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Fat embolism following traumatic injury with cerebral embolism and stroke in the presence of a patent foramen ovale

L. DeLong[1], J. D. Tobias[2,3]

[1]Heritage College of Osteopathic Medicine - Athens Campus, Athens, Ohio and Ohio University, USA
[2]Department of Pediatrics and the Division of Pediatric Critical Care Medicine, Nationwide Children's Hospital and the Ohio State University, Columbus, Ohio, USA
[3]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio; USA

Corresponding author: J. D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital, The Ohio State University College of Medicine, Columbus, Ohio, USA. E-mail: Joseph.Tobias@nationwidechildrens.org

Keypoints

1. Fat embolism syndrome (FES) includes a constellation of clinical signs and symptoms including hypoxemia, respiratory failure, petechial rash, and pyrexia.
2. FES occurs most commonly following orthopedic surgical procedures or trauma involving the femur or tibia.
3. A patent foramen ovale increases the incidence of embolic stroke following FES due to the potential for right-to-left shunting and paradoxical emboli.
4. Treatment of FES relies primarily on supportive care of the end-organ involvement with the primary goal being resuscitation and stabilization. PFO closure may be indicated to prevent the potential for recurrent paradoxical emboli.

Abstract

Fat embolism syndrome (FES) most commonly occurs 24-48 hours following trauma or orthopedic surgery. The signs and symptoms of FES are often difficult to identify or may be attributed to the primary event or a comorbid condition. Clinical manifestations vary depending on the clinical scenario, generally including hypoxemia, respiratory insufficiency, a petechial rash, and fever. We report a 13-year-old adolescent who presented with multiple end-organ effects including an embolic stroke in the presence of a patent foramen ovale related to FES following traumatic injury and orthopedic surgery. The proposed pathophysiological mechanisms and etiology of FES are reviewed, diagnostic criteria and work-up presented, and therapeutic interventions discussed.

Keywords

Fat embolism, fat embolism syndrome, trauma, patent foramen ovale

Introduction

Fat embolism syndrome (FES) was originally described in 1873.[1] Since then, clinical reports have demonstrated its occurrence in various clinical scenarios including orthopedic surgery, traumatic injury, and less frequently in non-trauma scenarios such as diabetes mellitus, pancreatitis, high dose corticosteroid therapy, and sickle cell disease.[2-5] Clinical manifestations vary significantly based on the clinical scenario and may include hypoxemia, respiratory failure, petechial rash, and pyrexia. In patients with severe systemic illnesses or trauma, the clinical manifestations may be difficult to detect or attributed to

the primary event or other comorbid conditions. We present a 13-year-old adolescent who presented with multiple end-organ effects including an embolic stroke in the presence of a patent foramen ovale related to FES following traumatic injury and orthopedic surgery. Diagnostic criteria for FES are presented, diagnostic work-up reviewed, and treatment algorithms discussed.

Case report

Review of this case and presentation in this format is in accordance with the guidelines of the Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio). The patient was a 13-year-old male who presented with multi-trauma while riding an all-terrain vehicle (ATV) that collided with a truck. The patient was not wearing a helmet. The patient had no significant past medical or surgical history prior to trauma. Due to the severity of the injury, endotracheal intubation occurred in the field prior to arrival in the emergency department (ED). On arrival to the ED, the patient's vital signs were stable and his Glasgow Coma Score (GCS) was 3T. The initial trauma survey showed diffuse bruising, facial and leg swelling, and diminished breath sounds on the right. A chest tube was placed for a right-sided pneumothorax. Additional injuries included a laceration of the kidney and liver, a grade 3 diffuse axonal injury to the brain, bilateral pulmonary contusions, a subdural hematoma along the left posterior falx and right tentorium, subarachnoid hemorrhage, subgaleal hematoma, right metacarpal fractures, and an open right femur fracture. The patient was admitted to the Pediatric ICU where intermittent hypotension was corrected with fluids before going to the OR for irrigation and debridement with placement of an external fixator to correct for the 6 cm. bone loss in the diaphysis of the right femur. A change in mental status, decreased responsiveness to painful stimuli, and left-sided hemiparesis, which were noted the morning following the operative procedure on the right femur, prompted investigation with computed tomography (CT) followed by magnetic resonance imaging. These studies revealed an embolic infarct in the right cerebellar hemisphere. Because of the concern for an embolic stroke, a transthoracic echocardiogram was obtained, which demonstrated a patent foramen ovale (PFO). The etiology of the stroke was suspected to be a fat emboli considering the PFO, traumatic event, and recent orthopedic procedure. One week following the injury, the patient was taken to the cardiac catheterization suite for percutaneous transcatheter closure of the PFO. Over the subsequent weeks, the patient's mental status, respiratory and cardiac status improved. His trachea was extubated and he was transferred to a long-term rehabilitation hospital. He was discharged home 2 months after the initial traumatic event. There was no residual focal neurologic deficits related to the embolic event. He is being followed-up in various outpatient clinics to ensure ongoing recovery from his orthopedic and traumatic CNS injuries.

Discussion

Although fat embolism and its clinical sequelae were first described in the literature over a century ago, there remains ongoing controversy regarding its pathophysiology.[1] The first mention of fat embolism was in 1664 from animal studies investigating the effects of the intravenous injection of fat on the body, which demonstrated the presence of fat globules in the pulmonary vessels.[1] In 1862, Zenker identified the presence of pulmonary fat emboli in a patient who died following a severe crush injury.[1] Shortly thereafter, Wagner was the first to correlate bone fractures with the development of fatty emboli in a cohort of 48 adults with long bone fractures who developed systemic signs and symptoms of FES.[5] The first clinical diagnosis of fat embolism syndrome (FES) was in 1873 when an autopsy report revealed a massive pulmonary fat embolism in a trauma patient who sustained a fractured femur following a fall from a roof.[1,5] The patient experienced dyspnea, cyanosis, hemoptysis, lethargy, and eventually became comatose immediately before death.[5]

FES has a nonspecific and variable clinical pattern consisting of a petechial rash, diffuse pulmonary infiltrates, hypoxemia, confusion, pyrexia, tachycardia, and tachypnea within 24-48 hours following trauma or orthopedic

surgery.[6,7] In 1974, Gurd and Wilson proposed major and minor criteria for the diagnosis of FES (table 1).[4] From Gurd and Wilson's criteria, a diagnosis of FES is suggested by the presence of at least one major criteria along with 4 minor criteria plus a laboratory feature of fat macroglobulinemia (the presence of large fat globules in circulation). However, fat macroglobulinemia was subsequently noted to be an unreliable finding in the diagnosis of FES due to the presence of large fat globules in healthy patients and in patients with fractures without the other signs and symptoms of FES.[4] In addition to the major and minor criteria, other laboratory findings that may further support FES include anemia, thrombocytopenia, and an elevated erythrocyte sedimentation rate.[4]

Table 1: Gurd and Wilson's Criteria for Fat Embolism Syndrome[4]

1. Major criteria
    a. Respiratory insufficiency
    b. Cerebral involvement
    c. Petechial rash
2. Minor criteria
    a. Pyrexia
    b. Tachycardia
    c. Retinal changes
    d. Jaundice
    e. Renal changes
3. Laboratory features
    a. Anemia
    b. Thrombocytopenia
    c. High erythrocyte sedimentation rate
    d. Fat macroglobulinemia

The ambiguity of the major features of FES and the potential that this may result in a missed diagnosis of FES have led to additional critiques and suggested modifications of the Gurd and Wilson criteria.[6,7] Lindeque et al further defined the respiratory insufficiency to include a sustained PaO_2 less than 60 mmHg, sustained $PaCO_2$ greater than 55 mmHg or pH less than 7.30, sustained respiratory rate greater than 35 breaths/minute after adequate sedation, and increased work of breathing indicated by the use of accessory respiratory muscles, dyspnea, tachycardia combined with anxiety.[7] Although a petechial rash has limited value in the diagnosis of FES because of its low incidence, its relatively short duration, and its potential to be missed, it is considered to be the only reliable criteria in patients under general anesthesia or those receiving sedation as respiratory insufficiency and CNS changes may not be readily noted or attributed to other features.[5-8] This was likely the case in our patient, in whom the diagnosis was delayed as mechanical ventilation and the need for sedation masked the CNS findings (hemiparesis) of the paradoxical embolism and stroke.

The majority of clinical scenarios involving fat embolism include patients who have undergone orthopedic surgery or trauma. Non-traumatic scenarios that may lead to fat embolism include diabetes mellitus, pancreatitis, high dose corticosteroid therapy, sickle cell disease, and liposuction.[5,6] Fat embolism has been estimated to occur in 90% of patients with long bone fractures or patients who have sustained multiple traumatic injuries.[5] In the majority of patients, despite the documentation of fat emboli during orthopedic surgical procedures, there are limited clinical sequelae.[9,10]

There are multiple theories that describe the potential pathophysiology behind the clinical presentation of FES. The *infloating/mechanical theory* suggests that fat can be forced out of the marrow into venous circulation with disruption of the intramedullary cavity during surgical procedures that create shear-mechanical pressure gradients exceeding 600 mmHg.[2] The resulting shower of fat emboli may coalesce forming thrombotic masses, pulmonary emboli, and/or right ventricular outflow tract obstruction.[2] It is suggested that the fat emboli travel through arteriovenous shunts to the systemic circulation including the brain.[2] The *free fatty acid and lipase theories* suggests an elevation of serum biochemical markers results in the formation of microscopic fat globules, fat emboli, and the initiation of an inflammatory process with vasculitis that damages pneumocytes and capillaries, leading to widespread end-organ involvement.[2,5] The *shock and coagulation theory* suggests that the hypovolemic nature of trauma patients results in altered circulation with a low flow state causing microaggregates to form in the lungs.[2] The resultant vascular damage from altered circulation leads to the activation and adherence of platelets to the bone marrow fat particles, which

further activates the coagulation cascade, potentially leading to circulatory collapse via a thromboembolic phenomenon.[2,5] Regardless of the exact mechanisms involved and although the process is initiated on the venous side of the circulation, it becomes systemic with multiple end-organ effects including those related to the CNS even in the absence of a PFO resulting in right-to-left shunting and paradoxical emboli.[11]

Fat embolism most commonly occurs following trauma with the onset of neurological symptoms, hypoxemia, and petechial rash generally within 24-48 hours after the event.[6,8] Anecdotal evidence in pediatric patients suggest an earlier progression within 2-4 hours of the event complicated by a rapid decline in mental status, cerebral edema, and unexplained hypoxemia.[11,12] The clinical sign most commonly described in patients with FES include respiratory insufficiency, usually occurring during the initial 12-24 hours.[8] These initial signs and symptoms including dyspnea, tachypnea, and hypoxemia may be missed because of the overlap with the symptomatology of acute lung injury.[8] Cerebral involvement typically presents concurrently with respiratory symptoms while a petechial rash may or may not be present in every patient with FES.[8]

In our patient, the initial signs and symptoms related to the respiratory and central nervous system were masked by the associated traumatic event and the use of sedative agents in the ICU setting during mechanical ventilation. However, CT and MR imaging obtained due to the eventual identification of left-sided paresis revealed an embolic stroke with areas of diffusion restriction within the right cerebellar hemisphere. Echocardiography demonstrated the presence of a PFO. Based on the clinical presentation, it was postulated that the CNS involvement was related primarily to paradoxical embolism through the PFO following a shower of fat emboli into the venous circulation from the femur fracture.

The presence of a PFO in patients with FES has been previously demonstrated to be a poor prognostic factor as it increases the risk for arterial emboli and severe neurological sequelae.[13,14] In these patients, surgical or device closure may be indicated to reduce the likelihood of a recurrent stroke.[15] In our patient, PFO closure was chosen as the stroke was indicative of a paradoxical embolism and future surgical procedures were likely necessary due to the associated orthopedic injuries. Given the potential for emboli during long bone surgery, the decision was made for device close of the PFO prior to these procedures to decrease the risk of paradoxical emboli.[13-15] In general, the treatment strategies for FES mainly rely on supportive measures with the primary goal of resuscitation and stabilization.[2] Early fixation of fractures is recommended to decrease the potential for subsequent emboli.[2,5] FES can manifest as multiple end organ effects, most commonly respiratory and CNS involvement.[2,8] The clinical signs and symptoms of FES are generally nonspecific and in the trauma or critically ill patient may be attributed to other causes including the primary event. As such, a high index of suspicion is needed in at risk patients.[16] Anecdotal evidence has suggested the potential efficacy of various therapeutic agents including corticosteroids, alcohol, dextran or heparin to stimulate lipase activity; however, there is limited prospective evidence-based medicine to support these interventions.[2,16]

In summary, we report a 13-year-old patient who presented with multiple injuries including long bone fractures following trauma and orthopedic surgery. The development of left-sided hemiparesis prompted CNS imaging that demonstrated an emboli stroke, which was attributed to FES. Further evaluation with transthoracic echocardiogram revealed a PFO. Because of the presence of paradoxical emboli and the need for future surgical procedures, device closure of the PFO was performed. Although CNS symptoms may occur with FES, they are generally thought to be a part of the systemic inflammatory response.[2] The presence of a PFO presents a unique scenario where paradoxical emboli may result in significant CNS involvement with FES.

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