Localized scleroderma and hemiatrophy in association with antibodies to double-stranded DNA

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Summary: Localized scleroderma involves primarily skin but also muscle, bone and synovium. Further associations and transitional forms have been reported. We report here two cases showing associations between localized scleroderma and vasculitis, mononeuritis multiplex, juvenile chronic arthritis and hemiatrophy. In particular our cases both possess antibodies to double-stranded DNA, a finding not previously reported.

Introduction

Localized scleroderma can occur as morphea, linear scleroderma or generalized morphea.¹ These form a distinct group both clinically and pathogenetically from systemic sclerosis. Localized scleroderma involves predominantly skin but can also involve muscle and joints. Other systemic associations are uncommon.

We report here two patients with localized scleroderma showing unusual associations.

Case reports

Case 1

A 50 year old woman (Figures 1 and 2) first presented in March 1977 with extensive morphea, widespread skin atrophy and right facial hemiatrophy. In addition she had left ulnar, partial right ulnar and left median nerve palsy which developed 2 weeks prior to presentation. Her blood pressure was 170/100 mmHg. Investigations revealed an ESR of 33 mm/h, a positive antinuclear factor (ANF) at a 1:400 titre and a homogeneous pattern. Anti-DNA antibodies and hand radiographs were normal. Histology showed features consistent with morphea. Her neurological symptoms responded to prednisolone 30 mg daily which was gradually withdrawn and finally stopped in 1979. In February 1980 she developed further left median, right ulnar and left lateral popliteal nerve lesions. No cause other than her scleroderma could be found

for these. Her blood pressure was 210/110 mmHg, ESR 42 mm/h, ANF remained positive at a 1:200 titre and rheumatoid factor (latex fixation method)

Figure 1 Photograph of a 50 year old female showing right facial hemiatrophy, morphea and skin atrophy.

Figure 2 Photograph of a 50 year old female showing vasculitic ulceration on the lateral aspect of her left foot.

was positive at a 1:320 titre. She responded once again to steroids while her blood pressure was controlled with atenolol and chlorthalidone. She had a recurrence of her peripheral nerve lesions in 1985 which persisted. By March 1988 she had in addition developed vasculitic ulcers over her lateral and medial malleoli with absent foot pulses. Investigations revealed an ESR of 24 mm/h, antinuclear factor positive at 1:50 titre, anti-DNA antibody positive with a titre of 893 IU/ml (normal < 50) and cryoglobulins had become detectable in her sera. The vasculitic nature of her ulcers was confirmed on biopsy. Her vasculitic ulcers and walking distance improved on azathioprine 100 mg daily and on increased prednisolone dose from 5 mg to 15 mg daily. Her blood pressure is now well controlled on nifedipine in place of atenolol and she remains improved one year later.

Case 2

A 14 year old boy was referred with juvenile chronic arthritis diagnosed 4 years earlier. This diagnosis was based on evidence of marked poly-articular synovitis involving his right elbow, knee and wrist. In addition the first and second proximal interphalangeal and metacarpophalangeal joints of his right hand were affected. Concurrently he developed progressive skin lesions of extensive linear scleroderma involving his right upper and lower limbs with accompanying unilateral right-sided hemiatrophy and a shortened right leg. His investigations performed at initial diagnosis had shown an ESR of 35 mm/h, positive rheumatoid factor (latex fixation) in a 1:80 titre and a positive ANF. He had subsequently been treated with penicillamine and physiotherapy. When seen, his clinical features were still present and in addition he had developed flexion deformities at his right elbow and knee joint. His right ankle showed restricted movement and he had a contracted right hand. His

ESR was now 24 mm/h. He was continued on penicillamine and given further physiotherapy. By 1985 he had developed subluxation of all toes of the right foot, and he was supplied with surgical shoes. In 1987 he developed right leg ulcers after dropping large tins on his right leg. Although these ulcers developed calcinosis cutis they responded to topical antibiotics. At no time did he show evidence of a heliotrope rash characteristic of dermatomyositis or of a lupus-type rash. Autoantibody screen performed now showed a strongly positive ANF in a 1:400 titre together with anti-DNA antibodies at 474 IU/ml (normal < 50). His ESR was 30 mm/h. Biochemistry including enzymes were normal, as were complement levels whilst histopathology including immunofluorescent staining was consistent with active linear scleroderma. He has no features of systemic lupus erythematosus and remains reasonably well.

In both cases an ELISA test kit (Diamedix, Florida, USA) which detects antibodies to only double-stranded DNA (specificity 100%) was used and confirmed using indirect immunofluorescence with *Crithidia luciliae*.

Discussion

Recent classifications recognize a distinction between systemic sclerosis, localized scleroderma and limited cutaneous scleroderma encompassing the CREST variant.^{1,2} Neither of our patients showed features in keeping with a diagnosis of systemic sclerosis or limited cutaneous scleroderma. Localized scleroderma is a distinctly different entity with visceral organ involvement occurring rarely,^{1,3} whilst limited cutaneous scleroderma is a part of systemic sclerosis. Considerable overlap between the various forms of localized scleroderma may occur as illustrated by the second case.

Both of our patients showed hemiatrophy although to differing extents. Hemiatrophy in association with scleroderma has been reported previously⁴⁻⁶ but in only one previous report from Britain.⁷ The pathogenic mechanism involved in this association is uncertain although it clearly involves impaired bone development. Idiopathic Romberg's facial hemiatrophy differs in that there is no cutaneous involvement. This delineation is not always clear-cut as scleroderma *en coup de sabre* can precede facial hemiatrophy while small cutaneous lesions may be missed in patients with idiopathic hemiatrophy. Total hemiatrophy as occurred with our second case is less common than facial hemiatrophy.⁷ It has been suggested that the underlying bony abnormality in hemiatrophy may make the involved side of the body more susceptible to scleroderma.⁶

Localized scleroderma has been reported in

association with various connective disorders including systemic lupus erythematosus.^{4,6,8} It can also be associated with juvenile chronic arthritis.⁹ On the other hand scleroderma can mimic juvenile chronic arthritis especially when nodules in association with joint and tendon contractures occur.^{9,10} An association between localized scleroderma and vasculitis as found in our first case is rare.¹⁰ Peripheral nerve lesions in association with localized scleroderma are similarly uncommon although well documented together with other forms of neurological injury. Surprisingly, this patient's nerve palsies responded to steroids even though most peripheral nerve lesions associated with scleroderma are non-inflammatory.^{11,12}

Serological abnormalities including the presence of rheumatoid factor and antinuclear antibodies have previously been well documented in patients with scleroderma.^{5,6,12-14} This is, however, the first report of localized scleroderma in association with double-stranded DNA antibodies in the absence of features of systemic lupus erythematosus, previous studies having shown only an association with single-stranded anti-DNA antibodies. Recently, Falanga *et al.*¹⁴ commented on this issue stating

that they could find no antibodies to double-stranded DNA in patients with localized scleroderma. They suggest that where such antibodies may appear to be present, this is as a result of using impure native DNA and that such antibodies react with single-stranded regions present. The sera of both our patients were analysed using an enzyme-linked immunoabsorbent assay specific for double-stranded DNA antibodies. It has recently been suggested that active linear scleroderma in children is occasionally associated with a severe synovitis and positive serology and that this forms a subgroup of juvenile scleroderma for which corticosteroids may be of benefit.¹⁵

The manner in which scleroderma differs from systemic sclerosis remains unresolved. Transitional forms have been described but remain controversial.^{5,16} In addition to involving muscle, bone and synovium, there is evidence that in children at least, scleroderma may be accompanied by visceral organ involvement.^{5,10} The presence of antibodies to double-stranded DNA in our two patients reported here gives further evidence of the presence of widespread immunological abnormalities in localized scleroderma and its variants.

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