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Pulmonary oedema in meningococcal meningitis

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Summary

Two cases of meningococcal meningitis complicated by pulmonary oedema are described. The pulmonary arterial wedge pressure was raised in the one case studied.

Profound sympathetic over-activity may be the cause of the pulmonary oedema occurring in this situation. If this is so, adrenergic blockade would appear to be a rational approach to therapy.

Introduction

Although pulmonary oedema is a recognized complication of intracranial lesions, it has only rarely been reported in relation to meningococcal meningitis and in none of these cases were any haemodynamic studies performed.

Case report no. 1.

A 21-year-old male presented to the casualty department with an extensive rash of sudden onset. This followed a 5-day history of general malaise and a 2-day history of abdominal pain. On examination he was extremely ill but fully conscious. He was cyanosed and an extensive purpuric rash was noted. There was no neck stiffness or localizing neurological signs. Blood pressure was 70/40 mmHg, pulse rate 120/min, and his extremities were cold and clammy. Investigations: haemoglobin 17 g/100 ml, white blood count 5,500/mm³, platelets 15,000/mm³. Gram-negative cocci were seen on the blood film. A diagnosis of meningococcal septicaemia was made, and resuscitative measures were begun. He was given hydrocortisone 200 mg, sulphadimidine 2 g, penicillin 6 megaunits. However, his condition rapidly deteriorated. He became very restless and began to

hyperventilate and cough up large quantities of frothy sputum. Intubation and artificial ventilation failed to improve his condition. Cardiac arrest occurred, and further resuscitation was unsuccessful.

At post-mortem examination there was evidence of basal meningitis but no other neurological abnormality. The lungs showed 'terminal pneumonia' and the heart gross dilatation of the right ventricle. The adrenal glands revealed some haemorrhage and oedema.

Case report no. 2

A 19-year-old labourer was admitted as an emergency with a 3-hr history of headache, vomiting and pain in the abdomen and legs. He had been well until the onset of this illness, and had no relevant past medical history. On examination he was restless and confused. His temperature was 40°C and there was marked neck stiffness. Pulse rate 90/min and hyperdynamic. Blood pressure 130/70 mmHg. The cardiovascular and respiratory systems were normal. No focal neurological signs were present, and in particular there was no papilloedema. Investigations: lumbar puncture revealed a pressure greater than 200 mm (although the patient was restless at the time). Cerebrospinal fluid protein 650 mg%, glucose 31 mg%; microscopy showed neutrophils 10,500/mm³, red cells 5,500/mm³ but no bacteria. On culture, however, a light growth of *Neisseria meningitis* was obtained. Haemoglobin 13.9 gm%, white blood count 16,000/mm³ with 69% neutrophils, 22% lymphocytes and 7% monocytes. Urea and electrolytes normal. Treatment was started with 20,000 u intrathecal penicillin, 4 g sulphadimidine stat. i.m., followed by 2 g 6-hourly.

Six hours after admission he became increasingly restless and started to scratch and excoriate the skin

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of his lower abdomen in an uncontrollable manner. He began to hyperventilate (respiration rate 36/min) and cough up large quantities of frothy, pink sputum and became centrally cyanosed. His blood pressure had risen to 170/75 mmHg, pulse rate 84/min and of good volume, although his extremities were cool and clammy. His pulse rate then rose rapidly to 150/min and his blood pressure fell to 80/60 mmHg. His jugular venous pressure was not raised. Widespread crepitations were heard throughout both lung fields. The chest X-ray showed frank pulmonary oedema, and the ECG a sinus tachycardia of 150/min without any other abnormality. Blood gases were Po_2 72 mmHg, Pco_2 16 mmHg, and pH 7.28. Diazepam 20 mg, frusemide 80 mg and hydrocortisone 100 mg were given intravenously without effect. In view of his critical state and continued gross hypoxia, intermittent positive pressure ventilation was started. This controlled his pulmonary oedema, and his blood pressure rose to 100/70 mmHg following the administration of 3 units of plasma.

Over the next 18 hr the patient's condition improved considerably, and he regained consciousness. His temperature had fallen to 36.8°C. He was tried off the ventilator, but that afternoon, 24 hrs after admission, pulmonary oedema recurred and intermittent positive pressure respiration was restarted. The central venous pressure was measured at this stage and found to be 33 mmHg (with the ventilator disconnected) with a blood pressure of 70/50 mmHg.

The following morning, 36 hr after admission, he had again become less cyanosed but was still in pulmonary oedema and continuing to produce large quantities of frothy sputum. At this stage a pulmonary wedge pressure measurement was taken via a Swann-Gantz catheter and found to be 30 mmHg with a central venous pressure of 25 mmHg. Blood pressure 130/70 mmHg; pulse rate 130/min (off the ventilator). Shortly afterwards the inflation pressure of the respirator was remaining at +10 cm H_2O during expiration, following which the patient developed widespread surgical emphysema. A new ventilator was substituted; the pressure fell to zero on expiration and the surgical emphysema regressed. A repeat lumbar puncture was performed and slightly turbid cerebrospinal fluid withdrawn. Microscopy revealed neutrophils 200/mm³ and red cells 800/mm³, but no organisms. Plasma urea 57 mg%. Normal urine output had been maintained throughout his illness. That night his pulmonary oedema worsened and he became hypoxic. At 9 a.m. the following morning cardiac arrest occurred and resuscitation was unsuccessful.

Post-mortem examination revealed a suppurative meningitis over the base of the brain but with no ventricular involvement. The intracranial vessels were engorged but not thrombosed. There was no

evidence of infarction, nor was there any abscess formation. The lungs weighed 880 and 960 g respectively and showed gross pulmonary oedema. There was no evidence of mucosal tearing in the trachea or bronchial tree to account for the surgical emphysema. There was sign of pneumonia. The heart and coronary arteries were normal, as were the adrenal glands.

Two specimens of frothy sputum were taken from the trachea, one shortly before death and one *post mortem*. Total protein content was measured and an electrophoretic strip performed. The results are shown in Table 1.

TABLE 1

Total protein (g/100 ml)	Albumin (g/100 ml)	Globulin			
		α_1	α_2	β	γ
<i>ante mortem</i> (0.4)	0.18	0.18	0.03	0.04	0.09
<i>post mortem</i> (0.4)	0.16	0.02	0.04	0.08	0.07

Discussion

The first of the cases died before any pressure measurements could be made. However, in the second case, central venous pressure and pulmonary wedge pressure were grossly elevated.

It is well recognized that pulmonary oedema can occur following a variety of intracranial lesions such as intracranial haemorrhage (Ducker, Simmons and Anderson, 1968; Ducker, Simmons and Martin, 1969; Weisman, 1939), and neoplasms (Cameron, 1948; Urabe *et al.*, 1961), but rarely intracranial infection. One report of the pathological findings in 200 cases of fatal meningococcal infections (Hardman and Earle, 1967) refers to the presence of pulmonary oedema in 60% of these cases. However, only two clinical reports of pulmonary oedema in acute meningococcal infection can be found (Kanter, Mauriello and Learner, 1956; Levin and Painter, 1966), and in neither instance was any attempt made to explain the pathogenesis of the pulmonary oedema.

Experimentally, 'neurogenic' pulmonary oedema has been produced by the intracisternal injection of veratrine (Worthen, Argano and Siwadlowski, 1969), thrombin and fibrinogen (Sarnoff and Sarnoff, 1952), intracarotid infusion of saline (Luisada and Sarnoff, 1946), and increased intracranial pressure (Ducker *et al.*, 1968).

Luisada (1967) and Sarnoff and Sarnoff (1952) have suggested that 'neurogenic' pulmonary oedema results from elevated left ventricular pressure due to a combination of peripheral vasoconstriction, systolic and diastolic overloading of the heart and increased myocardial stiffness as a consequence of profound

sympathetic overactivity. The second patient showed some features consistent with this hypothesis. Some hours after admission he began to show signs suggestive of increasing sympathetic activity. His systolic blood pressure rose from 130 to 175 mmHg and he became peripherally vasoconstricted. As the pulmonary oedema became established his blood pressure fell to 80/60 mmHg and his heart rate rose to 150/min. The pulmonary oedema persisted despite intermittent positive respiration and diuretic therapy. Evidence that the pulmonary oedema was secondary to left heart failure as a result of exaggerated sympathetic drive was provided by the grossly elevated pulmonary wedge pressure. It is unlikely that the pulmonary oedema was an exudate due to toxic damage to the capillary membrane because of the very low protein content of the oedema fluid.

If sympathetic overactivity is indeed the initiator of pulmonary oedema then a rational approach to treatment might be by the use of adrenergic blocking agents or stellate ganglion blockade which have been shown to be effective experimentally (Ducker *et al.*, 1968; Worthen *et al.*, 1969). The very high mortality in this situation makes such an approach worthwhile. Further haemodynamic studies in 'neurogenic' pulmonary oedema might help elucidate the pathogenesis of this condition.

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