

REVIEW

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FAT EMBOLISM AND FAT EMBOLISM SYNDROME; MANAGEMENT TRENDS

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ABSTRACT... Fat Embolism and the associated Fat Embolism Syndrome is a serious and potentially life threatening condition. It tends to occur usually after fractures or intramedullary instrumentation of long bones. Non-traumatic conditions such as Diabetes Mellitus severe Burns, SLE, sickle cell disease and Pancreatitis can also lead to Fat Embolic syndrome. Young adults are commonly affected. Presentation consists of an asymptomatic interval followed by pulmonary and neurological manifestations combined with petechial haemorrhages. The diagnosis largely depends on high index of suspicion and exclusion of other conditions. Treatment of this condition remains supportive. Mortality associated with this condition is significant, ranging from 10-20%¹.

Key words: Fat embolic syndrome, FES, fat emboli, fat embolus, fat droplet in venous system, blunt trauma, fracture complication, altered mental status.

INTRODUCTION

Fat embolism syndrome most commonly follows long bone fractures². In 1862, Zenker first described this syndrome at autopsy. In 1873, von Bergmann clinically diagnosed fat embolism syndrome for the first time³. Exact incidence is not known. In retrospective reviews, incidence of FES is less than 1%. However, there is a greater incidence reported in prospective studies of 11-29%.

Classically it presents with asymptomatic interval followed by pulmonary, neurologic and skin

manifestations. It has a biphasic clinical course. The initial symptoms are probably caused by mechanical occlusion of blood vessels with fat globules that are too large to pass through the capillaries. Unlike other embolic events, the vascular occlusion in fat embolism is often temporary or incomplete since fat globules do not completely obstruct capillary blood flow. The late presentation is due to hydrolysis of the fat to more irritating free fatty acids which then migrate to other organs via the systemic circulation⁴.

There exists many controversies regarding diagnostic

protocols, role of investigations and treatment; so a review of available literature is being presented.

Pathophysiology

Mostly, the fat embolism occurs after blunt trauma complicated by long-bone fractures, but it has also occurred in association with acute pancreatitis⁵, diabetes mellitus, burns, joint reconstruction, liposuction, cardiopulmonary bypass, decompression sickness and parenteral Infusion of lipids, sickle cell crisis. Although it occasionally causes multi system dysfunction, the lungs are always involved and next is brain⁶.

Fat embolism syndrome is a poorly understood subject, there are controversies about its causation, pathophysiology, diagnosis and treatment. It is therefore difficult to determine the incidence of this disorder. It is most common after skeletal injury, and is most likely to occur in patients with multiple long bone and pelvic fractures, orthopedic procedures like reaming for intramedullary nailing⁷, hip and knee replacements when cement is injected⁸, resulting in increased pressure in the marrow canal⁹. In Patients undergoing nailing for fractures of long bone, Unreamed nailing and reamed nailing of the medullary cavity stand equal chances of developing pulmonary fat embolism¹⁰. Patients with fractures involving the middle and proximal parts of the femoral shaft are more likely to suffer. Fat embolism and FES are more in closed, rather than open fractures. Multiple fractures release a greater amount of fat into the marrow vessels than do single fractures, increasing the likelihood of FES¹¹. Age also seems to be a factor in the development of FES: Young men with fractures are at increased risk.

The mechanical theory: The initial symptoms are probably caused by mechanical occlusion of multiple blood vessels with fat globules that are too large to pass through the capillaries. Unlike other embolic events, the vascular occlusion in fat embolism is often temporary or incomplete since fat globules do not completely obstruct

capillary blood flow because of their fluidity and deformability^{12,13}.

The biochemical theory: Free fatty acids are toxic to pneumocytes and capillary endothelium in the lung, causing interstitial hemorrhage, edema and chemical pneumonitis; while coexisting shock, hypovolemia and sepsis, reduce liver flow and facilitate the development of FES by augmenting the toxic effects of free fatty acids.

Pulmonary Changes: are usually the earliest manifestations. These are seen in 75% of cases and progress to respiratory failure in about 10%. These include tachypnoea, dyspnoea and cyanosis. Hypoxaemia may be detected hours before the onset of respiratory symptoms. The "shock lung syndrome," whenever associated with trauma, is probably in part the consequence of fat emboli, though aspiration, disseminated intravascular coagulation, microatelectasis, pulmonary edema, and hemorrhage due to other lung insults may be important in the etiology of many cases.

Neurologic signs: are seen in 86% of patients and are usually nonspecific. These ranges from acute confusion, headache, stupor, coma, rigidity or convulsions. Cerebral edema leads to neurological deterioration¹⁴.

Dermatological Changes: A reddish brown petechial rash within 24-36 hours appears, distributed to the upper body, chest, neck, upper arm, axilla, shoulder, oral mucous membranes and conjunctivae is considered to be a pathognomonic sign of FES. It vanishes within seven days. It results from occlusion of dermal capillaries by fat and increased capillary fragility. The distribution is theorized to be related to fat particles floating in the aortic arch like oil in water and are embolized to non dependent skin areas via subclavian or carotid arteries.

Other signs: like tachycardia and pyrexia may occur but are non specific. Retinal changes include exudates, cotton wool spots, edema, haemorrhage, or intravascular

fat globules. Renal changes may present as lipuria while hepatic changes as jaundice.

Fat embolism is a clinical diagnosis. Many patients are likely to have a missed diagnosis because of subclinical illness or concurrent injury or illness. Patients with increased age, multiple underlying medical problems, and/or decreased physiologic reserves have worse outcomes than other patients.

Clinical Presentation

A thorough knowledge of the signs and symptoms of the syndrome and a high index of suspicion are needed if the diagnosis is to be made.

An asymptomatic latent period of about 12-48 hours precedes the clinical manifestations. The fulminant form presents as acute cor pulmonale, respiratory failure, and/or embolic phenomena leading to death within a few hours of injury.

Clinical fat embolism syndrome presents with tachycardia, tachypnea, elevated temperature, hypoxemia, hypocapnia, thrombocytopenia, and occasionally mild neurological symptoms¹⁵.

A petechial rash that appears on the upper anterior portion of the body, including the chest, neck, upper arm, axilla, shoulder, oral mucous membranes and conjunctivae is considered to be a diagnostic sign of FES. However, it appears late and often disappears within hours. It results from occlusion of dermal capillaries by fat and increased capillary fragility¹⁶.

CNS signs, including a change in level of consciousness, are not uncommon. They are usually nonspecific and have the features of diffuse encephalopathy: acute confusion, stupor, coma, rigidity, or convulsions. Hypoxemia is present in nearly all patients with FES, often to a paO_2 of well below 60 mmHg. Arterial hypoxemia in these patients has been attributed to

ventilation-perfusion inequality and intrapulmonary shunting. Acute cor pulmonale is manifested by respiratory distress, hypoxemia, hypotension and elevated central venous pressure. Increased alveolar to arterial oxygen gradient and neurologic deficits, including coma, may last days or weeks¹⁷.

Differential Diagnosis

A careful search for infectious agents and possibly the institution of empiric antibiotics are necessary until an infectious source is ruled out.

The differential diagnosis includes pulmonary embolism, cardiac or pulmonary contusion, septic shock, hypovolemia, intracranial injury, aspiration pneumonitis, ARDS and transfusion reactions.

Medicolegal aspects: Assuming altered mental state, fever, and hypoxia are due to fat embolism, the lack of a search for treatable or life threatening disorders before making the diagnosis may lead to litigation if such a disorder is discovered later. CT scan of the head is necessary to rule out intracranial pathology.

Diagnosis

Clinical examination is still the preferable diagnostic method in fat embolic syndrome as there is no universal criteria used for diagnosis; which is always made on clinical grounds. Various criteria were proposed as Gurd has classified major and minor criteria for.

Major Criteria: Axillary/subconjunctival petechiae, Hypoxemia ($PaO_2 < 60$ mmHg; $FiO_2 < 0.4$, Central Nervous System depression, Pulmonary edema

Minor Criteria: Tachycardia (> 120 /minute), Hyperthermia, Retinal fat emboli, Urinary fat globules, Decreased platelet count/haematocrit, Increased ESR, Fat globules in sputum

Criteria for diagnosis of fat embolic syndrome require at

least one sign from major criteria and four signs from minor criteria categories.

Schonfeld's criteria is quantitative means of diagnosing FES; petechiae 5, chest x-ray changes 4, hypoxemia ($\text{PaO}_2 < 9.3 \text{ kPa}$) 3, fever ($> 38^\circ\text{C}$) 1, tachycardia ($> 120 \text{ beats/min}$) 1, tachypnea ($> 30/\text{min}$) 1, confusion 1: cumulative score of > 5 is required for diagnosis^{18,19}.

Laboratory Studies

Laboratory tests are mostly nonspecific and there is no pathognomonic test during the course of a Fat Embolic Syndrome.

Urinary fat stains are not sensitive or specific enough for diagnosing fat embolism or for detecting a risk of it. Fat globules in the urine are common after trauma.

Thrombocytopenia, anemia, and hypofibrinogenemia are indicative of fat embolism syndrome: however, they are nonspecific. Patients often have a mild anemia. Blood lipid level is not helpful for diagnosis. Decreased hematocrit occurs within 24-48 hours and is attributed to intra-alveolar hemorrhage. There may also be alterations in coagulation and thrombocytopenia. Serum lipase level increases after bone injuries and is often misleading

During the acute phase of Fat Embolic Syndrome, there may be increase in FDPs, positive D Dimer test, thrombocytopenia and other coagulation abnormalities

Liver and renal function tests should be performed. Serum electrolytes are mandatory. Hypocalcemia may be present due to saponification of the circulating unbound free fatty acids.

Arterial blood gas: depending on the condition of patient, serial ABG's are carried to monitor treatment including fluids and oxygen therapy as well as ventilatory support.

Cytologic examination of urine, blood, CSF and sputum may detect fat globules

Bronchoalveolar Lavage with staining of alveolar macrophages fat to aid in the diagnosis or to predict possibility of fat embolic syndrome is controversial²⁰. BAL has been proposed to detect fat droplets in alveolar macrophages as a means to diagnose FES. However, the invasive nature of the procedure limits the usefulness of this technique.

The diagnostic value of noninvasive methods, like induced sputum, have not been evaluated and compared with BAL.

Imaging Studies

The classical chest x-ray of fat embolism syndrome shows multiple flocculent shadows (snow storm appearance). However, the spectrum includes a diffuse ground glass appearance. Later the picture may be complicated by infection or pulmonary edema.

CT Scan brain (plain) may be normal or may reveal diffuse white-matter petechial haemorrhages consistent with microvascular injury.

Helical CT Scan chest may be normal as the fat droplets are lodged in capillary beds. Parenchymal changes consistent with lung contusion. Acute lung injury, or ARDS may be evident.

Magnetic Resonance Imaging: Scant data exist regarding MRI findings in patients with fat embolic syndrome. Cerebral CT scan results are usually negative, while MRI, especially diffusion-weighted MRI²¹, is more sensitive. High-resolution CT (HRCT) findings of the lungs revealed bilateral ground-glass opacities and thickening of the interlobular septa, whereas in some cases centrilobular nodular opacities were present. HRCT was performed in patients in whom a clinical diagnosis of FES had been made. The specificity and sensitivity of HRCT is not

known.

ECG findings are usually normal but may show right heart strain or ischemia..

Nuclear medicine ventilation/perfusion imaging of the lungs, are essential to look for pulmonary embolism.

Transcranial Doppler sonography: can detect cerebral microembolic signals during intraoperative nailing of long bone fractures. as long as 4 days after injury.

Transesophageal echocardiography (TEE): During intramedullary reaming and nailing. Repeated showers of emboli have been noted to increase right heart and pulmonary artery pressures.

Treatment

Prophylaxis of fat embolic syndrome: Adequate immobilization of the fracture prior to transport and early operative fixation of long bone fractures.

Medical: Fat embolic syndrome is a self limiting disease. Treatment is essentially supportive, consisting of cardiovascular and respiratory resuscitation and stabilization. Maintenance of intravascular volume is important because shock can exacerbate the lung injury caused by FES. Albumin has been recommended for volume resuscitation because it not only restores blood volume but also binds free fatty acids, and may decrease the extent of lung injury. Adequate analgesia is important to limit the sympathomimetic response to injury

Other aspects of treatment include prophylaxis of deep vein thrombosis, prevention of stress related gastrointestinal bleeding, Nutrition,steroids.

No specific drug therapy for FES is currently used. High dose corticosteroids have been effective in preventing development of FES and is currently recommended. However, dose regimens were not standardized which

varies from 1..5 mg/kg methylprednisolone 8 hourly to 30 mg/kg 4 hourly

Dextrans and hypertonic dextrose , Aspirin, intravenous alcohol and Heparin: These agents may exacerbate bleeding. No clinical benefit has been conclusively demonstrated with any of these agents.

Judicious use of crystalloids, colloids, and diuretics is necessary, volume depletion may precipitate shock and organ dysfunction, but volume overload may worsen the hypoxia.

Continuous pulse oximetry monitoring in at-risk patients (i.e, those with long-bone fractures), may help in detecting desaturatives early, allowing early oxygen therapy and possibly steroids, decreasing the chances of hypoxic insult and possible systemic complications of FES. Ventilatory support and PEEP therapy may be helpful.

A dobutamine infusion 0-20 mg/kg/minute, Furosemide and Morphine 1/V, Nor-adrenaline infusion, Metaraminol mg/1/V Sodium Bicarbonate 8.4 % may be used.

Surgical: Early stabilization of long bone fractures is recommended to minimize bone marrow embolization into the venous system.

Ligation of the profunda vein has been tried in experimental animals and showed encouraging results.

DISCUSSION

In 1861, Zenker described the presence of fat droplets in the lungs of a railway worker who had suffered a severe thoracoabdominal crush injury at autopsy and later in 1873, Bargmann clinically diagnosed Fat Embolic syndrome in a patient with fracture of the femur. The work continued on understanding the pathophysiology and pathogenesis of fat embolism throughout the early 20th century and in 1969, Peltier published his work on

the pulmonary consequences of fat embolism and its treatment. Gurd in 1970 put together the various clinical manifestations, which he later called the Fat Embolic Syndrome.

Two events promote entrance of marrow contents into the circulation following a fracture: movement of unstable bone fragments and reaming of the medullary cavity for the placement of an internal fixation device. Fat Embolic syndrome is also reported after non-traumatic lesions such as DM, severe burns, pancreatitis etc. Age seems to be a factor in the development of Fat Embolic Syndrome; young men with fractures are at increased risk.

The possibility of co-existing shock, hypovolemia and sepsis all of which reduce liver flow, facilitate the pathogenesis of Fat Embolic Syndrome by exacerbating the toxic effects of free fatty acids cannot be ignored.

An asymptomatic latent period of about 12-48 hours precedes the clinical manifestations. The fulminant form presents as acute cor pulmonale, respiratory failure, and /or embolic phenomena leading to death within few hours of injury.

The incidence of the fat embolism syndrome with early internal fixation of fractures of the femur is less, as compared with delayed fixation. It is believed that fixation prevented motion at the fracture site, which can promote intravasation of fat from the marrow. Early internal fixation can both prevent and promote the problem, yet early fixation probably prevents intravasation more than it promotes.

There is controversy among orthopedic surgeons over the size of the nail, however. Thin nails are less strong, but they require minimal reaming of the marrow canal or none, as compared with heavier nails. Transesophageal echocardiography is likely to provide further information about the effects of intramedullary reaming and its effects

on the fat embolism syndrome. The technique may also help in the further refinement of orthopedic instrumentation.

Currently, treatment is supportive^{22,23}, consisting primarily of mechanical ventilation for respiratory failure. It is logical to assume that sooner the diagnosis is made, the more effective potential therapy will be. Many treatments have been used with varying success including heparin, intravenous ethanol, low-molecular-weight dextran, and corticosteroids^{24,25}. But these are administered in later stages of the disease. Approaches to early diagnosis are adopted, and follow two avenues: (1) preoperative and postoperative and (2) intraoperative diagnosis²⁶.

CONCLUSION

Fat Embolism Syndrome is a significant cause of morbidity and mortality in trauma patients and elective orthopedic surgery. Despite certain laboratory and radiologic aids, clinical suspicion is still the mainstay in diagnosis of fat embolism syndrome. All possible laboratory and imaging aids must be used to rule out other treatable conditions. Treatment is essentially supportive, consisting of cardiovascular and respiratory resuscitation and stabilization. Maintenance of intravascular volume is important because shock can exacerbate the lung injury caused by FES. Intravenous albumin and steroids remains the mainstay of therapy while ventilatory support, oxygen and heparin can improve the prognosis in many patients.

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