Figure 1 Anti-keratin antibodies (AKA) detected by indirect immunofluorescence on rat oesophagus. (A) Typical linear laminated labelling pattern restricted to the upper cornified layer observed in the serum of patients with rheumatoid arthritis. (B) Foamy pattern due to prozone effect in rheumatoid serum, with high titres of AKA and anticyclic citrullinated peptide antibodies; when diluted, this serum gives the typical pattern as observed in (A).

technique. An excess of antibodies can result in diffuse or faint staining.¹⁰

To confirm this hypothesis, some of the anti-CCP positive sera, usually diluted 1:20 for AKA determination, were then diluted in phosphate-buffered saline up to 1:200. Patients 6, 7 and 10 then showed the characteristic linear laminated pattern. These patients who were first considered to be AKA negative were in fact AKA positive!

To conclude, testing for autoantibodies is highly relevant in the diagnosis or exclusion of many systemic autoimmune diseases, including RA. Our data show that IIF is an interesting diagnostic tool, provided the biologist has trained staff, quality controls, proficiency testing and keeps in mind the possible occurrence of prozone effects. As much as possible, AKA and anti-CCP antibodies should always be combined for optimum diagnostic performance. Solid-phase assays, which may be too expensive in some countries, can detect only anti-CCP antibodies, whereas IIF could give extra information such as the presence of antinuclear antibodies when examining for AKA.

Authors' affiliations

Frederique Dubois-Galopin, Celine Beauvillain, Damien Dubois, Anne Pillet, Gilles Renier, Pascale Jeannin, Alain Chevailler, Immunology and Allergology Laboratory, CHU Angers, France
Charles Masson, Rheumatology, CHU Angers, France

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Correspondence to: A Chevailler, Laboratoire d'Immunologie et d'Allergologie, Hôpital Larrey, CHU 49933 Angers cedex 9, France; alchevailler@chu-angers.fr

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Successful treatment with bosentan for severe digital ischaemia in limited cutaneous systemic sclerosis

Emma P K Yu, Andrew J K Ostor, Frances C Hall

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We report the case of a patient with limited cutaneous systemic sclerosis, who developed progressive digital gangrene. This responded rapidly to bosentan.

A 38-year-old, previously well, male non-smoker presented with an ischaemic left index finger. On examination the distal left index finger was cyanosed; sclerodactyly and facial telangiectasia were also noted. Investigations revealed haemoglobin 10.7 g/dl (normocytic); erythrocyte sedimentation rate 94 mm in the first hour; normal C-reactive protein levels; positive antinuclear, anticentromere and anti-Ro antibodies;

normal complement components; no anticardiolipin antibodies, lupus anticoagulant activity or cryoglobulin; negative blood cultures; normal chest radiograph and ECG; arteriogram of the left arm revealed no arterial occlusion and was consistent with small vessel disease; and endoscopy revealed antral gastritis.

A diagnosis of limited cutaneous systemic sclerosis was made. The patient was treated with iloprost, nifedipine, clopidogrel, losartan, fluoxetine, lansoprazole and repeated blood transfusions. Despite this, he presented acutely with gangrene of seven fingers, constitutional symptoms and

Figure 1 Serial photographs of the baseline appearance of the patient's right fingers, before receiving bosentan, and progress over 6 months' treatment.

anaemia. During a 2-month inpatient stay, the ischaemia progressed despite treatment with iloprost, methylprednisolone, cyclophosphamide and cervical sympathectomy.

Bosentan (62.5 mg increasing to 125 mg twice daily) was commenced. Within 9 days of treatment, there was a marked improvement in perfusion of the viable tissue in the fingers and the constitutional symptoms. Serial photographs document the baseline appearance of the patient's right fingers, before receiving bosentan, and progress over 6 months' treatment (fig 1). Health Assessment Questionnaire scores improved from 2.0 pre-bosentan to 1.0 over this period (supplementary fig 2 available at <http://ard.bmj.com/supplemental>).

After 6 months of treatment, reduction of the dose of bosentan to 62.5 mg twice daily was associated with recurrent cyanosis in his right ring finger, which resolved on returning to 125 mg twice daily. Over 10 months of follow-up, the patient remained well, with no further requirement for blood transfusion (20 units of packed red blood cells had been administered over the preceding 20 months).

Microangiopathy in systemic sclerosis is thought to involve vasoconstriction and vascular remodelling.^{1,2} Endothelin 1 is a potent endothelium-derived vasoconstrictor and has been reported to promote vascular smooth muscle cell proliferation, inflammation and fibrosis.^{3,4} Endothelin receptor antagonists are an established treatment for pulmonary artery hypertension^{5,6} and may also decrease the number of new ulcers in systemic sclerosis.⁷ The putative antiproliferative and anti-inflammatory actions of bosentan provided the rationale for its use in this case.

It was striking that, despite treatment with a range of vasodilators, this patient's digital ischaemia continued to progress. Since small vessel vasculitis potentially contributed to the microangiopathy, the patient was treated with methylprednisolone and cyclophosphamide. In view of the risk of scleroderma renal crisis, blood pressure and renal function were monitored carefully. This combination of treatments, over 2 months, failed to halt the progression of digital ischaemia. However, there was a dramatic local and systemic response within 10 days of commencing bosentan. Inevitably, infarcted tissue autoamputated, but marked improvement in the perfusion of viable digital tissue was evident over a 6-month period.

This indicates that the potential of endothelin-receptor antagonists in the management of systemic sclerosis-related microangiopathy should be further evaluated.

Supplementary data containing fig 2 available at <http://ard.bmj.com/supplemental>

Authors' affiliations

Emma P K Yu, Andrew J K Ostor, Addenbrooke's Hospital, Cambridge, UK

Frances C Hall, University of Cambridge Department of Clinical Medicine, Addenbrooke's Hospital, Cambridge, UK

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Correspondence to: Dr F C Hall, Box 157, University of Cambridge Department of Clinical Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK; fch22@medschl.cam.ac.uk

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