FAT EMBOLISM ASSOCIATED WITH DRUG OVERDOSE

Case Report

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SUMMARY

A case history is presented of a patient who developed severe pulmonary oedema, when almost recovered from self-inflicted barbiturate overdose. The resulting hypoxia was resistant to oxygen therapy with IPPV and CPPB. A fatal outcome ensued 14 days after admission. The diagnosis of fat embolism was confirmed by the demonstration of fat globules greater than 10μ circulating in the plasma. The pathogenesis and differential diagnosis is discussed. Fat embolism should be considered when the diagnosis of pulmonary oedema is in doubt.

Fat embolism classically may occur following fractures of long bones. Recently it has been appreciated that it may also occur in any traumatized patient, regardless of the site of injury. This paper reports the occurrence of fat embolism in a patient being treated for barbiturate overdose.

CASE REPORT

A 27-year-old male was admitted unconscious to the resuscitation area of the Accident and Emergency Centre, an empty bottle of barbiturate tablets having been found by his bedside. He had previously attempted suicide with coal gas, and was under psychiatric care. He was apnoeic and cyanosed and although there was a palpable peripheral pulse, the blood pressure was unrecordable. Marked sinus bradycardia was observed on the electrocardiogram. There was no response to stimuli although the pupils were small, equal and reacted to light.

Immediate treatment consisted of endotracheal intubation and ventilation with 100% oxygen, intravenous fluid therapy with cortisol and isoprenaline. Central venous pressure and urinary output were monitored. His colour again deteriorated, blood pressure and pulse disappeared, although he continued to have an e.c.g. complex. The pupils became widely dilated but still reacted to light. External cardiac massage was commenced with a Blanketrol as the rectal temperature was only 32°C.

He remained grossly hypotensive for 7 hours before a gradual improvement in peripheral circulation and blood pressure occurred. IPPV was continued for 24 hours until spontaneous respiration was adequate to trigger the Bennett ventilator. After 48 hours he was extubated, as the laryngeal and cough reflexes were active. Consciousness gradually returned and on the third day he was awake and, although still drowsy, was able to relate his feelings of depression, getting drunk and then swallowing tablets. He thought he had taken the tablets some 12 hours before he was found unconscious.

Anuria followed and intravenous fluids were restricted to 1 litre per day after the initial fluid required for resuscitation. Serum potassium levels were controlled with an exchange ion (sodium polystyrene sulphonate; Resonium-A, Winthrop; 30 g rectally) 4-hourly from the day when the blood urea reached 300 mg/100 ml. Satisfactory progress was maintained until the seventh day, when the patient became restless, irritable and confused. The Pao₂ which had returned to normal, had fallen to 55 mm Hg on room air. Marked tachypnoea was present which was reflected in the low Paco₂ of 30 mm Hg. 70% oxygen was administered from the face mask using an injector (Puritan) humidifier. The chest X-ray which previously had only shown patchy atelectasis in the left upper lobe (fig. 1) now showed enlarged hila, woolly opacities and prominent vascular patterns (fig. 2).

The following day he had obvious arterial desaturation with Paco₂ of 35 mm Hg on 75% oxygen and was semi-conscious. Rectal temperature was 39°C and heart rate 140 beats/min. Since copious bright red frothy sputum was being coughed up the patient was reintubated and IPPV commenced using the Cape ventilator, respiratory control being achieved with pancuronium and opiates. Despite IPPV with 100% oxygen, his condition continued to deteriorate, the arterial oxygen tension being only 45 mm Hg after 1 hour, and almost continuous tracheal suction was required to remove oedema fluid from the


*Manufactured by Cincinnati Sub-Zero Products Inc.
Continuous positive pressure ventilation (CPPV) was then started with an end-expiratory pressure of 10 cm H$_2$O, and within half an hour there was a marked improvement in colour and pulmonary oedema was considerably reduced. It was now possible to maintain a $P_{aO_2}$ of 90 mm Hg on 70% oxygen. Peritoneal dialysate was changed to No. 62 hypertonic solution* for 24 hours to aid in the control of the oedema.

Any attempt to remove the expiratory retard resulted in the return of the oedema and a fall in oxygen tension. Tracheostomy was performed on the tenth day to facilitate ventilation and suction. On the next day fat globules, larger than 10 $\mu$ dia., were demonstrated in the serum and these persisted for 4 days (fig. 3). In the first 2 days after the sudden deterioration the haemoglobin fell from 12 to 7.4 g/100ml, while the ESR rose to 74 mm/hour.

Over the next few days there was little change in the pulmonary oedema, which could not be controlled without CPPV and acceptable oxygenation was obtained only with difficulty. The chest X-ray (fig. 4) now showed homogenous opacities.

Two weeks after admission he had a sudden cardiac arrest in asystole and resuscitation was unsuccessful.

**Postmortem findings.**

*Lungs* showed venous congestion of the pulmonary vessels, with marked oedema of the alveoli and parenchyma. Alveoli showed areas of focal haemorrhage and also areas of fibrinous exudate, with the formation of hyaline membrane. Fibroblastic proliferation with changes of early carnification was also marked. Large numbers of foam cells were present. Fat stains showed no fat emboli in any great amounts, but a few fine droplets were seen within the macrophages in some alveoli.

*Kidneys* showed a marked degree of cloudy swelling, and in areas they were lined by flat cuboidal epithelium indicative of tubular necrosis with re-epithelialization.

**DISCUSSION**

The occurrence of pulmonary oedema was rather puzzling in view of the fact that 1 week had elapsed since his initial resuscitation and, apart from anuria,

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*This solution (Dialaflex; Allen and Hanburys) contains the following m-equiv of ions per litre: sodium 141, calcium 3.6, magnesium 1.5, chloride 100.8, bicarbonate (as lactate) 44.6.
which was not unexpected in view of the prolonged hypotension, he appeared to have recovered fully from the drug overdosage. At no time was there any clinical or radiological evidence that the oedema could have been explained on the basis of an aspiration pneumonia. Apart from the initial fluids used during resuscitation, fluid intake was restricted and peritoneal dialysis had been in progress for 2 days prior to the onset of oedema. Overloading the circulation with fluid could, therefore, be excluded as a cause.

There was no evidence of any cardiac disease and an e.c.g. confirmed that no myocardial damage had occurred as a result of the prolonged hypotension, or as a result of external cardiac massage. A cardiac cause for the oedema was, therefore, unlikely.

Pulmonary oedema is not usually a feature of bronchopneumonia or a blood-clot embolus, although he did complain of pain in his left thigh, which was swollen and tender and seemed to be related to femoral artery puncture. Burger and Macklem (1965) consider that the development of acute pulmonary oxygen toxicity whilst breathing 100% oxygen is probably due to absorption atelectasis. Oxygen toxicity is unlikely to occur if the $P_{a_o_2}$ is maintained at normal levels, despite high alveolar tensions (Winter et al., 1967). Nash, Blennershasset and Pontoppidan (1967) have provided evidence of an association between the prolonged administration of high concentrations of oxygen and the development of chronic pulmonary disease. In this patient the $P_{a_o_2}$ was maintained close to normal and 100% oxygen was only administered for 12 hours, at the most. It was thus felt that the pulmonary oedema was unlikely to be due to oxygen toxicity.

Recent work by Gett, Jones and Shepherd (1971) has shown that sodium retention occurs during controlled ventilation, and thus sodium restriction was imposed. Large doses of steroids can cause salt and water retention, but in our patient steroids were only administered on the first day.

Chronic renal failure with associated uraemia can result in the occurrence of pulmonary oedema, but this is a radiological diagnosis consisting of consolidation in the mid-zone of both lungs, extending out from the hila with so-called "bat's wing" shadows (Day, Sisson and Vogt, 1929). It appears to be related to chronic venous congestion, rather than to the degree of nitrogen retention (Grainger, 1958).

The development of unconsciousness, the sudden recurrence of hypoxia, pyrexia, tachycardia and pulmonary oedema suggested that fat embolism could explain his sudden deterioration, although a petechial rash was not present. This diagnosis was confirmed by demonstrating fat globules (fig. 3) circulating in the serum (Gurd, 1970). Globules larger than 10μ are pathognomonic (Harman and Ragaz, 1950).

The origin of the emboli found in fat embolism has long been controversial. The classical theory is that emboli are released from traumatized bone marrow. This case, however, adds weight to the metabolic view of Lehman and Moore (1927) that fat droplets can arise by aggregation within the plasma itself.

It is generally accepted that fat embolism is associated with bone injury. Warren (1946) studied 100 fatal cases of fat embolism, 91 of which followed fracture of one or more bones. Four were due to blast injury without fracture, two to crush injury without fracture, and three followed extensive burns. Fat embolism has been reported in the absence of injury in such conditions as acute haemorrhagic pancreatitis, diabetes, chronic alcoholism, and the
nephrotic syndrome (Lynch, 1954; Lynch, Raphael and Dixon, 1959). It has also been found in association with certain poisons, including carbon tetachloride, phosphorus, mercuric chloride, phenol, potassium chloride, chloroform, arsenic and strychnine (Grondahl, 1911; Grosskloss, 1935-6; McMahon and Weiss, 1929). It must be emphasized that in all these patients fat embolism was a post-mortem finding. The frequency of pulmonary fat embolism found in routine necroscopy varies from zero (Robb-Smith, 1941) to 50% (Lehman and McNattin, 1928).

Recent studies (Gurd, 1970) have shown the diagnostic value of demonstrating fat globules in the serum and those in this patient (being larger than 10 μ) are pathognomonic of fat embolism (Harman and Ragaz, 1950). This diagnosis was supported by the large fall in haemoglobin.

In this patient the aetiology of fat embolism could be explained on the basis of barbiturate overdosage with hypotension and tissue ischaemia. This results in the release of catecholamines and the conversion of neutral fat into free fatty acids, which are reesterified into neutral fat and deposited in the peripheries (Carlson, 1966; Lasch, 1969).

It would appear that the pathological findings described are compatible with resolving pulmonary fat embolism, although this view was not shared by all our pathologists.

There is no doubt that this patient had a true fat embolism syndrome. The diagnosis made from clinical evidence was supported by demonstrating fat macroglobulaemia. This patient’s clinical history is extremely interesting because the circumstances are unusual and serve to emphasize that the diagnosis may be overlooked in the absence of bone or soft tissue injury, unless it is appreciated that fat embolism must always be considered if the aetiology of pulmonary oedema is in doubt.

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REFERENCES


EMBOLIE DE GRAISSE ASSOCIEE A UN SURDOSAGE MEDICAMENTEUX

DESCRIPTION D'UN CAS

Les auteurs présentent le cas d'un malade qui développait un oedème pulmonaire sévère, lorsqu'il s'était quasi rétabli d'un surdosage volontaire aux barbituriques. L'hypoxie résultante résista au traitement oxygenique avec IPPV et CPPB. Le malade décéda 14 jours après son entrée à l'hôpital. Le diagnostic d'embolie de graisse a été confirmé par la démonstration de globules de graisse, plus grandes que 10 μ, circulantes dans le plasma. La pathogénese et le diagnostic différentiel sont discutées. Il faut penser à l'embolie de graisse lorsque le diagnostic d'oedème pulmonaire est douteux.
FETT—EMBOLIE IN ZUSAMMENHANG MIT ÜBERDOSIERUNG VON MEDIKAMENTEN
BERICHT ÜBER EINEN FALL

ZUSAMMENFASSUNG

EMBOLISMO GRASOSO ASOCIADO CON SOBREDOSIFICACION DE UN MEDICAMENTO
COMMUNICACION DE UN CASO

RESUMEN
Se presenta la historia de un paciente que desarrolló edema pulmonar intenso al haberse casi recuperado de la sobredosificación barbitúrica que se administró el mismo. La hipoxia resultante fue resistente a la terapia por oxígeno con IPPV y CPPB. El paciente murió a los 14 días después del ingreso. El diagnóstico de embolismo graso fue confirmado por la demostración de glóbulo graso mayor de 10 μ circulando en el plasma. Se discute la patogénesis y diagnóstico diferencial. Hay que tener en cuenta el embolismo graso cuando hay dudas sobre el diagnóstico de edema pulmonar.