Illustrative Teaching Case

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Cerebral Fat Embolism
A Case of Rapid-Onset Coma

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Case
An 87-year-old woman with a history of a biparietal meningioma previously treated with resection and radiation therapy presented after a fall. On arrival, she was alert and interactive without external evidence of head trauma. Hip x-ray showed a subcapital fracture of the right femoral neck, and plans were made for surgical fixation. Two hours later, she became agitated, then confused, and somnolent. She had lip-smacking movements and nystagmus. She was given intravenous lorazepam 2 mg and levetiracetam 500 mg. Computed tomography of the head showed chronic changes expected from treatment of her convexity meningioma and no acute lesions. Over the next hour, she became stuporous and hypoxic requiring intubation and mechanical ventilation. Chest x-ray showed bilateral perihilar densities and small pleural effusions. Transthoracic echocardiogram showed a left ventricular ejection fraction of 75% with hypokinesis of the right ventricular wall and hypercontractility of the apex (McConnell’s sign), suggesting pulmonary embolus. Computed tomography angiogram of the chest showed posterobasilar atelectasis or consolidation with pulmonary emboli. Computed tomography angiogram of the chest showed posterobasilar atelectasis or consolidation with bilateral pleural effusions and no pulmonary emboli.

She was initially afebrile with a normal complete blood count and biochemistry profile. On hospital day 2, she developed a fever to 101.2°F with leukocytosis. She had no rash. Platelet count, initially 235K/µl, fell to 113K/µl on day 3. Follow-up head computed tomography showed only stable chronic edema from her meningioma. Initial electroencephalograms showed ongoing seizures in both parietal lobes; later electroencephalograms showed bilateral slowing and epileptiform discharges. She was treated with levetiracetam, valproic acid, and then midazolam infusion and transferred to our center after 1 week.

She was started on vancomycin, ceftriaxone, ampicillin, and acyclovir for possible infectious meningoencephalitis. Cerebrospinal fluid glucose was 57, protein 37.4, and there were 2 to 3 nucleated cells with lymphocytic predominance. Transthoracic echocardiogram showed no evidence of patent foramen ovale (PFO), and McConnell’s sign had resolved. Magnetic resonance imaging (MRI) of the brain (Figures 1 and 2) demonstrated many (>10) tiny scattered foci of faint restricted diffusion in the periventricular white matter and innumerable punctate foci of susceptibility artifact throughout the brain, including the hemispheric white matter, corpus callosum, basal ganglia, brain stem, and cerebellum. Magnetic resonance venography and angiography showed no evidence of acute thrombosis. A diagnosis of cerebral fat embolism (CFE) syndrome was made based on her MRI and rapid progression to coma and respiratory failure after hip fracture. After 2 weeks, she remained comatose with sluggishly reactive pupils bilaterally, limited oculocephalic reflexes, brisk corneal reflexes, and a cough. Her best motor response was reflex flexion of her legs. She was ultimately transitioned to comfort care and transferred to home hospice.

Discussion

Fat Embolism Syndrome
Fat embolism is a well-known complication of long bone and pelvic fractures. The reported incidence varies greatly in the literature depending on diagnostic criteria; from <1% using Gurd’s clinical criteria, to 11% using arterial oxygen tension differences, and up to 88% using transesophageal echocardiography in all patients undergoing orthopedic procedures, regardless of symptoms.1 The disruption of marrow-containing bone allows globules of marrow fat to pass into venous sinuses that drain the marrow and then into the systemic circulation. High pressure in marrow during orthopedic surgery may also force marrow fat into veins.1 Having reached the circulation, fat may cause symptoms as a result of embolic occlusion of arteries in the lung, brain, skin, and elsewhere. However, simple vascular occlusion with ischemia probably does not fully explain the fat embolism syndrome (FES). Much study implicates alternative, supplementary, biochemical mechanisms of tissue injury. Such biochemical pathways of injury result from the complex inflammatory response to free fatty acids released by...
the hydrolysis of embolized fat that has entered blood vessels. This inflammatory response may have local effects on the brain and other tissues and systemic consequences, including shock and anticoagulation.1–3

The great majority of patients with fat embolism do not develop clinical FES, which has an incidence of only 0.9 to 2.2% in patients with long bone fractures.4 Echocardiographic evidence of fat emboli was found in up to 40% of patients who required orthopedic intervention in a study by Pell et al.2 In a small case series of 5 patients with long bone fractures, all had positive transcranial Doppler monitoring for microembolic signals. All patients demonstrated absence of microembolic signals within 4 days of injury, suggesting that risk of fat emboli is highest within the first few days after trauma.5 Clinical symptoms of fat emboli usually develop gradually within 24 to 72 hours of injury, suggesting that risk of fat emboli is highest within the first few days after trauma.3

Cerebral Fat Embolism

CFE occurs after fat emboli enter the arterial circulation. Fat globules may enter the arterial circulation by 2 mechanisms. First, fat globules can enter the left atrium directly from the right heart through a shunt, such as a PFO (paradoxical embolism). Second, microglobules of fat may filter directly through the lung capillaries to reach the arterial system. These microemboli are small and malleable and may not lead to significant pulmonary injury. There is direct evidence of passage of fat through a PFO, yet the absence of PFO in many patients with CFE supports the latter mechanism in some patients.1,2 Therefore, PFO should be considered an additional risk factor for CFE but is not necessary for the syndrome.

The neurological findings in CFE vary greatly, ranging from mild confusion to coma, and rarely include seizures and focal findings.1–3 These signs can occur in isolation but more often are associated with and occur after respiratory failure. They may occur as a consequence of hypoxemia or cerebral embolism.1 The effects of CFE are often reversible and associated with a favorable outcome.1,3 Mortality ranges between 5% and 15% with most deaths attributable to respiratory failure.3 There are limited data on the cognitive outcomes of surviving patients with CFE; however, long-term studies of 2 young patients found a near-complete recovery at 4 months.6

CFE is a clinical diagnosis, but specific findings on neuroimaging studies can be strongly supportive. Computed tomographic scans are frequently normal in these patients. The characteristic MRI finding is the starfield pattern, demonstrating scattered foci of high-intensity restricted diffusion on diffusion-weighted imaging. This is most apparent in the acute phase, from 4 hours to the first few days from the time of injury. T2-weighted lesions may take several days to become apparent. These lesions are most commonly found in the deep white matter, including the basal ganglia, brain stem, and cerebellum.7 Multiple scattered foci of hypointensity on susceptibility-weighted imaging are indicative of cerebral microbleeds and can be useful in the acute setting.4 Such widespread petechial hemorrhage and bland microinfarction have been demonstrated on autopsy.9

Figure 1. Magnetic resonance imaging (MRI) of the brain of our patient with diffusion-weighted imaging (DWI; A), Apparent diffusion coefficient (ADC) (B), fluid attenuation inversion recovery sequence (FLAIR) (C) showing acute (solid arrow) and subacute (dashed arrow) cerebral infarctions.

Figure 2. Susceptibility-weighted imaging (SWI) featuring diffuse microhemorrhages.
Our patient presented to the hospital = 1 week from the time of injury, and lesions on diffusion-weighted imaging were not as apparent as with susceptibility-weighted imaging. Takahashi et al correlated clinical findings with those on MRI and found that the number of abnormal signals correlates with the Glasgow Coma Scale. They also demonstrated that good outcome was associated with dissipation of lesions and that patients with poor outcome were more likely to have persistent multiple infarctions 2 months after presentation. Early surgical stabilization should be considered, patients who had early fixation of fractures and those who make an association between the incidence of FES among presentation. Likely to have persistent multiple infarctions 2 months after lesions and that patients with poor outcome were more consistent with diffuse, scattered microhemorrhages. In the acute phase, and patients presenting later may instead demonstrate findings on susceptibility-weighted imaging consistent with diffuse, scattered microhemorrhages. In patients presenting early, prophylactic corticosteroids may be considered. The mainstay of therapy remains supportive respiratory and neurological care. Although there are reports of excellent recovery in patients with CFE, some do not survive. Prognosis should be considered in the context of concomitant illness and premorbid functional status.

There is no current treatment for FES or CFE other than supportive care to address both intrinsic lung pathology and airway protection in the setting of neurological impairment. Corticosteroids have been extensively studied with variable results, and their use is controversial. Gupta et al propose a regimen of methylprednisolone 1.5 mg/kg IV every 8 hours for 6 doses in a select group of patients with long bone or pelvic fractures at high risk of developing FES and without significant contraindications. Early fixation of fractures within 24 hours has been recommended to prevent further trauma at the injury site and thus decrease the incidence of FES. Several studies, however, have failed to make an association between the incidence of FES among patients who had early fixation of fractures and those who did not. Early surgical stabilization should be considered, though this intervention has not consistently been shown to decrease overall risk.

In summary, clinical FES and CFE are relatively uncommon, whereas the true incidence of fat emboli, mostly asymptomatic, is high in the setting of long bone and pelvic fractures. The diagnosis should be investigated in patients who develop respiratory distress, new neurological symptoms, and petechial rash. Imaging studies are critical in the diagnosis of CFE, especially MRI. The classically described starfield pattern may only be present in the acute phase, and patients presenting later may instead demonstrate findings on susceptibility-weighted imaging consistent with diffuse, scattered microhemorrhages. In patients presenting early, prophylactic corticosteroids may be considered. The mainstay of therapy remains supportive respiratory and neurological care. Although there are reports of excellent recovery in patients with CFE, some do not survive. Prognosis should be considered in the context of concomitant illness and premorbid functional status.

**Take-home Points**

- Cerebral fat embolism should be considered in all patients with long bone or pelvic fractures who develop respiratory distress and or neurological deficits.
- Cerebral fat embolism may occur without the presence of a patent foramen ovale.
- Diffusion-weighted imaging often demonstrates the characteristic starfield pattern; diffuse microhemorrhages on susceptibility-weighted imaging may be the only characteristic finding if outside of the acute period.
- There is no consensus on treatment, but a select, high-risk population may benefit from high-dose systemic steroids.

**Disclosures**

None.

**References**


**Key Words:** angiography • cerebrovascular disease • computed tomography • embolism • embolism, fat • stroke
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