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Fulminant Desquamative Interstitial Pneumonitis

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SUMMARY

A previously well, 48-year-old female presented with a short history of respiratory distress and fever for which no cause could be found. Open lung biopsy was not contributory. She died within nine days of presentation of hypoxia and multi-organ failure. Post mortem examination revealed the pattern of desquamative interstitial pneumonitis.

Key Words:LUNG: pneumonitis, interstitial, desquamative

Desquamative interstitial pneumonitis is a diffuse and uniform inflammatory process that involves the interstitium and air spaces of the lung, characterized by the presence of large mononuclear cells in the distal air spaces. The mononuclear cells were believed by early investigators to be "desquamated" from alveolar walls. It was first described as a distinct entity by Liebow et al[1] in 1965. However, debate continues as to whether desquamative interstitial pneumonitis is an early form of usual interstitial pneumonitis[2,3] or a clinicopathological entity of its own[4-6]. The distinct morphological characteristic of desquamative interstitial pneumonitis is the increased numbers of intra-alveolar macrophages with only mild interstitial fibrosis compared with usual interstitial pneumonitis where there is a heterogeneous pattern of inflammation, fibrosis, and honeycomb change interspersed with normal lung[4-6].

We describe a case of fulminant respiratory failure which, on histological examination, progressed from normal lung to the typical features of desquamative interstitial pneumonitis over five days. This rapid progression and the absence of causative factors suggest that desquamative interstitial pneumonitis can occur as a distinct clinical entity.

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CASE REPORT

A 48-year-old female was referred to the intensive care unit at the Royal Adelaide Hospital after presenting at another hospital 24 hours previously. On presentation to the referring hospital, she gave a two-week history of lethargy, anorexia, frontal headache and lumbar back pain. Five days prior to presentation she developed progressive dyspnoea. There was no cough, sputum or haemoptysis. Over this later period symptoms included heartburn and diarrhoea.

Past medical history included cholecystectomy for acalculous cholecystitis, excision of a lump in the breast which proved benign, bilateral salpingo-oophorectomy and hysterectomy for endometriosis. There was a history of rheumatic fever as a child, and an episode of pneumonia which did not require hospital admission 11 years previously. She was on no medication, had a 60 pack year smoking history and took alcohol occasionally.

On examination she was distressed with dyspnoea and tachypnoea (40 breaths per minute). She was sweating with flushed facies and had a temperature of 38.6°C per axilla. Heart rate was 110 beats per minute and blood pressure was 110/70 mmHg. On auscultation of the chest fine inspiratory crackles were present at both bases. Splenomegaly was noted. The remainder of the examination was unremarkable.

A chest roentgenogram demonstrated only minimal pulmonary venous congestion with no other consolidative or infiltrative lesions. On facemask oxygen at 50%, arterial blood gases were pH 7.48, P_aCO_2 26.5mmHg, P_aO_2 82mmHg. The serum sodium was 125 mmol/l, potassium 3.4 mmol/l, chloride 91 mmol/l and bicarbonate 20 mmol/l. Urea and creatinine were normal. The bilirubin was 52 mmol/l, albumin 33g/l, alkaline phosphatase 103 IU/l, alanine amino transferase 304 IU/l and lactate dehydrogenase 865 IU/l.

Haemoglobin was 12.6 g/dl, white blood cell count 10.8×10^3 per microlitre with 83% neutrophils. The platelet count was 51×10^3 per microlitre. Biochemical and microbiological examination of the cerebrospinal fluid was normal. An electrocardiogram was normal and the transthoracic echocardiogram demonstrated minimal mitral regurgitation. A ventilation/perfusion scan was normal. The patient was treated with frusemide, benzylpenicillin, ceftriaxone, gentamicin and erythromycin after blood, sputum and urine samples were taken for culture and serology.

Intubation and ventilation was performed for increasing respiratory distress. Pulmonary artery wedge pressure was 16 mmHg, cardiac index 3.3 $l.min^{-1}.m^{-2}$ and the systemic vascular resistance was 667 $dyn.s.cm^{-5}$. Inotropes and fluids were used to optimize cardiac index and maintain mean arterial pressure. Mild disseminated intravascular coagulation (DIC) was demonstrated with a fibrinogen of 1.0 g/l (N1.5-4.0) and D-dimer fibrinogen degradation products of 0.5 mg/l (N<0.25).

Throughout her admission repeated cultures of urine, sputum and blood were negative. Serology for *Mycoplasma pneumoniae*, influenza A and B, adenovirus, legionella, toxoplasma, hepatitis B and C were all negative. Human immunodeficiency virus 1 and 2 was not detected by enzyme immunoassay. A nasopharyngeal aspirate was also negative for adenovirus, influenza A and B, *Mycoplasma pneumoniae*, para-influenza 1, 2 and 3 and respiratory syncytial virus on enzyme immunoassay. Extractable nuclear antigen autoantibodies, glomerular basement membrane antibodies, antineutrophil cytoplasmic antibodies and anticardiolipin antibodies were not detected. Antibody to double stranded DNA was reported as less than 5 IU/ml (N<8 IU/ml). Rheumatoid factor was negative. A short synacthen test demonstrated a normal stress response. Serial chest X-rays showed a progressive bilateral interstitial infiltrate which was most prominent in the left upper lobe.

An open lung biopsy was performed from the left upper lobe on the third day after her admission. This showed only a small amount of intra- alveolar proteinaceous fluid consistent with pulmonary oedema (Figure1). There was no interstitial inflammation or consolidation. Occasional platelet thrombi in capillary size vessels were present consistent with the mild disseminated intravascular coagulation evident from the coagulation studies. The following day a splenectomy was performed for rupture of the enlarged 340 gram spleen. Histology showed congestive and ischaemic changes with white pulp cellular changes that were reactive in nature. Anaerobic and aerobic culture of splenic tissue was negative. The multiorgan failure escalated with onset of acute renal failure and worsening jaundice, hypoxia and hypotension. Despite maximal supportive therapy including continuous veno-venous haemodiafiltration, the patient died of hypoxia and multiple organ failure on day 8 of her intensive care admission.

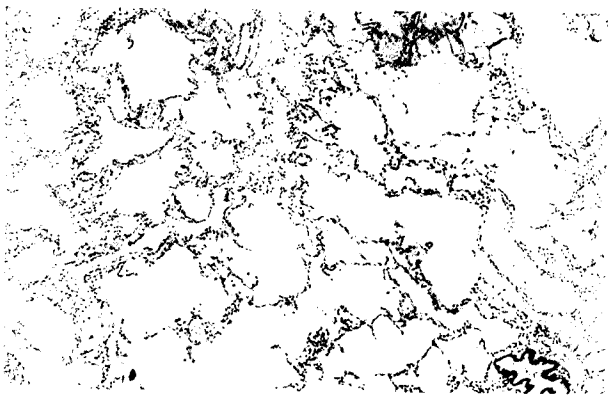

FIGURE 1: Open lung biopsy showing patchy oedema fluid. No alveolar cellular infiltrate is present.

At post mortem examination the lungs were heavy at 850 grams (left) and 900 grams (right). Histological examination of the lungs revealed bilateral, widespread filling of alveolar spaces by non-vacuolated macrophages indicative of desquamative interstitial pneumonitis (Figure 2). Interstitial oedema and minor lymphocytic infiltrate caused widening of the alveolar walls but no interstitial fibrosis or eosinophillia were present (Figure 3). Histology of the normal appearing brain demonstrated a lymphocytic meningitis with parenchymal perivascular lymphocytic cuffing consistent with intercurrent viral infection. The remainder of the post mortem

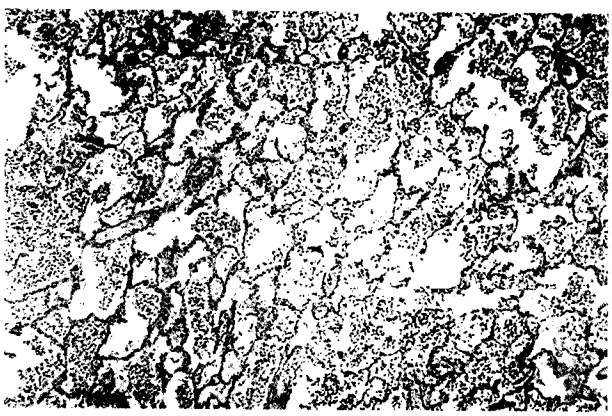

FIGURE 2: Post mortem lung showing filling of alveolar spaces with mononuclear cells in a desquamative pattern.

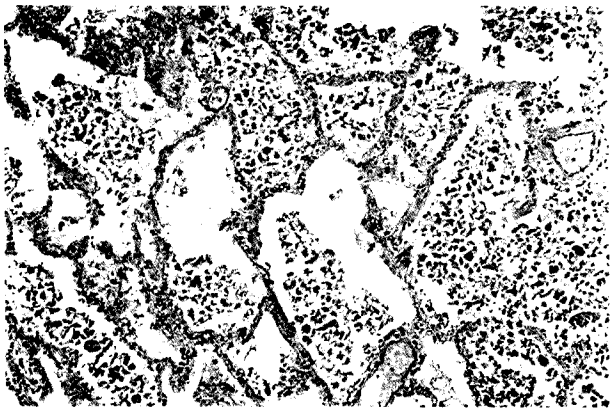

FIGURE 3: High power view of intra-alveolar cellular infiltrate. Minimal interstitial inflammation is present.

examination showed changes related to multi-organ failure. Post mortem cultures of lung tissue were negative for mycobacterial species, viruses, fungi and pathogenic bacteria.

DISCUSSION

Interstitial pneumonias have been classified into three types by Liebow and Carrington on the basis of their histologic appearance and clinical course: usual interstitial peumonitis, lymphoid interstitial pneumonitis and desquamative interstitial pneumonitis. The Hamman-Rich syndrome is a fuliminant form of usual interstitial pneumonitis. The distinction of the desquamative from the usual is important as desquamative interstitial pneumonitis is a chronic indolent condition that is corticosteroid responsive with a much better survival rate than that reported for usual interstitial pneumonitis[4]. This report describes a particularly fulminant case of histologically proven desquamative interstitial pneumonitis that was fatal.

This patient presented with pneumonia and signs of the systemic inflammatory response syndrome and initial therapy was directed at the various causes of pneumonia. However, the patient did not respond and no bacterial, viral or autoimmune cause was identified despite extensive, repeated investigations. Open lung biopsy was not diagnostic. Five days later at post mortem there was histological evidence of widespread desquamative interstitial pneumonitis. None of the known aetiologies of desquamative interstitial pneumonia (such as drugs, infective agents, eosinophillic granuloma and particulate matter) can easily be associated with this case.

The most likely explanation for this patient's presentation was a desquamative interstitial pneumonitis secondary to a viral infection. However, despite the clinical and pathologic suspicion of viral infection, this could not be substantiated, with repeated cultures, negative serology and lack of viral inclusion bodies on histopathology. Although an acute presentation of desquamative interstitial pneumonitis is uncharacteristic, there are two other similar case reports in the literature[7,8].

As desquamative interstitial pneumonitis is a diffuse disease with uniform involvement of the lung, it is unlikely that the negative lung biopsy was a sampling error, but demonstrates in this case the rapid progression of a usually indolent disease. Had this diagnosis been suspected, steroid therapy would have been instituted[4]. Recent advances in computer tomography of the chest may distinguish between pulmonary oedema and interstitial lung disease, but this technology was not available in our institution at the time of this patient's presentation.

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