Current Anaesthesia & Critical Care 21 (2010) 277–281

Contents lists available at ScienceDirect

Current Anaesthesia & Critical Care

journal homepage: www.elsevier.com/locate/cacc

POINTS OF VIEW

Fat embolism – An update

Pratik Sinha, Nick Bunker*, Neil Soni

Chelsea and Westminster Hospital, 369 Fulham Road, London SW10 9NH, UK

Keywords:
Incidence
Aetiology
Pathophysiology
Diagnosis
Treatment

SUMMARY

Fat embolism syndrome is an unexpected and alarming complication that is difficult to actively prevent, hard to diagnose with confidence and has limitations in effective treatment modalities. The syndrome is a melange of respiratory, haematological, neurological and cutaneous symptoms and signs associated with trauma and other disparate surgical and medical conditions. The pathogenesis is still debated. It is clear that fat emboli are quite common yet the clinical syndrome is rare. Diagnosis is by pattern recognition as befits a syndrome, but the recently defined features on MRI could now be used to increase the probability of the diagnosis. Various therapeutic options have been tried and failed. At present steroids have a single meta-analysis suggesting benefit but it is in the trauma population where they may be contra indicated for other reasons, i.e. infection, so their place is ill defined. Supportive treatment is the mainstay.

1. Definition

It is important to differentiate fat in the circulation and the syndrome that is sometimes seen as a consequence. Fat in the circulation is probably quite common and embolisation can occur. Fat embolism syndrome (FES) is when there is fat in the circulation and it is associated with an identifiable clinical pattern of symptoms and signs.

The classic description of the syndrome is the combination of respiratory failure associated with neurological disturbance and a petechial rash often in the absence of any obvious cause.

2. Pathophysiology

The mechanism of fat embolism syndrome is not clear. It is clear that fat frequently gets into the circulation and can be demonstrated on both sides of the circulation. It is clear that fat can cause embolisation. Yet the syndrome is relatively uncommon. As a syndrome the range of effects implies diffuse damage at more than one site. This could be due to embolisation or may be associated with a different secondary mechanism. It is hard to tie all the effects seen in FES to embolus as a sole mechanism. Several theories have been postulated but the two main contenders are the mechanical and biochemical theories.

2.1. Fat embolus theory: mechanical

Fat globules can be physically forced into the venous system during trauma. In surgical situations high pressures are exerted in the marrow and this may force fat into the blood stream. The normal marrow pressure is 30–50 mmHg but this can be dramatically increased (up to 800 mmHg) during intra-medullary reaming and insertion of intra-medullary devices.[1] The presence of fat micro emboli can be clearly shown with ultrasonography in a relatively high percentage of patients albeit they are micro emboli and in small numbers.[2,3] Micro emboli seem to be seen most during manipulation of the intra-medullary cavity. Circumstantial evidence for the importance of intra-medullary fat comes from the observation that in previously reamed femoral cavities during redo replacements the incidence is low.[4] The use of cement is also associated with fat embolic phenomena but it is also seen in cement-less prosthesis.[5] Various models of fat injection or subjecting the medullary marrow to high pressures can all be shown to produce emboli and to result in cardiorespiratory problems. It has also been shown that the use of external fixation in trauma is associated with a lower incidence of FES than intra-medullary fixation.[6]

2.2. Free fatty acid theory: biochemical

This is in two parts. The first is the theory that trauma results in the release of lipases into the plasma that destabilise circulating fat molecules resulting in their saponification and de-emulsification. In animal studies exogenous fat in the circulation has been shown

* Corresponding author.
E-mail address: nickbunker@doctors.net.uk (N. Bunker).

0953-7112/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.cacc.2010.03.003

to cause the release of phospholipase A2, methylguanidine and proinflammatory cytokines. The significance of this phenomenon in vivo is unknown. In the same model fat droplets and fibrin thrombi were found in several organs.[7]

A more appealing biochemical theory invokes the histotoxic effects of free fatty acids (FFA). It is known that FFA's can cause severe vasculitis in animal models and in the lung this can disrupt pulmonary architecture fairly rapidly. If the free fatty acids are near the endothelium they can cause disruption of the integrity of the endothelial membrane and capillary wall leading to haemorrhage and oedema. Although bone marrow is predominantly neutral fat, in the acute inflammatory milieu it is possible that FFA activity may be important.[8–10] If in vivo there is hydrolysis of neutral fats to FFA's it could explain the interval before the probable time of fat release and the onset of signs and symptoms. In the clinical setting following long bone surgery FFA levels were found to be significantly higher in patients with multiple injuries and associated with significantly lower oxygen tension.[11]

2.3. Thrombocytopaenia

Part of the syndrome is often a falling platelet count. In the trauma population with hypovolaemia and coagulopathy there may be an association between sluggish, hypoxaemic circulation and possible 'sludging' of blood.[12] Coagulation abnormalities are encountered frequently in FES. The combination of activation of platelets, vascular endothelial effects and microaggregate collection might be catalysed by the presence of fat.

2.4. Systemic and paradoxical embolisation

Given that fat is released into the venous return to the right heart, it is a curiosity that it causes systemic effects, sometimes without pulmonary effects.[13,14] It has been suggested that this could be via a patent foramen ovale (PFO) which is not uncommon in the general population, with an incidence of about 25%.[15] Although closure of PFO does reduce emboli, whether a PFO was present or not makes no difference to the incidence of FES and it is clear that emboli are seen in patients without PFO.[3,16–18] Transpulmonary systemic fat embolisation does occur and has been shown in dogs without a patent foramen ovale.[19] The size and deformability of the fat micelles may allow this pulmonary transit.

There is no clear individual mechanism that can readily explain all the abnormalities seen in the syndrome. As shall be discussed later the distribution of lesions on cerebral MRI might provide clues towards multiple mechanisms but to date it is conjecture.

3. Clinical features of the syndrome

3.1. Associations

There are several reported causes of fat embolism syndrome. These are listed below and may be considered as preconditions where fat embolism syndrome (FES) might be seen. Trauma with long bone fractures and major elective orthopaedic procedures are the most common causes. Other causes are rarer. Liposuction has the potential to force fat into the circulation and there are many case reports of it causing Fat Embolism Syndrome (FES). Medical conditions such as hepatic necrosis or the fatty liver may predispose. Drugs such as intralipid,, parenteral nutrition or propofol have the potential to cause the syndrome although the mechanisms may differ in that the fat emulsions may coalesce and cause mechanical obstruction of the vascular tree and hence local damage. FES is implicated in sickle cell disease. In an acute sickle crisis the pulmonary macrophages often stain positive for fat and Bronchoalveolar Lavage may be a useful adjunct to diagnosis.[20] Bone marrow necrosis may release fat and certainly non-specific markers such as lipases are raised. In a recent study the incidence appeared very high (33%).[20–22]

Main causes
- Trauma – long bone fractures
- Joint replacements – prosthetic placement
- Scoliosis surgery

Mechanical disruption of adipocytes
- Soft tissue injury. (Crush and Blast injuries)
- Liposuction
- Liver failure – fatty liver.

Mechanical disruption of the bone marrow
- Bone marrow harvest
- Bone marrow transplant

Exogenous fat
- Parenteral nutrition
- Propofol infusion
- Lymphograophy

Non-specific
- Burns
- Extra corporeal circulation
- Acute sickle crisis
- Acute pancreatitis
- Decompression sickness
- Altitude sickness

3.2. Diagnosis

Fat embolism syndrome is a collection of symptoms and signs. As with any syndrome it is a clinical pattern rather than an easily defined entity. It is helpful to consider the condition in terms of preconditions that need to exist, symptoms that may occur and physical signs that may or may not be present and to a lesser or greater degree. It may even then be a diagnosis of exclusion as it overlaps with other conditions.

While many of the signs may be suggestive of the condition, none are absolutely pathognomonic.

It is also important to emphasise the wide range of clinical presentation from almost imperceptible sub-clinical signs to the more common gradual onset or the fulminating crisis with pulmonary and systemic embolisation of fat, right ventricular failure and cardiovascular collapse.

FES can present in a fulminant manner after the trauma or during the operation. The more classical onset is gradual over 12–36 h following injury or surgery, with increasing hypoxaemia often associated with neurological symptoms such as confusion, drowsiness, or coma. It may be accompanied by fever and a characteristic petechial rash, often in the axillae but may be on the face or in the conjunctivae.

To diagnose this syndrome requires the right preconditions to exist (see associations above). Gurd's classification is helpful and can be seen in Table 1.

In order to diagnose FES, 1 major and 4 minor criteria are required. Although various reports describe the presence of fat globules in the blood or sputum this requirement poses several problems. While the original guidelines require daily testing for fat globules it has been contentious. Fat globules can be found in both trauma patients and more worryingly in healthy volunteers with no