Case Report
Étude de cas

Fat embolism syndrome in a patient demonstrating only neurologic symptoms

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Fat embolism syndrome (FES) is a recognized complication of both long bone fractures and intramedullary orthopedic procedures. The usual presenting features are respiratory failure, neurologic dysfunction and petechiae. In this report, a 25-year-old woman with FES presented with serious neurologic symptoms and signs in the absence of respiratory dysfunction. The diagnosis is essentially a clinical one, but nuclear magnetic resonance imaging of the brain revealed distinctive lesions that may help future diagnosis of FES.

L'embolie graisseuse est une complication reconnue dans le cas des fractures des os longs et des interventions orthopédiques intramédullaires. Les caractéristiques habituelles sont l'insuffisance respiratoire, la dysfonction neurologique et les pétéchies. Dans ce compte rendu, une femme âgée de 25 ans qui avait une embolie graisseuse présentait de sérieux signes et symptômes neurologiques sans dysfonction respiratoire. Le diagnostic est essentiellement clinique, mais une image par résonance magnétique nucléaire du cerveau a révélé la présence de lésions distinctes qui pourront aider à l'avenir à diagnostiquer une embolie graisseuse.

Fat embolism syndrome (FES) is a serious and potentially lethal complication of both long bone fractures and orthopedic procedures that require intramedullary manipulation. Both intramedullary reaming and pressurized methylmethacrylate cement have been reported to cause FES in patients who undergo total hip and knee arthroplasty.[1–3] The full syndrome becomes manifest within 8 to 72 hours of injury or operation and is characterized by respiratory failure with resulting hypoxemia, focal or global neurologic dysfunction and thrombocytopenia with a petechial rash.[3–6] Although FES continues to be a clinical diagnosis, nuclear magnetic resonance imaging (MRI) of the brain has revealed typical lesions and may aid in the diagnosis.[7–11]

Case report

A 25-year-old woman presented with a history of seronegative juvenile rheumatoid arthritis since the age of 7 years, involving hips, knees, elbows, right ankle, left wrist, neck and temporomandibular joints. She had no previous cardiorespiratory or neurologic disorders and had no known allergies to any medications. She was taking prednisone, ibuprofen, methotrexate and ferrous sulfate. She appeared to be in good health but her hip joints were very sore and their range of motion was restricted. Results of preoperative blood work were normal except for a slight anemia (hemoglobin level 104 g/L and platelet count 336 $\times 10^9$/L).

She chose to have bilateral hip arthoplasty with insertion of noncemented prostheses. Premedication included cefazolin (1 g intravenously), hydrocortisone (100 mg intravenously) and indomethacin (50 mg rectally). Induction and intubation were achieved with intravenously administered thiopental and vecuronium. Anesthesia was maintained with endotracheal nitrous oxide and oxygen

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(66%:34%) and isoflurane (1%), plus intravenously administered fentanyl and morphine. She also received doxacurium for muscle relaxation titrated using a peripheral nerve stimulator. During the entire 3-hour operation her oxygen saturation remained between 97% and 99%, her end-tidal carbon dioxide level was between 34 mm Hg and 40 mm Hg, and her electrocardiogram, blood pressure and body temperature were stable. The arthroplasty procedure was uncomplicated, with an estimated blood loss of 400 mL. Two intraoperative hemoglobin measurements were made: 83 g/L after the first arthroplasty and 81 g/L after the second. At the end of surgery, muscle relaxation was reversed with glycopyrrolate and neostigmine and the patient was transferred to the postanesthetic room awake and responsive to commands.

Initially the patient was stable and awake with a 10/10 recovery room score. She received 2 fluid boluses for tachycardia in the first 2 hours but remained otherwise well. A repeat complete blood count revealed a hemoglobin level of 63 g/L and a platelet count of 182 $\times 10^9$/L. Two units of packed red blood cells were transfused over the following 2 hours as well as a further dose of hydrocortisone (100 mg intravenously). On examination 7.15 hours postoperatively, she was somnolent but still able to open her eyes and follow other commands. The post-transfusion complete blood count showed a hemoglobin level of 67 g/L and a platelet count of 43×10^9/L. At 7.75 hours postoperatively, the patient became unresponsive, would not follow commands and did not withdraw from painful stimuli, but her vital signs remained stablewith a 5/10 recovery room score. Electrolyte levels and blood glucose level were normal, the prothrombin time was increased at 17.8 seconds (international normalized ratio 2.0), and arterial blood gases on 8 L of oxygen by mask were pH 7.38, arterial oxygen partial pressure (Pa_{O_2}) of 189.7 mm Hg, arterial carbon dioxide partial pressure (P_{CO_2}) of 39.2 mm Hg, bicarbonate 20.5 mmol/L, oxygen saturation 100%, and alveolar:arterial gradient of 283.

The patient did not respond to the intravenous administration of naloxone (0.4 mg), and a second transfusion of 2 more units of packed red blood cells was begun. On physical examination conducted at 8.25 hours postoperatively her pupils were equal (3 to 4 mm) and reactive to light bilaterally; she would open her eyes only to loud noises and had a roving gaze, she maintained a gag reflex, both upper and lower extremities showed no movement or withdrawal from pain, and her deep tendon reflexes were normal. At 9.5 hours, the patient was comatose with a 3/10 recovery score and began to require increasing airway support. At 9.75 hours, she was reintubated and transferred to the intensive care unit.

Her cardiovascular and respiratory status remained stable in the intensive care unit throughout her course. Initially she was fully ventilated using synchronized intermittent mandatory ventilation with a tidal volume of 600 mL, respiratory rate of 12/min, positive end-expiratory pressure of 5 cm H_2O, and peak airway pressures of 28 to 32 cm H_2O. Her arterial blood gas measurements stabilized on 60% oxygen at pH 7.44, Pa_{O_2} 262 mm Hg, Pa_{CO_2} 34 mm Hg, bicarbonate 23 mmol/L, oxygen saturation 100% and alveolar:arterial gradient 87.

A chest film taken on admission to the intensive care unit showed no abnormality, and serial examinations for 6 consecutive days showed no evidence of adult respiratory distress syndrome. She continued to receive regular doses of cefazolin (1 g) and hydrocortisone (100 mg intravenously). CT of the head done soon after her arrival showed no evidence of edema, hemorrhage or hydrocephalus and the scan was reported as normal. An electroencephalogram obtained the following day described triphasic delta frequency waves suggestive of an encephalopathy. Findings on physical examination remained the same except her gaze deviated to the left, cold calorics showed no corrective nystagmus on the left, a positive Babinski reflex was noted on the left and she demonstrated flexor posturing of the right side and flaccidity of the left side.

Another 2 units of packed red blood cells were needed to keep her hemoglobin level at 90 g/L, and 10 units of platelets were used to increase her count from 63×10^9/L to 100×10^9/L.

On the third postoperative day, the patient began to open her eyes spontaneously and withdraw all limbs to noxious stimuli. Again, a repeat head CT scan was normal. Her ventilation and oxygen requirements decreased, and she was switched to a pressure support ventilator mode. A transthoracic echocardiogram failed to show an embolic source or a right to left intracardiac shunt. By the 5th postoperative day, she showed significant improvement, opening her eyes and performing weak hand grip to command. She was extubated the following day. MRI of the head showed multiple high-intensity lesions (T_2 weighted) scattered throughout the deep white matter and basal ganglia of both cerebral hemispheres and the left cerebellar peduncle (Fig. 1). These same lesions were of low intensity on T_1 weighting. On postoperative day 8, the patient was able to speak and move all limbs. Her right side was stronger than her left, her hemoglobin level was 105 g/L and

her platelet count was 286×10^9/L. She was transferred to the orthopedic ward.

During her first week on the ward, her motor strength improved quickly and she showed few signs of cortical dysfunction. She was discharged from hospital 3 weeks after her operation ambulating with a walker for support. At her first outpatient visit 6 weeks later, she showed absolutely no evidence of neurologic dysfunction and was rehabilitating very quickly with respect to her bilateral hip arthroplasties. A 5-month follow-up MRI study showed complete resolution of all the previously seen brain lesions (Fig. 2).

Discussion

FES comprises a constellation of physical symptoms, signs and laboratory test results. These occur in patients who have suffered fractures, especially long bone fractures, or who have undergone orthopedic procedures, most commonly in intramedullary manipulations and the insertion of hip and knee prostheses.[1–3,12–16] Diagnosis of FES continues to be a challenge because of a great variance in both clinical and laboratory presentation. Classically, patients present with respiratory failure with resulting hypoxemia, focal or global neurologic dysfunction and thrombocytopenia with a petechial rash.[3–6] Less commonly patients may also display anemia, coagulopathy, increased lipase, lipiduria, retinopathy, tachycardia and pyrexia.[3,5,6,17] The onset ranges from a few hours to a few days after injury or operation with approximately 90% of cases occurring within 3 days.[18]

The pathogenesis of FES remains unresolved. Two main theories have been proposed to explain its etiology. First, the mechanical model postulates that medullary fat is forced into the venous system.[3,6] This occurs when medullary contents are exposed to damaged vessels and by increased medullary pressures created by fracture manipulation and hematomas as well as intramedullary orthopedic procedures such as reaming, pressurizing cement and prothesis insertions.[1–3,12–16] The medullary fat then embolizes to the lung and invades the systemic circulation to affect all other organs.[3,19–21] Second, the sedimentation theory proposes that increased catecholamines and plasma lipase help mobilize lipids from fat stores and destabilize the resulting high concentration of plasma fat causing the formation of fat droplets within the entire circulatory system.[3,6]

The lipid droplets embolized in the microcirculation of the various organs cause a sludging of the circulation with resulting localized hypoxia.[3,22,23] In addition, thromboplastin release induces platelets to adhere to fat globules with consequent coagulation activation.[3,6,17] Peltier[6] has suggested that the thrombocytopenia resulting from the consumptive platelet coagulopathy can be used as a strong diagnostic sign. It is also thought that capillaries are damaged by the plasma lipase-

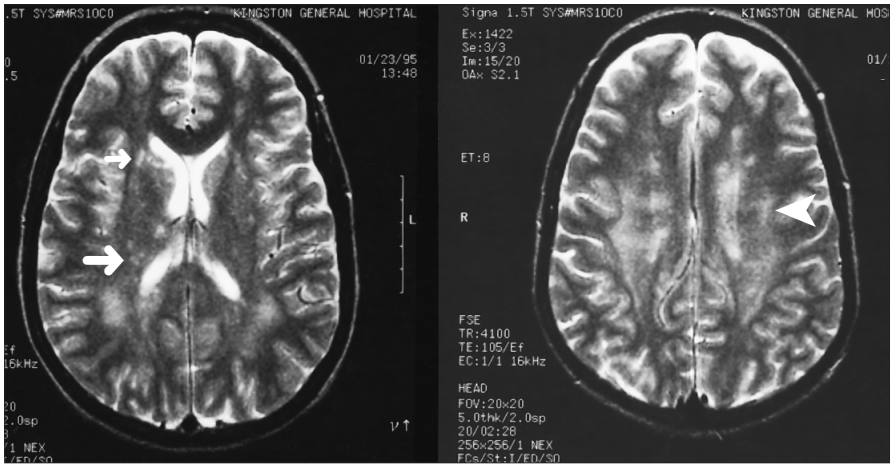

FIG. 1. Axial T_2-weighted magnetic resonance images showing high intensity lesions in the periventricular deep white matter (arrowhead) and the thalamus (large arrow) and basal ganglia (small arrow).

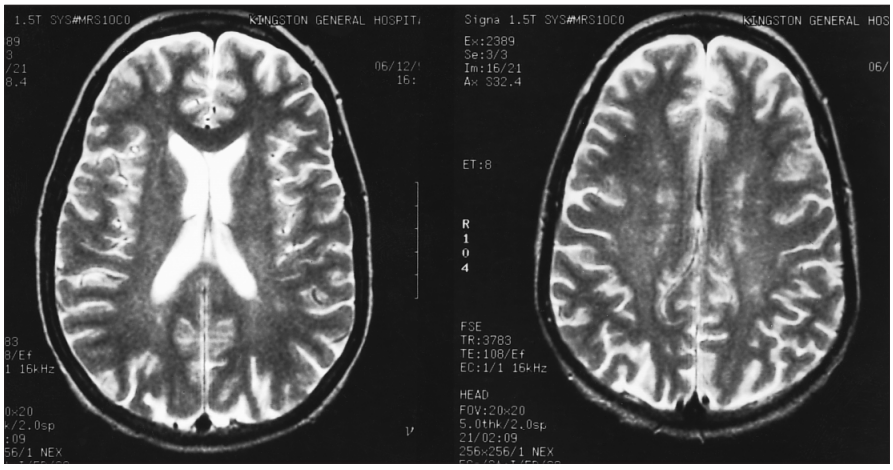

FIG. 2. Axial T_2-weighted magnetic resonance images 5 months later showing complete resolution of the lesions seen on the initial brain scan (Fig. 1).

mediated hydrolysis of neutral fat particles into histotoxic free fatty acids that results in the final common pathways of end-organ dysfunction.[3,6,17]

The patient we present suffered rapid neurologic deterioration and subsequent coma, requiring intubation for airway protection. She initially had an increased alveolar:arterial gradient in the absence of hypoxemia but adult respiratory distress syndrome never developed. Other supporting evidence for the diagnosis of FES included an acute precipitous thrombocytopenia and persistent anemia, not in keeping with the patient's estimated blood loss and resistant to blood transfusion, and an unexplained coagulopathy (elevated prothrombin time). No other source for the patient's depressed neurologic state was found on any physical examination or investigation, and a chart review did not find any anesthetists' or nurses' errors such as drug errors or unrecognized hypotension. In addition our patient underwent bilateral total hip arthroplasties, which would have exposed her to a very large embolic marrow-fat load.

This is an infrequent presentation for FES that has been reported previously and illustrates that cerebral fat embolism need not necessarily be associated with respiratory failure.[9,11,24–26] Prior theories on FES attribute the coexistence of neurologic dysfunction and respiratory failure to the resulting global arterial hypoxemia.[3] This case suggests that fat emboli were able to pass through the pulmonary vasculature to the systemic circulation to cause neurologic dysfunction. Byrick and associates[27] were able to confirm the transpulmonary passage of marrow fat within 3 hours of cemented arthroplasty in the dog model, excluding right to left cardiac shunts. This evidence supports the theory that the localized ischemic effects of cerebral fat emboli could be the primary contributor to the neurologic manifestations of FES.

Autopsy histologic studies of cerebral fat embolism describe multiple small infarcts with perivascular hemorrhage in the basal ganglia, the thalamus, the brain stem and the deep white matter of the cerebral hemispheres and cerebellum.[26] A number of MRI studies on FES have now reported visualizing hypointense lesions on T_1-weighted images and hyperintense lesions on T_2-weighted images in a similar pattern to the one we have described.[7–11] Anegawa and associates[7] and Erdem and associates[8] have postulated that the MRI lesions represent the small infarcts seen in pathological studies. In addition, follow-up studies have shown resolution of the brain lesions demonstrated on MRI at 1 to 3 months, parallelling the patients' clinical course.[8,9,11] Our case clearly demonstrates these typical MRI lesions in the appropriate distribution with complete resolution at 5 months. The MRI results coupled with a clinical presentation of isolated neurologic FES also support the idea that cerebral fat emboli, not hypoxemia or cerebral edema, causes neurologic dysfunction in FES.

An explanation for the predominantly neurologic presentation of FES in our patient eludes us. The mechanical theory would require fat emboli to pass through the pulmonary circulation without causing clinical disease before being carried to the brain. Possibly the brain is more susceptible to the effects fat embolism than the other organ systems and our patient's good health provided her with a large enough pulmonary reserve to avoid hypoxemia. Respiratory symptoms in classical FES are commonly preceded by neurologic manifestations, which could indicate the brain's increased sensitivity to fat emboli.[4,5,17]

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