have sacroiliitis 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 sacroiliitis 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.

**Rheumatology key message**

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

**Disclosure statement:** The authors have declared no conflicts of interest.

S. Levy, V. Sandhu

1Department of Rheumatology, St Georges Hospital, Tooting, London, UK

Accepted 7 August 2008

Correspondence to: S. Levy, Department of Rheumatology, Kings College Hospital, Denmark Hill, London SE5 9RS, UK. E-mail: sarahlevy@doctors.net.uk


Rheumatology 2008;47:1734–1735
doi:10.1093/rheumatology/ken367
Advance Access publication 23 September 2008

**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-1 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...
laboratory features may on occasions be indistinguishable from idiopathic scleroderma. The only unusual feature in this case is male gender, as 80% of the cases of SSc occur in women. The mechanism of interrelationship between scleroderma and malignancy has not been proven but most hypothesis favour imbalance of the immune system: it is postulated that a humoral or cell-mediated immune process initiated by the malignancy may be responsible for the development of scleroderma [2, 4, 5]. HCL is an indolent form of B-cell lymphoma. Hairy cells produce fibronectin and cytokines such as fibroblast growth factor, TGF-β and TNF-α. The first three have been deemed responsible for bone marrow fibrosis whilst the latter is thought to cause marrow inhibition [7]. Activated fibroblasts are recognized as the effector cells responsible for the fibrotic changes in scleroderma. Their activation and regulation results from complex cell-cell, cell-cytokine and cell-matrix interactions mediated by a variety of cytokines and growth factors [8]. TGF-β promotes extracellular matrix synthesis and myofibroblast differentiation and is implicated as a key driver of the activated scleroderma fibroblast phenotype [9]. Interestingly, TGF-β and other cytokines are produced in excess in HCL. Given that the interplay between a number of cytokines and growth factors is thought to underlie the pathogenesis of both conditions, it is reasonable, although purely speculative, to infer that both pathologies may have common pathogenic links.

Cladribine is a purine analogue with cytotoxic effects in proliferating and quiescent hairy cells [10]. Death of hairy cells will result in interruption of the production of TGF-β and other cytokines, which may explain why treatment of HCL halted the progression of scleroderma in our case. This shows parallelism with recent publications on the use of imatinib (a tyrosine kinase inhibitor) in myeloproliferative syndromes: clues to occult neoplasia. Semin Arthritis Rheum 1999;29:43–55.

Clinical suspects should retain a high index of suspicion for an underlying malignancy in patients presenting with scleroderma even when age of onset and clinical features are unremarkable.