AN UPDATE ON
FAT EMBOLISM SYNDROME (FES)

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HISTORICAL BACKGROUND

Fat Embolism Syndrome (FES) has been recognized since the late 1800's and extensively described following traumatic, surgical and atraumatic conditions. Fat Emboli were first noted by FA Zenker in 1861 in a railroad worker with a thoraco-lumbar crush injury.[1] After about a decade, FES was first described by Von Bergman in 1873.[2] This patient had a fractured femur who died and the diagnosis confirmed by post mortem examination.

DEFINITION

FES may be defined as a complex alteration of hemostasis which occurs as an infrequent complication of fractures of pelvis and or long bones and manifests clinically as acute respiratory insufficiency.[3]

Incidence: Exact incidence is not known. In retrospective reviews, incidence of FES is less than 1%.[4,5] However, there is a greater incidence reported in prospective studies of 11–29%.[6-9]

Causes: It includes long bone fractures especially fractures involving the middle and proximal parts of the femoral shaft, blunt trauma, acute pancreatitis, burns, joint reconstruction[10], liposuction, cardiopulmonary bypass, decompression sickness, parenteral lipid infusion[11], sickle cell crisis.[12]

Risk factors: It is most common after skeletal injury and more likely in long bone and pelvic fractures, closed fractures, movement of unstable bone fragments and reaming of medullary cavity, multiple fractures and in young men.

PATHOPHYSIOLOGY

Many aspects of the fat embolism syndrome remain poorly understood. Several theories have been proposed for its pathogenesis.

Mechanical Theory: The classical mechanical theory by Gossling H. et al[13] states that large fat droplets are released into the venous system. FES results from physical obstruction of the pulmonary and systemic vasculature with embolized fat .

Biochemical theory: This theory proposed by Baker et al[14], incriminates free fatty acids. According to this theory, local hydrolysis of triglyceride emboli by pneumocyte lipase together with excessive mobilization of free fatty acids from peripheral adipose tissue by the catecholamines results in toxic pulmonary concentration of these acids. The biochemical theory helps explain non-traumatic forms of FES.

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CLINICAL FEATURES

A high index of suspicion is needed for the diagnosis of FES. Its classic presentation consists of an asymptomatic interval of about 12-72 hours followed by triad of pulmonary changes, cerebral dysfunction, and petechial rash. The syndrome follows a biphasic clinical course. The initial symptoms are probably caused by mechanical occlusion of multiple blood vessels with fat globules. The late presentation is thought to be a result of hydrolysis of the fat to more irritating free fatty acids which then migrate to other organs via the systemic circulation.

Pulmonary Changes: Pulmonary signs are usually the earliest manifestations. These are seen in 75% of cases which may progress to respiratory failure in 10%. These include tachypnoea, dyspnoea and cyanosis. Hypoxaemia may be detected hours before the onset of respiratory symptoms.[15]

Cerebral Changes: CNS signs seen in 86% of patients are usually nonspecific and ranges from acute confusion, headache, stupor, coma, rigidity or convulsions.[16] Cerebral edema contributes to the neurological deterioration.

Dermatological Changes: A reddish-brown nonpalpable petechiae rash within 24-36 hours[17] appears, usually distributed to the upper body–chest, neck and conjunctivae. Resolution occurs within seven days. It results from occlusion of dermal capillaries by fat and increased capillary fragility.[18] The distribution is theorized to the related fat particles floating in the aortic archlike oil in water and are embolized to non-dependent skin areas via subclavian or carotid arteries.[19]

Several other signs like tachycardia and pyrexia may occur but are non-specific.[20] Retinal changes include exudates, cotton-wool spots, edema, haemorrhage, or intravascular fat globules.[21] Renal changes may present as lipuria while hepatic changes as jaundice.

DIAGNOSIS

There is no universal criteria used for diagnosis which is always made on clinical grounds. Various criteria were proposed by different authors. According to Gurd et al[15] diagnosis of FES requires at least one sign from major criteria and at least four signs from the minor criteria category (Table-I). Schonfeld et al[9] proposed a quantitative means of diagnosing fat embolism syndrome (Table-II). Lindegue et al[8] suggested that the FES can be diagnosed on the basis of respiratory status alone. (Table-III)

Table-I: Gurd's Criteria

Major criteria (one necessary for diagnosis)	Petechial rash Respiratory insufficiency Cerebral involvement
Minor criteria (four necessary for diagnosis)	Tachycardia >120 beats/min Fever >39.4°C Retinal signs – fat or petechiae Jaundice Renal signs – anuria or oliguria
Laboratory findings (one necessary for diagnosis)	Thrombocytopenia Anemia High ESR Fat macroglobulinemia

Table-II: Schonfeld's criteria

Petechiae	5
Chest *x-ray* changes (Diffuse alveolar infiltrates)	4
Hypoxemia (PaO2 <9.3kPa)	3
Fever (>38°C)	1
Tachycardia (>120 beats/min)	1
Tachypnea (>30 breaths/min)	1
Confusion	1

Cumulative score >5 required for diagnosis

Table-III: Lindeque's criteria

1. Sustained pO_2<8 kPa
2. Sustained pCO_2 of >7.3 kPa or a pH <7.3
3. Sustained respiratory rate >35 breaths/min despite sedation
4. Increased work of breathing: dyspnea, accessory muscle use, tachycardia and anxiety.

Laboratory Studies: Laboratory studies are mostly non-specific. Thrombocytopenia, anemia and hypofibrinogenemia can occur. Cytologic examination of urine, blood, CSF and sputum may detect fat globules.[22] Decreased hematocrit occurs within 24-48 hours and is attributed to intra-alveolar hemorrhage. ECG findings are usually normal but may show right heart strain or ischemia.[23]

IMAGING STUDIES

Chest x-ray: It may show evenly distributed, fleck-like pulmonary shadows (*Snow Storm* appearance), increased pulmonary markings and dilatation of the right side of the heart.

CT scan Head: It is performed because of alterations in mental status. It may be normal or may reveal diffuse white-matter petechial hemorrhages consistent with microvascular injury.

Ventilation/perfusion imaging of the lungs: It is performed for suspicion of pulmonary embolus, the findings may be normal or may demonstrate subsegmental perfusion defects.

Magnetic Resonance Imaging: MRI has shown to be more sensitive than CT in the identification of cerebral FES. In one small patient group, multiple, nonconfluent, hyperintense lesions were seen on proton-density and T2-weighted images characteristically located along the boundary zones of the major vascular territories.[24]

Transcranial Doppler: In a small case study, five patients with trauma were monitored with intracranial Doppler, two during intraoperative nailing of long bone fractures. Cerebral microembolic signals were detected as long as 4 days after injury.[25]

PROCEDURES

Bronchoalveolar lavage: Lipid inclusions commonly appear in patients with traumatic and nontraumatic respiratory failure. Some authors suggest that fat droplets within cells recovered by lavage may be both rapid and specific in diagnosis of fat embolism syndrome.[26,27]

TREATMENT

Medical: 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 in addition to balanced electrolyte solution, because it not only restores blood volume but also binds fatty acids and may decrease the extent of lung injury. Adequate analgesia is important to limit the sympathomimetic response to injury.[28]

No specific drug therapy for FES is currently recommended. High dose corticosteroids have been effective in preventing development of FES in several trials, but controversy on this issue still persists. However, dose regimens were not standardized which varies from 1.5 mg/kg methylprednisolone 8 hourly to 30 mg/kg 4 hourly.[7,8] Other drugs, such as heparin, intravenous alcohol, dextrans and hypertonic dextrose have not proved to be of any benefit.[29]

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

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 diagnosis is still the mainstay of diagnosis of fat embolism syndrome.

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