Case Report

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Cerebral fat emboli monitoring using transcranial Doppler ultrasound and confirmation of a successful treatment response: a case report

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Fat emboli syndrome is a rare and potentially fatal condition that most commonly manifests after traumatic long-bone fractures. Cerebral fat emboli are one of the most feared complications leading to permanent neurologic injury, though methods for optimal monitoring in high-risk patients are lacking. We present a case of a 16-year-old female patient who presented to the emergency department following a motor vehicle collision with multiple injuries, including a comminuted femoral shaft and pelvic ring fracture, as well as an acute basilar artery occlusion due to fat embolism. Continuous transcranial Doppler ultrasound (TCD) of the bilateral middle cerebral arteries was utilized for emboli detection and evaluation of right-to-left shunt. The patient was found to have a high burden of microemboli on TCD in combination with a right-to-left shunt conferring increased risk of additional neurologic injury. Following surgical fixation of her orthopedic injuries, repeated TCD assessment demonstrated no further evidence of microemboli thus demonstrating efficacious response to definitive treatment. This report highlights the utility of TCD for early monitoring and detection of cerebral emboli in patients at risk for fat emboli syndrome as well as evaluating response to intervention.

Keywords: Ultrasound; Embolism; Stroke; Case reports

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INTRODUCTION

Fat embolism syndrome (FES) is a rare, potentially life-threatening condition, resulting from the release of fat globules into the microcirculation causing end-organ damage [1]. It is most commonly encountered following skeletal trauma resulting in long-bone or pelvic fractures as well as high-risk orthopedic surgical procedures such as intramedullary nailing. It is less frequently described in other conditions, including pancreatitis, liposuction, sickle cell disease, and osteomyelitis [1,2]. FES is classically characterized by respiratory failure, fever, petechial rash, and neurologic symptoms manifesting 24 to 72 hours after a precipitating

event; however, most patients do not exhibit the full spectrum of clinical findings [1]. While most patients have evidence of fat globules in their blood following long-bone fracture, the proportion who develop FES is much lower, with estimates of approximately 0.1% to 0.3% for isolated fractures, although the risk increases nearly 10-fold with multiple fractures [2,3].

One of the most worrisome complications of FES is cerebral fat embolism (CFE), which can be variable in presentation and manifest with acute altered mental status, seizures, and/or focal neurologic deficits [1]. The diagnosis of FES and CFE can be elusive and requires a high index of clinical suspicion, as there are no specific diagnostic tests with sufficiently high predictive value. Magnetic resonance imaging (MRI) is the most sensitive technique to establish a diagnosis of CFE and classically demonstrates a "starfield pattern" with widespread nonconfluent microinfarcts throughout the bilateral hemispheres [4]. While MRI is a useful modality for diagnosis of CFE, it is incapable of predicting the risk of recurrent embolism. In contrast, transcranial Doppler ultrasound (TCD) provides a portable and noninvasive diagnostic approach for assessing CFE in real time. Prior investigations using TCD for CFE detection in long-bone fractures have found a high frequency and intensity of emboli, particularly in patients with a patent foramen ovale (PFO), which are directly correlated with risk of developing neurologic symptoms [5,6]. Given these advantages, screening high-risk trauma patients with point of care TCD may allow for early detection, risk stratification, and timely interventions in patients with CFE.

We report the case of an otherwise healthy 16-year-old female patient who presented following a motor vehicle collision with femur and pelvic fractures leading to CFE/FES with large vessel occlusion (LVO). TCD was utilized to diagnose ongoing emboli and demonstrated resolution after definitive treatment with fracture fixation.

CASE REPORT

The patient was an otherwise healthy 16-year-old female patient who presented to the emergency department following a high-speed motor vehicle collision. The patient received a chest needle decompression in the field for presumed pneumothorax. Upon arrival to the emergency department, she was found to have a Glasgow Coma Scale of 3 and was intubated emergently for airway protection. She subsequently had bilateral chest tubes placed in the setting of shock and was resuscitated with an appropriate hemodynamic response.

A full trauma workup revealed a left femoral shaft comminuted fracture (Fig. 1A), complete zone 2 sacral fracture, lateral compression type 1 pelvic ring injury, multiple rib fractures, mandible fracture, and a C1 fracture with atlanto-occipital dislocation. Head computed tomography (CT) demonstrated subarachnoid hemorrhage at the basal cisterns, intraventricular hemorrhage, and diffuse cerebral edema. A CT angiogram of the head and neck was performed and showed an LVO of the basilar artery. The patient was then taken emergently to interventional neuroradiology for mechanical thrombectomy with successful recanalization of the basilar artery through residual right posterior cerebral artery occlusion (Fig. 1B). The clot appeared to be composed of adipose-like tissue. An external ventricular drain was placed given severe traumatic brain injury with initial low pressure. The patient was subsequently taken emergently to surgery for an occiput to C2 posterior spinal fusion for atlanto-occipital dislocation.

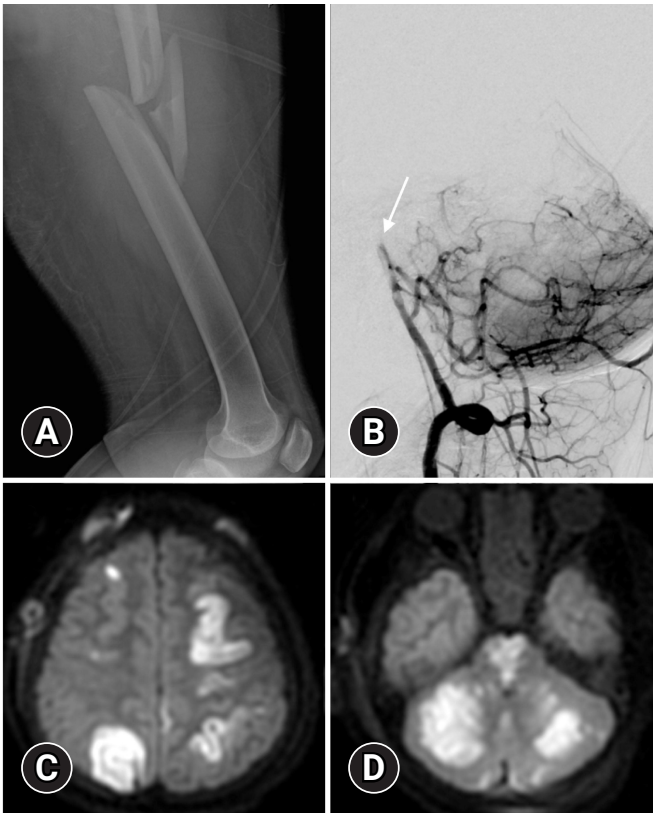

Fig. 1. Multimodal imaging findings. (A) Acute comminuted left femoral shaft fracture. (B) Large vessel occlusion (arrow) in the mid basilar artery on digital subtraction angiography. (C) Multiple areas of diffusion restriction in the supratentorial brain on magnetic resonance imaging, consistent with cytotoxic edema. (D) Diffusion-weighted imaging signal abnormalities in the paramedian pons and bilateral cerebellar hemispheres on magnetic resonance imaging.

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CFE was considered the likely mechanism of the basilar artery occlusion in the setting of long-bone and pelvic fractures, as well as evidence of fat material in the retrieved basilar thrombus. Prolonged TCD monitoring of the bilateral middle cerebral arteries (MCAs) was performed on hospital day 2 to evaluate the risk of ongoing embolization and demonstrated bilateral spontaneous microembolic signals (MES; 14 MES over 30 minutes; range, 7–14 dB) suggesting a proximal source (Fig. 2). Subsequent TCD evaluation on hospital day 3 demonstrated ongoing MES in the bilateral MCAs (10 MES over 30 minutes; range, 7–15 dB). A transthoracic echocardiogram (TTE) was performed with agitated saline to evaluate for PFO; however, it demonstrated no evidence of an intracardiac shunt.

A repeat CT demonstrated new evolving multifocal infarcts involving the right parietal, left frontoparietal and cerebellum consistent with embolic cerebral infarcts. Given the evidence of new multifocal embolic infarcts, the absence of other vascular injuries, and TCD demonstrating continuous MES in the bilateral cerebral hemispheres, CFE was felt to be most likely in the setting of her multiple orthopedic injuries. The patient was then taken for expedited closed reduction of the femur fracture, as well as closed reduction and percutaneous fixation of the pelvic ring injury on hospital day 5 to reduce the risk of further fat embolization. Repeat TCD obtained on hospital days 6 and 7 following fracture stabilization demonstrated a complete absence of MES in the bilateral MCAs, suggesting a successful treatment response (Fig. 3). A TCD study with agitated saline was also performed following surgery to evaluate for right-to-left shunt (RLS) and confirmed the presence of a grade II shunt despite a repeat TTE continuing to find no evidence of PFO.

Despite evidence for resolution of CFE, the patient's examination remained poor and notable for absent eye opening and flexor posturing to noxious stimuli. A brain MRI was obtained on hospital day 6 demonstrating multifocal ischemic strokes involving the brainstem in addition to bilateral cerebellar, occipital, frontoparietal and thalamic structures (Fig. 1C, D). In the setting of substantial neurologic injury and after extensive family meetings with palliative care, the family decided to pursue comfort care measures and she died following compassionate extubation.

Ethics statement

Informed consent for publication of the research details and clinical images was obtained from the legally authorized representative of the patient.

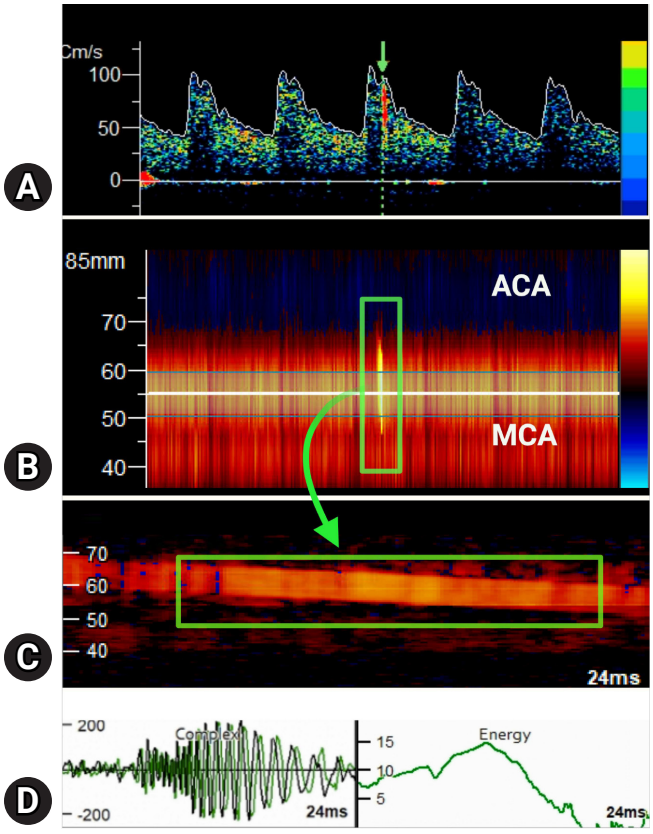

Fig. 2. Transcranial Doppler ultrasound (Viasonix Dolphin/XF, Imaging Monitoring USA) results. (A) Transcranial Doppler spectral waveform of the left middle cerebral artery (MCA) obtained via transtemporal approach with a high-intensity transient signal (HITS) noted (arrow). (B) Power M-mode with a red band extending from 35 to 65 mm denoting anterograde blood flow in the MCA and a blue band extending from 65 to 75 mm denoting retrograde flow in the anterior cerebral artery (ACA). Note the HITS in green box, which is brief (<0.3 seconds) and unidirectional (slightly negatively slanted orientation, reflecting movement towards probe over time as blood flows laterally through MCA). (C) High-resolution M-mode allows further characterization of HITS (green box) at 24 msec resolution to confirm that the signal is unidirectional along its entire length, increasing the likelihood that it reflects true microemboli and is not an artifact (D) Complex velocity analysis demonstrates matching Doppler shift frequencies for HITS (green waveform) and blood flow (black waveform) suggesting that both are in-phase, increasing the likelihood of a true embolic signature rather than an artifact. Energy measurement showing that the event is of sufficiently high intensity (15 dB) to be consistent with microembolic signal.

DISCUSSION

Patients with CFE may present with a constellation of neurologic symptoms either in isolation or in combination with other end-organ damage related to FES. The precise pathophysiologic mechanisms underlying FES remain elusive, although two mod-

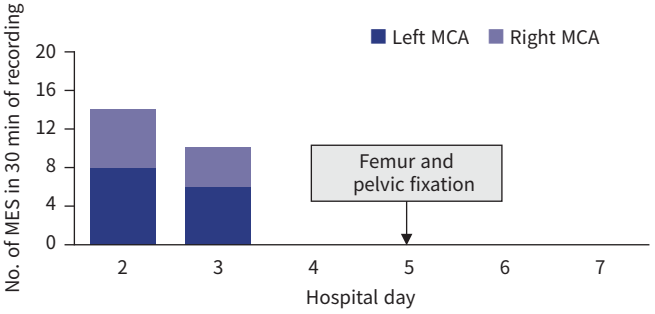

Fig. 3. Chronological graph of transcranial Doppler ultrasound findings in the right and left middle cerebral artery (MCA) by hospital day. Recordings performed on hospital days 2, 3, 6, and 7. Surgical fixation occurred on hospital day 5. MES, microembolic signals.

els predominate. The mechanical theory hypothesizes that the traumatic release of fat particles into the venous system enters the systemic circulation via intracardiac or pulmonary shunts, causing vasculature occlusion and tissue ischemia [7]. The biochemical theory, in contrast, proposes that increased lipase levels following trauma lead to catalyzation of fat globules into free fatty acids in the bloodstream, which pass through the pulmonary vasculature and cause endothelial damage with resulting microthrombi formation and a widespread inflammatory response [1,7]. The latter model likely better accounts for the typical delay in systemic manifestations, including acute respiratory distress syndrome and diffuse petechial rash, following an inciting event and provides a rationale for the development of neurologic symptoms even in the absence of an RLS.

While the full spectrum of clinical manifestations related to FES can likely be explained by an overlap of these two mechanisms, the occurrence of an acute presentation with LVO is almost certainly related to shunted macroembolic material. Compared to classic CFE neuroimaging findings of diffuse punctate infarcts throughout the subcortical white matter suggestive of microvascular cytotoxic injury, fat emboli–related LVO, such as in our patient's case, has been rarely reported in the literature and results in blockage of a major cerebral artery with symptoms of acute stroke. In a recent meta-analysis, 18 cases of LVO related to CFE were identified, and in contrast to typical features of FES, 77% experienced neurologic symptoms within 6 hours of the injury and rarely exhibited other systemic manifestations of FES [8]. Furthermore, the majority of patients screened had evidence of PFO, further supporting the role of fat macrothrombi shunting into the systemic circulation, resulting in mechanical occlusion of the cerebral vasculature. Although the overall mortality of FES is approximately 10%, with a large proportion achieving functional recovery within a year even after presenting with coma or posturing, LVO cases appear to be associated with more severe neurologic injury, often necessitating aggressive intervention including decompressive hemicraniectomy for management of malignant cerebral edema, with a higher likelihood of mortality (Table 1) [8–17]. Though limited to case reports, urgent recognition and revascularization via endovascular thrombectomy is the favored approach for LVO due to fat emboli, with some reports of good functional outcomes [8,14,17].

For patients presenting with CFE outside of an LVO, the management is largely supportive and focused on optimizing hemodynamics and respiratory status. Given their potent anti-inflammatory properties, prophylactic corticosteroids have been widely studied and appear to decrease the incidence of FES, though notably without a mortality benefit, and their use remains controversial due to increased risk of infection, delayed wound healing, and metabolic derangements [18]. The most well-established intervention to decrease the incidence and severity of FES is early immobilization and fixation [19]. Although circulatory levels of fat emboli transiently increase during closed manipulation and surgical fixation, evidence suggests the risk of FES increases by over twofold when the time to operation is delayed longer than 24 hours [1,2,19]. However, certain trauma patients may not be stable enough for expedited orthopedic surgery, for example, those patients with significant polytrauma or severe traumatic brain injury, contributing to delays in the definitive management of skeletal injuries. In these cases, risk-stratifying based on CFE burden would be invaluable to identify patients at the highest risk for neurologic deterioration.

While several clinical criteria exist for FES, none are designed to predict the risk of CFE, and no diagnostic modalities are widely utilized to predict the occurrence of cerebral ischemia [20]. TCD monitoring is highly efficacious for detection of spontaneous microemboli entering the cerebral circulation and has been validated to predict ischemic stroke risk in a variety of conditions, including carotid stenosis, blunt cerebrovascular injury, infective endocarditis, and cardiac thrombus [21]. MES are defined as high-intensity transient signals at least 3 dB greater than the spectral background, short duration (< 300 msec) and unidirectional, in keeping with the direction of blood flow in the parent vessel (Fig. 2) [21]. TCD is well suited for the critical care setting as it is portable and noninvasive; furthermore, with recent innovations in robotic headset technology, prolonged continuous monitoring is feasible even without experienced operators for real-time cerebral hemodynamic assessment and evaluation of embolic events. Furthermore, TCD possesses nearly three times higher sensitivity for PFO assessment compared to TTE, as ex-

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Table 1. Cases of cerebral fat emboli with large vessel occlusion

Study	Age (yr)	Sex	Presumed etiology	Timing of symptom onset	Imaging finding	Presence of shunt	Treatment	Outcome
van Oostenbrugge et al. [9] (1996)	40	Female	Intramedullary fixation in the setting of pathologic fractures from metastatic adenocarcinoma	Immediately post-operatively	Malignant cerebral edema throughout the left MCA territory	PFO detected on autopsy	Supportive care	Herniation and death
Wang et al. [10] (2009)	52	Female	Sternotomy for mechanical mitral valve replacement	Within 24 hr of operation	Hypodensity in right MCA	Not reported	Not reported	Died 2 days after injury
Kellogg et al. [11] (2013)	58	Male	Mechanical fall with intertrochanteric femoral fracture	6 hr after hospital admission	Malignant cerebral edema throughout the right MCA territory with midline shift	Not reported	Initial supportive care, decompressive hemicraniectomy	Tracheostomy gastrostomy tube and left hemiplegia 6 mo after injury
Piuzzi et al. [12] (2014)	80	Male	Femoral revision surgery	15 min after arrival to recovery room	Hypodensity in the right MCA, post-procedure CT noted hemorrhagic transformation and mass effect	PFO detected on TEE	Intraarterial thrombolysis and mechanical thrombectomy	Discharged with hemiparesis and cognitive impairment though died 3 mo later
Avila [13] (2017)	70	Female	Sternotomy for aortic valve replacement	Immediately post-operatively	Hypodensity in the right MCA, cerebral edema and herniation	Not reported	Decompressive hemicraniectomy	Discharged to nursing home and died of cardiac arrest 1 mo later
Maier et al. [17] (2019)	56	Male	Right knee replacement	Immediately post-operatively	Hypodense left MCA	PFO with septal aneurysm detected on TTE	Endovascular thrombectomy of left MCA	Good recovery
Fowler et al. [14] (2021)	70	Male	Motor vehicle collision (no discernable fracture)	Immediately following trauma	Right MCA territory infarct	Not reported	Endovascular thrombectomy of right ICA and MCA	Mild left hemiparesis, discharged to home
Koh et al. [15] (2021)	91	Female	Femur fracture with hemiarthroplasty	Immediately post-operatively	Hypodense right MCA with surrounding edema and loss of gray-white differentiation	Not reported	Supportive care	Died 1 wk after injury
Ooi et al. [8] (2021)	71	Male	Elective knee replacement	Immediately post-operatively	Large-territory left MCA infarct with hemorrhagic transformation	Large detected PFO on TEE	Endovascular thrombectomy of left MCA	Persistent global aphasia and right hemiparesis at 60 days
	47	Male	Sternotomy for mechanical mitral valve replacement	48 hr after surgery	Bilateral occipital and cerebellar infarcts	None detected on TTE	Endovascular thrombectomy and stenting of basilar artery	Regained ability to walk at 12 mo from stroke
	69	Female	Intertrochanteric femoral fracture with intramedullary nailing	Immediately post-operatively	Extensive left MCA territory infarct with microhemorrhages and cerebral edema	PFO detected on TTE	Hyperbaric oxygen and dexamethasone, decompressive hemicraniectomy	Died while hospitalized
Kamal et al. [16] (2024)	69	Female	Mechanical fall with femur fracture and ORIF	Immediately post-operatively	Left MCA territory infarction with cerebral edema	Not reported	Supportive care	Died while hospitalized

MCA, middle cerebral artery; PFO, patent foramen ovale; CT, computed tomography; TTE, transthoracic echocardiography; ICA, internal carotid artery; ORIF, open reduction and internal fixation.

hibited in our patient, making it an ideal diagnostic modality for noninvasive detection of RLS when evaluating the risk of paradoxical emboli [22].

Prior investigations by Forteza et al. [5,6] demonstrated that spontaneous MES on TCD were common in patients with long-bone fractures and that a combination of RLS, high frequency of MES (>4 per hour), and high signal intensity (>13 dB) was highly predictive of developing neurologic symptoms (positive predictive value 86%, negative predictive value 97%). Furthermore, TCD characterizes the embolism size in FES, which correlates with risk of neurologic deficits, as patients with RLS on average have higher signal intensities, suggestive of a larger mass, than those without a shunt [5,23]. In our patient, the persistent elevation in MES frequency (10–14 over 30 minutes) with high intensity (7–15 dB) in combination with radiographic evidence of new cerebral infarcts justified surgical fixation to mitigate the risk of further cerebral injury. Ideally, the presence of persistent MES in this clinical setting could be used to proceed with surgical fixation before significant cerebral injury occurs. Another benefit of daily TCD assessment is the evaluation of response to intervention. Our case is the first to characterize the resolution of microemboli on TCD following surgical fixation of fractures in FES, thus confirming an efficacious treatment response. Other investigations have reported similar utility of TCD emboli detection to gauge response to initiation of anticoagulation in cerebrovascular dissection as well as confirming successful PFO closure [23,24].

In summary, we report a case of FES following skeletal trauma with CFE initially presenting with basilar LVO requiring thrombectomy. Although the patient ultimately died due to substantial neurologic injury related to their initial brainstem ischemic stroke, the case highlights the utility of TCD microemboli detection in critically ill patients at risk of FES to gauge risk of cerebral embolic events as well as to confirm the response to definitive therapy.

ARTICLE INFORMATION

Author contributions

Conceptualization: RM, IN, CC, JRV; Investigation: MJ, HN, KR, AA, JRV; Methodology: MJ, JRV; Visualization: HN, KR, AA; Writing–original draft: MJ, JRV; Writing–review & editing: RM, IN, CC, JRV. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Data availability

Data sharing is not applicable as no new data were created or analyzed in this study.

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