Journal of Clinical & Experimental Cardiology

Choudhuri R, et al., J Clin Exp Cardiolog 2014, 5:8
DOI: 10.4172/2155-9880.1000332

Case Report Open Access

Fat Embolism Syndrome and Role of Immunomodulation: A Case Report

Rajat Choudhuri, Sandeep Kumar Kar*, Dhiman Adhikari and Chaitali Sen Dasgupta

Department of Anaesthesiology and Cardiac Anaesthesiology, IPGME&R/SSKM Hospital, Kolkata, West Bengal, India

***Corresponding author:** Sandeep Kumar Kar, Clinical Tutor, I.P.G.M.E&R Kolkata, Cardiac Anaesthesiology, AJC Bose road 220, Kolkata 700020, India, Tel: +919477234900; E-mail: sndpkar@yahoo.co.in

Rec date: Jun 05, 2014, **Acc date:** Aug 28, 2014, **Pub date:** Sept 08, 2014

Introduction

Fat embolism is a dramatic form of embolism leading to a syndrome which is a constellation of clinical manifestations that develops when fat globules appear in blood and act as emboli. In the age of increasing orthopaedic interventions provoking fat embolization, the risk of perioperative cardiorespiratory emergencies is also increasing.

In 1862, Zenker first described fat embolism at autopsy, but even after so many years of research, no specific agent such as aspirin, hypertonic saline, low molecular weight dextran, sildenafil or methyl prednisolone have been of definite benefit.

This case report is a step which highlights targeting this syndrome from the pathophysiologic point of view through immunomodulators, the role of which might be beneficial in the definitive treatment of fat embolism syndrome.

Case Report

A 21 years young healthy boy was admitted in the emergency following a road traffic accident, which on evaluation was found to reveal compound fracture shaft of right femur. After initial protocolised trauma management and resuscitation, including external fixation of the damaged limb, the patient was planned to put up for open reduction and internal fixation of the shaft right femur as his vitals were permitting the operative intervention.

But within 24 hours, it was noted that the oxygen saturation was decreasing along with the appearance of petechial rashes with sub-conjunctival haemorrhage. He was now being shifted to intensive care unit where he was oxygenated with reservoir face mask but tachypnoea was creeping with decreasing PaO2/FiO2 (ratio of partial pressure arterial oxygen and fraction of inspired oxygen) ratio. Further 12 hours down the line he started to become drowsy progressing to a comatose condition. As per team decision, he was intubated with endotrachel tube and sedation was ongoing and the operation was deferred.

Apart from the routine protocolised investigations, chest x-ray, electrocardiogram (ECG), d-dimer assay, coagulation profiles were also done. Bronchoalveolar lavage (BAL) fluid was being evaluated for any pathogen and fat globules. Tumour necrosis factor alpha (TNF-α) titre was estimated in blood as well as in the bronchoalveolar fluid. Urine was studied for routine pathological parameters and fat globules. CT scan of brain, CT Pulmonary angiography, magnetic resonance imaging of (MRI) brain was being done after partial stabilization of the situation on next day. Bilateral lower limbs arterio-venous Doppler, duplex scan and V/Q (ventilation/perfusion) mismatch was searched for.

Till then we were ventilating the patient with lung protective strategy along with ongoing routine intensive care measures where we identified that the peak pressures were high. The compliance of the lung was worsening so positive end expiratory pressure (PEEP) requirement was titrated to get the best pulmonary mechanics.

In the T2 Diffusion weighted imaging of brain it was revealed to have diffused foci of hyperintensity in the deep white matter, basal ganglia and periventricular region. CT brain revealed non-specific cerebral oedema. Chest X-ray showed patchy infiltrates in perihilar and basilar region. CT pulmonary angiography proved filling defects in few subsegmental branches of pulmonary artery in the lower lobe of lungs with partial to complete luminal obstruction, likely to be due to embolism, patchy alveolar consolidation with ground glass attenuation in their distribution. Fat globules were present both in urine and BAL fluid and increased TNF-α titres found in both blood and BAL fluid. Sepsis screen of the patient didn't uncover any pathogen in blood, urine, sputum or the wound tissue. But the patient was fighting with life encompassing central nervous system (CNS), pulmonary, circulatory dysfunctions.

Apart from continuing with empiric antibiotic patient was administered 4 lakhs I.U. of ulinastatin per day, glutamine 100 ml twice daily and omega-3 (Ω-3) fatty acids with ongoing enteral calorie supplementation.

From Third day of the above therapy the ventilator parameters started improving, oxygen requirement reduced and respiratory rate reduced.

On the sixth day after starting the immunomodulatory therapy, patient could be successfully weaned off the ventilator and it was substantiated by clinically significant reduction in the TNF-α titres in BAL fluid and blood which we were evaluating with the ongoing immunomodulatory therapy.

Patient was then rehabilitated over another fortnight when the orthopaedic surgeons in consultation with the team of cardiologist, pulmonologist, intensivists and anaesthesiologists decided to put up the case for definitive operative intervention.

Perioperative procedure was successfully conducted with the means of central neuraxial blockade namely combined spinal epidural technique with precautionary measures for stepping up to general anaesthesia if condition worsens. Post operatively after 72 hours observation in intensive care unit he was planned to be discharged and he had an uneventful recovery period.

Discussion

Fat embolism syndrome should be considered in the differential diagnosis of cardiorespiratory and neurological deterioration after trauma and orthopaedic surgery but though the first case was

diagnosed in the year 1873 by Von Bergman, target treatment towards this syndrome has not come up without controversies. The incidence can vary from 0.25% to 35 % [1] (Table 1,2).

Criterion	Features
Gurd and Wilson (FES=1 Major+1 Minor+Fat microglulinemia)	Major Criteria Respiratory insufficiency Cerebral involvement Petechial rash Minor criteria Pyrexia Tachycardia Retinal changes Jaundice Renal changes (anuria or oliguria) Thrombocytopenia (a drop of >50% of the admission thrombocyte value) High erythrocyte sedimentation rate Fat microglobulinemia
Fat Metabolism index (FES=5 or more)	Diffuse petechiae (5 points) Alveolar infiltrates (4 points) Hypoxemia (<70 mm of Hg) (3 points) Confusion (1 points) Fever 38 ®C Heart rate >120 per minute Respiratory rate >30 per minute
Lindeque criteria (FES=femur fracture ± tibia fracture+1 feature)	A sustained PaO_2<60 mm Hg A sustained PaO_2>55 mm Hg or pH>7.3 A sustained respiratory rate >35/ min even after adequate sedation Increased work of breathing judged by dyspnea, use of accessory muscle, tachycardia and anxiety.

Table 1: Three criteria to define Fat embolism syndrome [2]

General factors	Males Age 10-39 years Posttraumatic hypovolemic state Reduced cardiopulmonary reserve
Injury related factors	Multiple fractures Bilateral femur fractures Femur shaft fractures Lower extremity fractures Traumatic fractures Concomitant pulmonary injury
Surgery related factors	Intramedullary reamed and unreamed nailing after femoral fracture Joint replacement after femoral fracture Bilateral procedure Joint replacement with high volume prosthesis

Table 2: Risk factors for fat embolism syndrome [1]

1) Trauma

Causes of Fat embolism syndrome are [1]-

2) Non-Traumatic: a) Disease (pancreatitis, crush injury, alcoholic fatty liver etc.)

b) Drug (lipids > 3.8 gm/kg/day)

c) Procedure related (intraosseous fluid and drug administration)

Exact pathophysiology of fat embolism syndrome is not known but two theories have been put forwarded-

1) Mechanical Hypothesis: Increased intramedullary pressure forces marrow particles, fat or bone fragments into the circulation via the open sinusoids causing obstruction of the small pulmonary (20 micrometer in diameter) and systemic vessels [3,4].

2) Biochemical Hypothesis : Fat globules being acted upon by lipoprotein lipase releases free fatty acids causing direct injury to pneumocytes and lung endothelial cells through their inflammatory effects Chemical mediators including platelet activating factor, phospholipase A2, cGMP, serotonin, nitric oxide have been implicated in the pathogenesis of fat embolism syndrome [1,5,6]

Clinical presentations are multi systemic involving pulmonary system, CNS, CVS, skin, eyes, renal and circulatory systems [7]. Diagnostic aids are mainly laboratory based and image based parameters as stated in case summary [8]. Fat embolism is basically a diagnosis of exclusion.

Immunomodulation is defined as modulation of the immune respone with naturally occurring nutrients in order to limit tissue injury, reduce infection rates and morbidity [9].

Koji Ito demonstrated that ulinastatin is a human urinary trypsin inhibitor which inhibits the production of TNF-α involved in potentiating the leukocyte activation having a role in development of oleic acid induced lung injury [10].

Pacht ER et al. demonstrated that enteral diet enriched in eicosapentaenoic acid and gamma linolenic acid for at least 4-7 days significantly reduced BAL fluid interleukin (IL-8), TNF- α, total proteins, neutrophils and significantly improved oxygenation and reduced vascular permeability. Hence it can be an essentially helpful aid in acute respiratory distress syndrome (ARDS) [11].

Role of Glutamine:

A) In systemic inflammatory response syndrome (SIRS):

1) Decreases Simplified Acute Physiology Score (SAPS) II Scores, leukocytes and natural killer (NK) cell count, which might be associated with suppressing inflammation and improving clinical recovery.

2) B and T lymphocytes increased → Improves immune system.

3) Decreases infection related complications and length of hospital stay [12].

B) As stress handler: Glutamine is an essential precursor of glutamate for the synthesis of glutathione (GSH) which is a tripeptide protecting cells from oxidative stress.

C) As an immunonutrient and immunomodulator: Glutamine is essential for immune nutrition in the critically ill. Impairment of immune system functioning contributes to the development of sepsis. Glutamine is required by the cells of the immune system both as a primary fuel and as a carbon and nitrogen donor for nucleotide precursor synthesis. Glutamine is essential for optimal immune cell functioning for monocytes, lymphocytes and neutrophils. It helps in nitrogen transport maintaining cellular redox state [13-15].

Summary

This case report highlights the importance of immune activated biochemical predominant pathway of fat embolism syndrome, which triggered the usage of immunomodulators. Immunomodulators significantly altered the disease process and hence it provokes further research into the role of immunomodulation in fat embolism syndrome, the human studies of which are extremely rare.

Conclusion

With the age of increasing trauma incidents and orthopaedic surgeries, leading to perioperative cardiorespiratory emergencies, it is important that clinicians be knowledgeable regarding fat embolism syndrome and its associated presentations. Keeping in mind the pathophysiological sequence of events, it is imperative that further research works in the field of immunomodulation is required to manage and break the cycle of immune mediated morbidity in fat embloism syndrome.

References

1. Akhtar S (2009) Fat embolism. Anesthesiol Clin 27: 533-550, table of contents.
2. Guard AR, Wilson RE (1974) The FES. J Bone Joint Surg Br 56: 408-416.
3. Batra P (1987) The fat embolism syndrome. J Thorac Imaging 2: 12-17.
4. Findlay JM, DeMajo W (1984) Cerebral fat embolism. Can Med Assoc J 131: 755-757.
5. Peltier LF (1956) Fat embolism. III. The toxic properties of neutral fat and free fatty acids. Surgery 40: 665-670.
6. Kao SJ, Chen HI (2008) Nitric oxide mediates acute lung injury caused by fat embolism in isolated rat's lungs. J Trauma 64: 462-469.
7. Capan LM, Miller SM, Patel KP (1993) Fat embolism. Anesthesiol Clin N America 11: 25-54.
8. Taviloglu K, Yanar H (2007) Fat embolism syndrome. Surg Today 37: 5-8.
9. Karagiorga G, Nakos G, Galiatsou E, Lekka ME (2006) Biochemical parameters of bronchoalveolar lavage fluid in fat embolism. Intensive Care Med 32: 116-123.
10. Ito K, Mizutani A, Kira S, Mori M, Iwasaka H, et al. (2005) Effect of Ulinastatin, a human urinary trypsin inhibitor, on the oleic acid-induced acute lung injury in rats via the inhibition of activated leukocytes. Injury 36: 387-394.
11. Pacht ER, DeMichele SJ, Nelson JC (2003) Enteral nutrition with eicosapentaenoic acid, gamma linolenic acid, and antioxidants reduces alveolar inflammatory mediators and protein influx in patients with acute respiratory distress syndrome. Crit Care Med 31: 491-500.
12. Cetinbas F, Yelken B, Gulbas Z (2010) Role of glutamine administration on cellular immunity after total parenteral nutrition enriched with glutamine in patients with systemic inflammatory response syndrome. J Crit Care 25: 661.
13. Cai G, Yan J, Zhang Z, Yu Y (2008) Immunomodulatory effects of glutamine-enriched nutritional support in elderly patients with severe sepsis: a prospective, randomized, controlled study. J Organ Dysfunction 4: 31-37.
14. Wilmore DW, Shabert JK (1998) Role of glutamine in immunologic responses. Nutrition 14: 618-626.
15. Andrews FJ, Griffiths RD (2002) Glutamine: essential for immune nutrition in the critically ill. Br J Nutr 87 Suppl 1: S3-8.