Fat Embolism Syndrome with Cerebral Involvement in a Multitrauma Patient

Fat embolism syndrome (FES) is a serious 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.


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.\textsuperscript{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.\textsuperscript{3,4}

\section*{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 4\textsuperscript{th} day and later followed 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 2\textsuperscript{nd} 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 basal ganglia.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Multiple millimetric hyperintense lesions in bilateral cerebral hemispheres, centrum semiovale, corpus callosum, and basal ganglia.}
\end{figure}
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/μL, Hgb: 6.89 g/dL, Hct: 19.3%, Plt: 224 K/μL, PTsec 11.9 s, 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, 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, polychromasia 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. 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. 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. 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.**

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>Respiratory insufficiency (96% of cases)</td>
<td>8</td>
</tr>
<tr>
<td>Cerebral involvement (59% of cases)</td>
<td>4</td>
</tr>
<tr>
<td>Petechial rash (33% of cases)</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia (usually &lt;39° C)</td>
<td>1</td>
</tr>
<tr>
<td>Tachycardia (&gt;120 beats/min)</td>
<td>1</td>
</tr>
<tr>
<td>Retinal changes (fat emboli or petechiae)</td>
<td>1</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1</td>
</tr>
<tr>
<td>Renal changes (aruria or oliguria)</td>
<td>1</td>
</tr>
<tr>
<td>Anemia (drop of &gt;20% of the hemoglobin value measured at admission)</td>
<td>1</td>
</tr>
<tr>
<td>Thrombocytopenia (a drop of &gt;50% of the thrombocyte value measured at admission)</td>
<td>1</td>
</tr>
<tr>
<td>High erythrocyte sedimentation rate (&lt;71 mm/hour)</td>
<td>1</td>
</tr>
<tr>
<td>Fat macroglobulinemia</td>
<td>1</td>
</tr>
</tbody>
</table>

**TABLE 2: Schonfeld’s Fat Embolism Index (FEI) Score.**

<table>
<thead>
<tr>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Diffuse petechiae</td>
</tr>
<tr>
<td>4</td>
<td>Alveolar infiltrates</td>
</tr>
<tr>
<td>3</td>
<td>Hypoxemia (&lt; 70 mmHg)</td>
</tr>
<tr>
<td>1</td>
<td>Confusion</td>
</tr>
<tr>
<td>1</td>
<td>Fever (&gt; 38° C)</td>
</tr>
<tr>
<td>1</td>
<td>Tachycardia (&gt; 120 b/m)</td>
</tr>
<tr>
<td>1</td>
<td>Tachypnea (&gt; 30 /m)</td>
</tr>
</tbody>
</table>
FFAs and consequent rupture of thin-walled capillaries. 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. 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. 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 semioval 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. 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. 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 cathecolamines, 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). The lipid spherules embolized into the microcirculation of various organs prompt localized hypoxia by sludging of the circulation. Thromboplastin release also induces platelets to adhere lipid spherules, resulting in coagulation activation. 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. 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 Funding: Ateş Duman; Materials: Jale Bengi Çelik.
REFERENCES


