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Neutrophilic alveolitis in Sweet's syndrome

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Abstract

In a case of Sweet's syndrome (acute febrile neutrophilic dermatosis) neutrophilic alveolitis was found by lung biopsy. Pulmonary disease in this condition may be underrecognised yet, like the dermatological features, it responds rapidly to corticosteroids.

In 1964 Sweet described "acute febrile neutrophilic dermatosis," a condition characterised clinically by multiple erythematous and painful skin plaques and histologically by a dense neutrophilic infiltration of the dermis without vasculitis.[1] An underlying internal malignancy is found in 10–15% of cases.[2] Associated non-cutaneous features include pyrexia, peripheral blood neutrophilia, a raised erythrocyte sedimentation rate (ESR), episcleritis, arthralgia, proteinuria, and hepatitis.[1–4] Pulmonary lesions, proved by biopsy, have been reported in three patients only[5–7]; in all cases they were severe and associated with a myeloproliferative disorder. We report a further patient with Sweet's syndrome and biopsy proved neutrophilic alveolitis.

Case report

A 72 year old woman presented with a five day history of a pustular rash on her hands. Her medical history was unremarkable but she was having long term treatment with fenbufen for osteoarthritis and oxprenolol and frusemide for hypertension. She had had no previous lung disease and had not smoked cigarettes for 20 years. She complained of mild breathlessness but had no cough or sputum. She had tender, dusky, erythematous plaques studded with pustules on the dorsum of both hands. On her face there were erythematous plaques associated with pronounced facial oedema. Her sclera were injected and showed changes of a nodular episcleritis. On auscultation of her chest bilateral lung crackles were audible. She was afebrile and examination otherwise showed no abnormalities. On admission her chest radiograph showed patchy infiltration of the right upper lobe, which progressed over the next two weeks with the development of further shadowing in the left midzone (fig 1) despite empirical treatment with flucloxacillin and ampicillin. Sputum cultures were sterile and serological tests for viruses, chlamydia, *Mycoplasma pneumoniae*, and *Legionella pneumophila* gave negative results. Her haemoglobin concentration was 12·7 g/dl with a normal blood film, the white cell count was 14·1 × 10^9/l (75% neutrophils) and her erythrocyte sedimentation rate was 119 mm in one hour. Results of liver function tests and serum creatinine, calcium, and electrolyte concentrations were normal. Urine analysis showed 1+ proteinuria but no casts were seen by microscopy and urine culture was negative. Results of tests for serum rheumatoid factor and antinuclear and antineutrophil cytoplasmic antibodies were negative; concentrations of immunoglobulins, angiotensin converting enzyme, and complement components C_3 and C_4 were normal. HLA typing showed A3 AW19 B7 B27. Pulmonary function tests showed a vital capacity of 1·5 l (62% predicted), FEV_1 1·0 l (52%), total lung capacity 4·2 l (89%), and transfer factor for carbon monoxide (TLCO) 4·03 mmol/min/kPa (95% predicted). Bronchoscopy showed inflammation of the right upper lobe bronchus but secretions were mucoid and not overtly purulent. Analysis of fluid obtained from the right upper lobe by bronchoalveolar lavage showed a white cell count of 11·2 × 10^9/l (91% neutrophils, 2% eosinophils, and 7% macrophages). Culture of the fluid was sterile, cytological examination showed no malignant cells, and culture for mycobacteria was negative.

Skin biopsy (fig 2A) showed a pronounced neutrophilic infiltration in the upper dermis with some leucocytoclasis. There was no evidence of vasculitis and immunofluorescence studies gave negative results. Gram staining of fluid from a pustule showed mature polymorphs but no organisms and culture was negative. Transbronchial biopsy was performed from the right upper lobe. The lung parenchyma was collapsed and showed interstitial infiltration by large numbers of neutrophils, with occasional eosinophils and small numbers of lymphocytes. Small groups of macrophages were present in alveoli (fig 2B). There was no evidence of granulomatous inflammation. The biopsy specimen contained a small piece of cartilagenous bronchus showing active chronic inflammation of the mucosa and submucosa with infiltration by numerous neutrophils and small numbers of lymphocytes, plasma cells, and eosinophils.

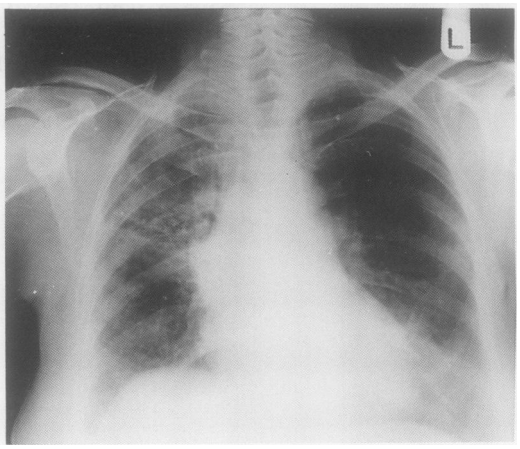

Figure 1 Chest radiograph showing areas of ill defined consolidation particularly affecting the right upper and left mid zones with reduction in the volume of the right lung.

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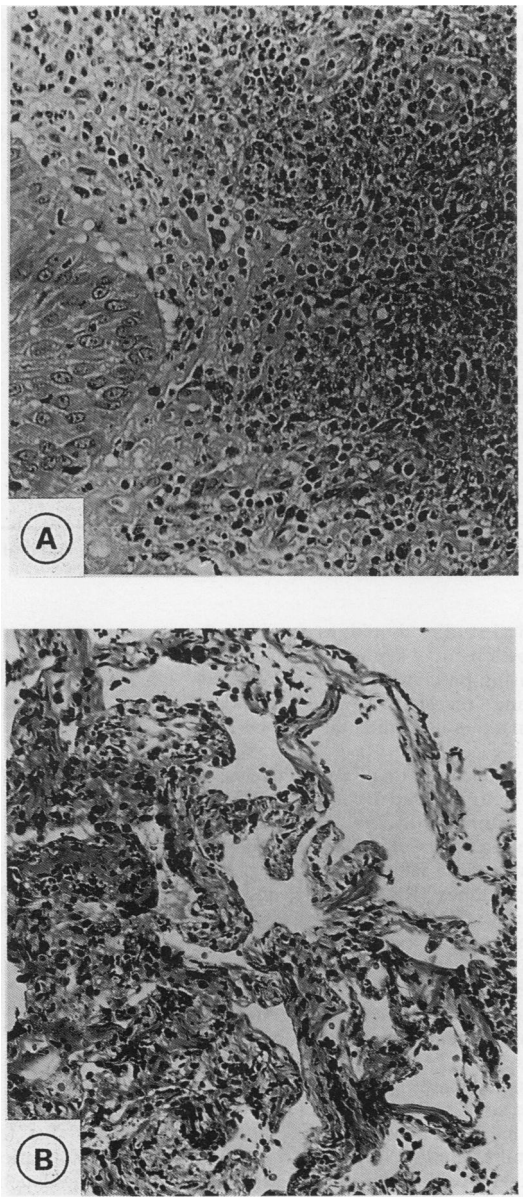

Figure 2 Skin biopsy specimen (A) showing a dense inflammatory dermal infiltrate with a large proportion of neutrophils and transbronchial lung biopsy specimen (B) showing interstitial infiltration by neutrophils without acute vasculitis.

A diagnosis of Sweet's syndrome with pulmonary manifestations was made and treatment with prednisolone 40 mg daily was started. There was a rapid improvement in her rash, which resolved over eight weeks. Her breathlessness resolved and pulmonary function improved, vital capacity rising to 2·0 l (83% predicted), FEV_1 to 1·45 l (78%), total lung capacity to 5·05 l (107%), and transfer factor to 5·59 mmol/min/kPa (134%). There was rapid clearing of the radiographic shadowing but some reticulonodular shadowing persisted in the right upper lobe, suggesting some residual fibrosis.

Discussion

We report a case in which skin changes typical of Sweet's syndrome (acute febrile neutrophilic dermatosis) were accompanied by inflammatory changes in the lung, shown histologically to be neutrophilic alveolitis. Investigations for infective causes gave negative results and the pulmonary shadowing progressed during antibiotic treatment but responded to steroids. Biopsy proved pulmonary disease in Sweet's syndrome has been reported on three occasions, in each case associated with a myeloproliferative disorder.[5-7] The pulmonary disease in these cases was severe, necessitating mechanical ventilatory support in one patient and leading to fatal respiratory failure in another. Overall 10–15% of cases of Sweet's syndrome have been associated with malignancy—acute myelogenous leukaemia in nearly half. Our patient has responded well to corticosteroids and has shown no evidence of underlying malignancy during a follow up of 11 months.

Previous cases have been diagnosed by open lung biopsy but our experience suggests that transbronchial biopsy provides adequate tissue to establish the diagnosis. Bronchoalveolar lavage was particularly helpful in excluding infection and in showing evidence of florid neutrophilic alveolitis. This distinction between infection and sterile inflammation is crucial as the disease does not respond to antibiotics but does respond to corticosteroids. Lung manifestations in this syndrome may be more common than has been realised because in a few further reported cases pulmonary infiltrates responded to corticosteroids but the diagnosis was not established by biopsy.[8-10]

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