Perioperative management of massive fat embolism syndrome presenting as refractory status epilepticus

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ABSTRACT

Fat embolism syndrome (FES) most commonly can occur after trauma in patients with long bone fractures. While the majority of FES cases present as a mild decrease in mental status, some may manifest as seizure activity. We describe a case of a young patient with traumatic fractures who developed FES leading to refractory status epilepticus and simultaneously required damage controlled orthopedic surgery. The role of imaging modalities including magnetic resonance imaging, transcranial Doppler, and transesophageal echocardiography in diagnosis is discussed, and a multidisciplinary approach to successful perioperative management is described.

Key Words: Fat embolism syndrome, multidisciplinary care, perioperative management, refractory status epilepticus

INTRODUCTION

Acute trauma with long bone fractures of the lower extremities is a known risk factor for fat embolism. Fat embolism syndrome (FES) occurs in a subset of patients who have fat emboli and consists of neurologic, respiratory, and cutaneous manifestations. Along with FES, paradoxical cerebral emboli can occur through venoarterial shunts and present as multifocal ischemic strokes. Neurologic dysfunction from FES is a poor prognostic indicator although the syndrome is usually self-limited and resolves with supportive management.

Cerebral fat emboli are usually diagnosed based on clinical picture and can be confirmed with diagnostic studies such as magnetic resonance imaging (MRI) or transcranial Dopplers (TCD). In some cases of cerebral fat emboli, an intracardiac shunt exists allowing the passage of fat globules into the arterial circulation and to cerebral arteries. We present the case of a young patient with lower extremity trauma who developed refractory status epilepticus (rSE) due to FES necessitating prolonged anticonvulsant therapy, while at the same time, requiring surgical fixation of the fractures. To our knowledge, this case introduces two novel aspects to the literature: (1) perioperative management with transesophageal echocardiography (TEE) and intraoperative TCD to guide surgical approach in a patient with rSE to limit the degree of fat embolization and (2) a treatment strategy for refractory seizures due to cerebral FES (CFES) [Table 1]. Both strategies lead to excellent functional recovery and intact neurological status.

CASE REPORT

The patient is a 26-year-old man with no significant medical history who arrived to the trauma resuscitation bay after a jet-ski accident. Significant injuries included left proximal femur and distal tibial fractures, left L5 transverse process fracture, left sacral ala fracture, and a Grade 1 splenic laceration. The patient had intact neurological status on arrival with Glasgow Coma Scale of 15, and computed tomography (CT) scan of his brain was negative for acute pathology. His leg injuries
were stabilized with a short leg splint and a proximal tibial traction pin, and he was admitted to the surgical Intensive Care Unit for observation. On hospital day (HD) 1, the patient developed acute agitation, hypoxemic respiratory failure, tachycardia, hypertension, and a petechial rash throughout his upper extremities and thorax. He was intubated and sent for a repeat CT scan of his brain, which was negative for any acute process, and FES was suspected. The patient subsequently developed seizures on HD 2, which were confirmed by continuous electroencephalography (cEEG), and was started on anticonvulsant therapy with lacosamide and levetiracetam. Further workup with TCD revealed multiple microembolic signals in the distribution of the middle cerebral arteries (MCAs) bilaterally [Figure 1a] cerebral arteries (MCAs) bilaterally [Figure 1]. In addition, MRI of the brain revealed innumerable scattered supratentorial and infratentorial parenchymal punctate areas of high T2/fluid-attenuated inversion-recovery signal [Figure 2], consistent with multifocal embolic strokes and FES. Due to the bilateral distribution of the emboli, an echocardiogram was performed for suspected intracardiac shunt. Transesophageal echocardiography (TEE) was negative for a patent foramen ovale (PFO) [Figure 3] but did show the passage of bubbles into the left atrium seven beats after injection. These findings were consistent with severe FES and an intrapulmonary shunt as the underlying etiology of the patients’ paradoxical emboli.

By HD4, the patients’ seizure activity evolved into Stage 2 status epilepticus [Figure 4] despite antiepileptic therapy consisting of levetiracetam, lacosamide, a propofol infusion, and midazolam as needed. Unstable lower extremity fractures were considered as a contributing factor to ongoing showering of fat emboli, and after multidisciplinary discussion, the patient was taken to the operating room (OR) on HD 5 for stabilization of fractures with an external fixation. After an uneventful general anesthetic with invasive arterial monitoring, he remained intubated and was brought back to the trauma Intensive Care Unit. Since the patient remained in rSE, a midazolam load of 0.2 mg/kg was given, followed by high-dose infusion at a rate of 0.5 mg/kg/hr on HD 6. Burst suppression was achieved within 24 h, and the infusion was weaned off starting on HD 8 with the goal of decreasing by 0.5 mg/hr every 3 h. Throughout the weaning process, there were no further episodes of seizures on cEEG, but there were episodes of rhythmic
Table 1: Summary of pertinent clinical findings and novel aspects of the case

| MRI findings showing diffuse, bilateral hyperdensities | Citation |
|--------------------------------------------------------|----------|
| Existence of right-to-left intrapulmonary shunt         | Figure 2 |
| Convulsive status epilepticus due to CFES, treated with an anesthetic dose of midazolam | Figure 3 |
| Complete neurological recovery in a patient with rSE due to CFES | Figure 4 |
| Use of TCD for both diagnosis and guidance of surgical repair | Fernández-Torre JL, et al., 2015 |

delta activity. The infusion of midazolam ended on HD 27.

Mental status and respiratory function of the patient improved over the subsequent days, and he was weaned off mechanical ventilation a few days after an uneventful percutaneous tracheostomy was performed in the Intensive Care Unit. The patient was taken back to the OR on HD 36 for a definitive treatment of the fractures with open reduction and internal fixation. Due to the history of severe FES, the decision was made to proceed with intraoperative TCD monitoring of the bilateral MCAs allowing early detection of fat emboli [Figure 1b], which in turn would allow modification of operative technique. Only one microembolic signal was detected throughout the procedure. The patient had an uneventful postoperative recovery. His mental status returned to baseline and he was able to ambulate without assistance before transfer to inpatient rehabilitation facility.

**DISCUSSION**

This case illustrates the effective multispecialty peroperative care of a patient with traumatic long bone fractures who suffered rSE secondary to CFES. To the best of the authors’ knowledge, this case is the first report of a favorable outcome in such a patient. A recent report described the case of an 82-year-old female who suffered rSE due to CFES after knee prosthesis surgery requiring multiple antiepileptic medications who unfortunately succumbed due to her complications.[4] There are other reports of multifocal strokes from cerebral fat emboli after long bone fractures with good neurologic recovery; however, none of the patients developed rSE.[2,3]

Although fat emboli are present in the vast majority of patients who suffer long bone fractures, FES only develops in a minority of cases.[6] FES consists of a constellation of cutaneous, respiratory, neurologic, and nonspecific inflammatory signs and symptoms and is diagnosed using criteria put forth by Gurd and Wilson.[7] Two competing theories have been proposed to explain the presentation of FES.[1] The biochemical hypothesis holds that the end organ dysfunction seen is the result of toxic effects of free fatty acids produced as a result of lipoprotein lipase breaking down the released bone marrow fat. The mechanical hypothesis states that either trauma or increased intramedullary pressures lead to intravascular dissemination of fat globules that then exert their effects on end organs through obstruction of small vessels. These globules gain access to the arterial circulation either through a right-to-left intracardiac shunt or through an intrapulmonary shunt.

FES can present as a heterogeneous mixture of nonspecific signs and symptoms. The lack of a gold standard for diagnosis as well as various methods used to document the incidence of FES has led to the great variability in reported incidence ranging from 0.25% to 35%.[1] Therefore, clinicians must have a high degree of suspicion for ordering imaging studies if FES is suspected. Specific pathognomonic imaging findings on MRI[8] and TCD[9] have been used to detect emboli and their sequelae in the perioperative period. Given that our patient developed hypoxemic respiratory failure and acute mental status changes after long bone fractures, early use of TCD and MRI for detection of emboli was warranted. TCD was positive for numerous embolic signals, and the T2-weighted MRI findings were consistent with those described by Takahashi et al.[8]

Patients with FES can present with a range of nonspecific findings, including restlessness, acute anxiety, and drowsiness.[1] Before 2015, CFES had not been documented as a cause of acute status epilepticus in an adult patient,[6] despite the known relationship between acute status epilepticus and cerebrovascular accidents.[10] The present case highlights the rarity of such a presentation as well as the therapeutic dilemma faced by practitioners confronted by rSE. According to the most recent guidelines from the American Epilepsy Society,[11] benzodiazepines are the initial therapy of choice for convulsive status epilepticus. Unfortunately, there is currently no evidence-based preferred second- or third-line treatment for refractory seizures though an anesthetic dose of a barbiturate, midazolam, or propofol is recommended for rSE.[12] In our patient, control of SE and burst suppression was achieved once high-dose midazolam infusion was initiated after failing dual antiepileptic therapy and propofol infusion. Gradual decrease in the dose of midazolam leading to a prolonged wean of the benzodiazepine over nearly 3 weeks prevented the recurrence of any seizure activity.

Our patient developed CFES before definitive repair of his traumatic injuries. In such a patient, treatment must be aimed at decreasing the further embolic burden from the injured bones as well as investigating and possibly closing the site of paradoxical embolization. Initially, our patient’s fractures were stabilized with an external fixation system and required definitive repair. Further investigation to locate the source of the paradoxical emboli revealed no intracardiac shunt. However, there was
evidence of intrapulmonary shunt on TEE. Asymptomatic intracardiac shunts are a common anatomical variation with the American Heart Association and the American Stroke Association recommending against closure of PFO as primary prevention for stroke.[10] However, with regard to FES, Forteza et al. documented a case of a pediatric patient with FES who was found to have a PFO. After closure of the PFO, there was a significant reduction in the number and intensity of embolic signals.[3] With the lack of correctable venoarterial shunt in our patient, multidisciplinary discussion between the critical care, trauma, and orthopedic team determined that it would be advantageous to do the definitive repair using a plating technique. There is evidence in an animal model of FES that this approach, plating instead of intramedullary nailing, decreases lung injury.[13] Intramedullary nailing is associated with increased medullary pressures and the presence of fat emboli during both reaming and nail insertion.[14] TCD has been used intraoperatively to detect embolic events during orthopedic surgery.[9] This modality was used in two ways in our patient: first as a diagnostic tool when his neurologic function declined and then as an intraoperative monitor during definitive surgical repair.

CONCLUSION

FES can occur after traumatic fractures and requires a high degree of suspicion to make the diagnosis with the available imaging and monitoring modalities. SE is a rare manifestation of FES, which requires aggressive pharmacologic management with antiepileptics and benzodiazepines to allow for good neurologic recovery.

Consent

Written informed consent was obtained for the presentation of the case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient’s health care proxy has given their consent for the images and other clinical information to be reported in the journal. The patient’s health care proxy understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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