duman;* ***Data Collection and/or Processing:*** *Ömür İlban;* ***Analysis and/or Interpretation:*** *Ömür İlban;* ***Literature Review:*** *Mehmet Ali Baş;* ***Writing the Article:*** *Ömür İlban, Mehmet Ali Baş;* ***Critical Review:*** *Jale Bengi Çelik;* ***References and Fundings:*** *Ateş Duman;* ***Materials:*** *Jale Bengi Çelik.*

REFERENCES

1. Bulger EM, Smith DG, Maier RV, Jurkovich GJ. Fat embolism syndrome. A 10-year review. Arch Surg. 1997;132(4):435-9.
2. Horton DP, Ferriero DM, Mentzer WC. Nontraumatic fat embolism syndrome in sickle cell anemia. Pediatr Neurol. 1995;12(1):77-80.
3. Levy D. The fat embolism syndrome. A review. Clin Orthop Relat Res. 1990;(261):281-6.
4. Madenoğlu H, Koç K, Karaoğlu S. [Fat embolism syndrome (case report)]. Cerrahi Tıp Arşivi. 1993;3:30-40.
5. Schonfeld SA, Ploysongsang Y, DiLisio R, Crissman JD, Miller E, Hammerschmidt DE, et al. Fat embolism prophylaxis with corticosteroid. A prospective study in high-risk patients. Ann Int Med. 1983;99(4):438-43.
6. Tachakra SS. Distribution of skin petechiae in fat embolism rash. Lancet. 1976;1(7954):284-5.
7. Jaffe FA. Petechial hemorrhages. A review of pathogenesis. Am J Forensic Med Pathol. 1994;15(3):203-7.
8. Gando S. Hemostasis and thrombosis in trauma patients. Semin Thromb Hemost. 2015;41(1):26-34.
9. Parizel PM, Demey HE, Veeckmans G, Verstreken F, Cras P, Jorens PG, et al. Early diagnosis of cerebral fat embolism syndrome by diffusion-weighted MRI (starfield pattern). Stroke. 2001;32(12):2942-4.
10. Aravapalli A, Fox J, Lazaridis C. Cerebral fat embolism and the "starfield" pattern: a case report. Cases J. 2009;2:212.
11. Butteriss DJ, Mahad D, Soh C, Walls T, Weir D, Birchall D. Reversible cytotoxic cerebral edema in cerebral fat embolism. AJNR Am J Neuroradiol. 2006;27(3):620-3.
12. Mellor A, Soni N. Fat embolism. Anaesthesia. 2001;56(2):145-54.
13. Pape HC, Zelle BA, Hildebrand F, Giannoudis PV, Krettek C, van Griensven M. Reamed femoral nailing in sheep: does irrigation and aspiration of intramedullary contents alter the systemic response. J Bone Joint Surg Am. 2005;87(11):2515-22.
14. Giannoudis PV, Tzioupis C, Pape HC. Fat embolism: the reaming controversy. Injury. 2006;37 Suppl 4:S50-8.
15. Klein C, Sprecher C, Rahn BA, Green J, Müller CA. Unreamed or RIA reamed nailing: an experimental sheep study using comparative histological assessment of affected bone tissue in an acute fracture model. Injury. 2010;41 Suppl 2:S32-7.
16. Kerstell J. Pathogenesis of post-traumatic fat embolism. Am J Surg. 1971;121(6):712-5.
17. Adar R. [Editorial: pathogenesis and treatment of fat emboli]. Harefuah. 1972;83(11):491-3.
18. Schnaid E, Lamprey JM, Viljoen MJ, Joffe BI, Seftel HC. The early biochemical and hormonal profile of patients with long bone fractures at risk of fat embolism syndrome. J Trauma. 1987;27(3):309-11.
19. ten Duis HJ. The fat embolism syndrome. Injury. 1997;28(2):77-85.
20. Hulman G. Fat macroglobule formation from chylomicrons and non-traumatic fat embolism. Clin Chim Acta. 1988;177(2):173-8.
21. Müller C, Rahn BA, Pfister U, Meinig RP. The incidence, pathogenesis, diagnosis, and treatment of fat embolism. Orthop Rev. 1994;23(2):107-17.
22. Replogle RL. The nature of blood sludging, and its relationship to the pathophysiological mechanisms of trauma and shock. J Trauma. 1969;9 (8):675-83.
23. Robb HJ. Microembolism in the pathophysiology of shock. Angiology. 1965;16:405-11.
24. Peltier LF. Fat embolism. A perspective. Clin Orthop Relat Res. 1988;(232):263-70.
25. Jacobson DM, Terrence CF, Reinmuth OM. The neurologic manifestations of fat embolism. Neurology. 1986;36(6):847-51.
26. Fabian TC. Unravelling the fat embolism syndrome. N Engl J Med. 1993;329(13):961-3.
27. Fabian TC, Hoots AV, Stanford DS, Patterson CR, Mangiante EC. Fat embolism syndrome: prospective evaluation in 92 fracture patients. Crit Care Med. 1990;18(1):42-6.
28. Kallenbach J, Lewis M, Zaltzman M, Feldman C, Orford A, Zwi S. 'Low-dose' corticosteroid prophylaxis against fat embolism. J Trauma. 1987;27(10):1173-6.
29. 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.