Ankylosing spondylitis and pulmonary sarcoidosis—a case report and discussion of the literature

Sir, Co-occurrence of sacroiliitis and sarcoidosis is rarely reported, but when it occurs it is a cause of diagnostic confusion [1]. The two conditions may co-exist either due to sarcoid deposition within the SI joint or due to the development of two distinct conditions (sarcoid and SpA) within the same patient [1]. Recent reports of the development of pulmonary sarcoidosis in patients with AS treated with anti-TNF-α therapy makes correct diagnosis in these cases critical [2, 3]. We present the case of a 31-yr-old man with a 23-yr history of AS, who was found to have radiological and histological evidence of pulmonary sarcoidosis while undergoing preliminary assessment for anti-TNF-α therapy.

The patient came under the care of our clinic in 1999. Plain radiographs at that time showed sclerosis and ankylosis of both SI joints (Fig. 1a), and Schober’s test and chest expansion were well maintained at 5 cm. Auscultation of the chest was normal. Initially he was managed with oral naproxen and physiotherapy. Oral SSZ was started when his symptoms worsened.

In 2005, he reported increasing spinal pain and stiffness and examination revealed that his spinal movements had deteriorated, with Schober’s test and chest expansion at 2 cm. At this point, the use of TNF-α blocking therapy was discussed with the patient. A routine chest radiograph at this time, however, revealed reticular–nodular shadowing mainly in the mid- and upper zones (Fig. 1b). High-resolution CT scanning of the lungs showed enlarged mediastinal and hilar lymph nodes with extensive mid- and upper zone fibrosis consistent with pulmonary sarcoidosis. Transbronchial lung biopsy revealed non-necrotizing granulomata and bronchioalveolar lavage revealed a chronic inflammatory picture. There was no evidence of tuberculosis on prolonged culture. Pulmonary function tests showed an FEV1 of 2.73 l (69% of predicted), an FVC of 3.01 l (62% of predicted) and a transfer factor of 1.68 l (107% of predicted). There were no previous chest radiographs within the hospital for comparison. Direct questioning revealed that the patient had had symptoms of breathlessness since adolescence, but had not reported this and had modified his activities to avoid exertion. Later in life he had found that his spinal symptoms were the main limit to his activity.

Tissue typing revealed that along with HLA B27 the patient carried DR4, which has been associated with late onset of sarcoidosis, and DQB1*06, which has been associated with susceptibility to sarcoid [4].

There have been only five other reported cases of sarcoidosis developing in a patient with established AS [1, 5–7]. All of these patients were HLA-B27 positive and presented initially with saccroiliitis but then went on to develop pulmonary sarcoidosis (in one case with skin nodules [1]) with non-necrotizing granulomata on lung biopsy. There have been nine reported cases (six before 1975) in which features of SpA and sarcoidosis have co-existed [1, 5, 6, 8]. In one case, biopsy of the SI joint revealed sarcoid, and in the four cases where HLA typing was available, all were B27 negative but carried HLA types that have been associated with sarcoidosis (B8, B13, B35 and A9), making sarcoid of the SI joint the most likely diagnosis.

A recent cross-sectional study of a UK sarcoid population found that radiological sacroiliitis occurred in 6.6% of the patients compared with 1.9% of the normal population [9]. These data, however, do not support a true association between SpA and sarcoidosis, as only one of the four patients found to...
have sacroilitis on X-ray was HLA-B27 positive. It may be, however, that sacroilitis of the SI joint may be more common than previously thought. A single European study found that isolated pulmonary sarcoid was associated with HLA-B27 [10], making a true association between SpA and sarcoid possible, but this finding has not been replicated and the relatively high prevalence of the two conditions (1:1000 for AS and 0.04–64/1000 for sarcoidosis [7]) makes sporadic co-occurrence likely.

In conclusion, co-existence of SpA and pulmonary sarcoid is rare, but sacroilitis of the SI joint may be more common than previously thought. Treatment with TNF-α blockade may precipitate de novo pulmonary sarcoid and with the increasing use of these drugs for the treatment of SpA accurate diagnosis in patients who present with both sacroilitis and sarcoid is critical. The clinician should be aware that patients with SpA of sufficient severity to warrant treatment with anti-TNF agents may not report symptoms of pulmonary sarcoid due to limitation of their activity by musculoskeletal symptoms. We would therefore recommend that all AS patients undergo thorough assessment and monitoring of respiratory function prior to and during treatment with TNF-α blockers.

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**Rheumatology key message**

- Reduced exercise capacity in AS may mask the symptoms of pulmonary sarcoidosis.

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**Paraneoplastic scleroderma secondary to hairy cell leukaemia successfully treated with cladribine**

Sir, We read with interest the report by Sfikakis et al. on the use of imatinib in refractory dcSSc [1]. We would like to share our own experience. We report a 55-yr-old man with rapidly progressive scleroderma associated with hairy cell leukaemia (HCL). The progression of scleroderma was stopped by treating the underlying malignancy with cladribine (2-chlorodeoxyadenosine).

The patient presented with a 2-month history of severe ankle pain, swollen hands, dyspnoea and fatigue. Physical examination was unremarkable. Baseline tests revealed a pancytopenia and he was referred to haematology. Peripheral blood count showed mononuclear cells with morphology suggestive of HCL. Flow cytometry showed a population of B cell expressing CD22, CD20, CD25, CD103 and CD11C. Bone marrow aspirate confirmed the diagnosis (Fig. 1). Chemotherapy was deferred until peripheral blood count dropped to treatment threshold. However, his dyspnoea worsened and he developed RP. Investigations included CXR (normal), echocardiogram (normal) and blood tests showing positive ANA reactivity with anti-topoisomerase-I antibodies. This prompted a review by rheumatology at which point the patient complained of persistent swelling, stiffness and RP in his hands, difficulty in opening his mouth, early satiety and regurgitation, dyspnoea on minimal exertion and severe fatigue. Examination revealed abnormal nail-fold capillaries, active RP, poor grip strength and diffuse thickening of the skin in hands, forearms and feet. Mouth aperture was reduced. A diagnosis of dcSSc was made 3 months after the diagnosis of HCL. The severity and rapid progression of scleroderma occurring in the context of recently diagnosed HCL suggested a paraneoplastic origin. Although a conservative approach to management of HCL would otherwise have been taken, it was decided to treat the patient with cladribine due to his concurrent scleroderma. This resulted in total remission (bone marrow <1% hairy cells), almost complete resolution of skin sclerosis and overall symptomatic improvement. RP remained but was controlled by oral vasodilators. To date, HCL remains in remission and the progression of scleroderma has stopped.

Paraneoplastic scleroderma has been reported in small numbers in association with carcinomas of breast [2], ovary, uterus [3] and prostate [4]; metastatic melanoma and bronchial carcinomas; HCL [5] and other lymphomas. The definition of paraneoplastic scleroderma is supported by a close temporal relationship between the presentation of scleroderma and malignancy [2–5], scleroderma following the progression of the malignancy [3, 5] and a much more rapid and severe progression of scleroderma than usual [2, 4]. These observations are also present in the case we report. Although some case series have highlighted the atypical features of scleroderma occurring in the context of malignancy, such as absence of hallmark autoantibodies or disproportionate palmar fibrosis [6], our case illustrates that the clinical and

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**Fig. 1.** Bone marrow trephine labelled with anti-CD20 showing hairy cells.