October 2020 Critical Care Case of the Month: Unexplained Encephalopathy Following Elective Plastic Surgery

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A 29-year-old woman with no significant medical history presents to the hospital due to progressive encephalopathy, 5 days after undergoing an elective abdominoplasty with abdominal liposuction and breast augmentation. She is somnolent on exam, and is hypoxic to ~60% saturation on room air. She is emergently intubated in the emergency department prior to being admitted to the MICU, and is started on broad-spectrum antibiotics and n-acetyl cysteine (NAC). She has evidence of acute liver failure but her initial work-up for acute liver failure is entirely unrevealing, and her liver function and hemodynamics improve without additional intervention over the initial 3 days of hospitalization. Unfortunately, her mental status does not improve. Despite weaning of all sedation, she shows limited signs of awareness. A lumbar puncture, CT of the head, and electroencephalogram (EEG) are performed and are unremarkable.

What should be ***done next***?

1. Brain magnetic resonance (MRI) imaging
2. Myelography
3. Neurology consultation
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

The cause for her non-responsiveness is unclear. Neurology was consulted and suggested an MRI of the brain which is below. Compared to CT scanning MRI has a much greater range of available soft tissue contrast, depicts anatomy in greater detail, and is more sensitive and specific for abnormalities within the brain itself.

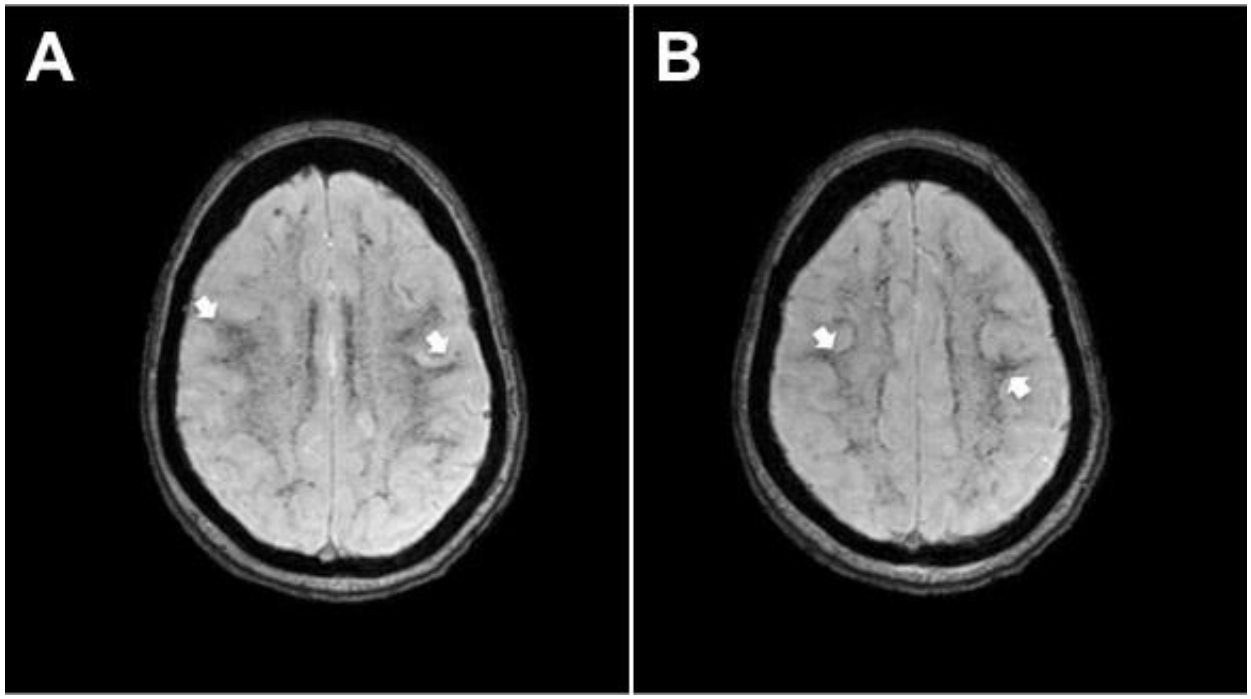

Figure 1. Selected T2 weighted images from a brain MRI on hospital day 3.

What unifying ***diagnosis*** can explain these findings?

1. Anoxic brain injury
2. Cardioembolic stroke
3. Fat embolism syndrome
4. Status epilepticus
5. Toxic metabolic encephalopathy

Correct!
3. Fat embolism syndrome

The MRI brain reveals diffuse white matter abnormality with fine, granular abnormal lesions in a “starfield” pattern (arrows) consistent with cerebral fat embolism syndrome (FES).

FES is the clinical syndrome that follows the presence of fat globules in the pulmonary or peripheral circulation (1). FES is most common after traumatic orthopedic injuries (typically long bone fractures), and pulmonary fat emboli have been reported in up to 82% of blunt trauma patients at autopsy (2,3). However, FES is also known to complicate soft tissue trauma and non-traumatic events. These include elective orthopedic surgeries, cosmetic procedures that cause adipose tissue damage (plastic surgeries, implant placements, and even depot drug delivery), pancreatitis, and bony/soft tissue infections (4,5). Our patient developed FES after an elective liposuction procedure. A literature search published by Duran *et al.* (6) found 15 cases in the literature (Sept 1986 – Mar 2017) of fat embolism after liposuction, 6 of which occurred in the United States.

What is the ***classic triad*** of symptoms seen in fat emboli syndrome?

1. Neurologic changes, acute liver injury, and rash
2. Respiratory distress, neurologic changes, and acute liver injury
3. Respiratory distress, neurologic changes, and rash
4. Respiratory distress, shock, and acute liver injury
5. Shock, neurologic changes, and rash

Correct!
3. Respiratory distress, neurologic changes, and rash

The classic triad of symptoms in FES includes respiratory distress, neurologic changes, and a petechial rash. Symptoms typically present 24 to 72 hours after a trauma, with an insidious onset of dyspnea and hypoxemia. Neurologic symptoms follow the pulmonary complaints in up to 80% of patients. Commonly, patients develop confusion and agitation, which can progress to focal deficits with upper motor neuron signs, focal seizures, and coma (1,4). Unresponsiveness can be the initial presentation (4). The classic petechial rash occurs only in 20 to 50% of patients. Interestingly, the rash in FES is only found anteriorly on the body in nondependent areas (1). In Duran's review of the 15 reported cases of liposuction-related FES, symptoms began at a mean of 25.6 hours after the start of surgery, with the most common presentation being dyspnea (10/15 patients), followed by fever (7/15 patients) and altered consciousness (6/15 patients) (6).

There are no validated diagnostic criteria for diagnosing FES, and diagnosis is primarily clinical. For cerebral fat emboli syndrome specifically, head CT is often normal (3). MRI typically shows diffuse hyperintense punctate lesions ("starfield pattern") within the white and deep gray matter on diffusion-weighted and T2-weighted images (7,8).

Interestingly, there are no reports in the literature of acute liver failure in fat emboli syndrome. It is possible that our patient developed shock liver due to intra-operative hypotension, septic shock or an anesthetic drug reaction that was entirely unrelated to her fat emboli syndrome. Her liver abnormalities resolved with supportive care measures.

At this point, the patient is hemodynamically stable and is on minimal ventilator settings, but is unable to wake up.

What is your ***next step*** in treatment?

1. Corticosteroids
2. Heparin drip
3. Supportive care
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

Treatment for fat embolism syndrome is primarily supportive. Several studies have assessed adjunctive pharmacologic therapies for FES, including heparin, aspirin, statins, and anti-inflammatory agents, with overall inconclusive results and a lack of high quality evidence (5). The most commonly studied agent has been corticosteroids. A 2009 meta-analysis of 7 studies (n=389) by Bederman *et al.* (9) found that administration of corticosteroids to patients with long bone fractures reduced the risk of FES by 78%, with a number needed to treat (NNT) of 8. Notably, the authors of this article found the quality of the trials to be poor, and found no differences in mortality with steroid use (9). A similar meta-analysis by Sen *et al.* (10) from 2011 identified 7 randomized trials (n=483) that evaluated corticosteroids in patients with lower limb fractures. They found a decreased risk of FES with steroid use; 9/223 patients in the steroid-receiving group compared with 60/260 patients in the control group developed FES, respectively ($p<0.05$). Again, the authors expressed concerns about the lack of uniformities in the studies, making it difficult to draw definitive conclusions about steroid use.

What is the ***underlying mechanism*** of fat emboli syndrome?

1. Mechanical obstruction resulting from release of fat thrombi into the pulmonary and systemic vasculature
2. Release of micro-fat emboli into the venous system, resulting in disseminated intravascular coagulation (DIC)
3. Systemic inflammatory response to high concentrations of free fatty acids in the vasculature
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

Two pathophysiologic mechanisms behind FES have been proposed which are not mutually exclusive: mechanical and biochemical. The first, mechanical theory was proposed by Gauss in 1924, and suggests that trauma of long bones causes damage to fat in the marrow and intraosseus blood vessels, subsequently releasing fat droplets into the vasculature (1,4,5). These fat droplets cause mechanical obstruction in lung capillaries, or may pass directly into the systemic circulation via a patent foramen ovale or as microglobules that can filter directly through lung capillaries. It is unclear why symptoms of FES are typically delayed in this proposed mechanism.

Lehman and Moore described an alternative biochemical theory in 1927, which proposes that symptoms of FES are attributable to a proinflammatory state. They suggest that once fat globules reach the pulmonary capillaries, they are hydrolyzed by lipase produced by pneumocytes, leading to high concentrations of free fatty acids that cause a localized inflammatory response (5). It is likely that the clinical symptoms of FES are a combination of these two theories, and occur from both mechanical vascular obstruction and the body's inflammatory response to embolized fat.

Our patient ultimately was treated supportively, without the addition of steroids. With this, she had slow, progressive improvement in her mentation. She was extubated on hospital day 11, was discharged home on hospital day 16, and seen in neurology clinic 6 weeks later. At this follow-up visit, she was noted to have mild cognitive impairment but was otherwise thought to be doing well. She had returned to working part time.

References

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