

Scleroderma in childhood

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Ansell, B. M., Nasseh, G. A., and Bywaters, E. G. L. (1976). *Annals of the Rheumatic Diseases*, 35, 189–197. **Scleroderma in childhood.** Scleroderma in childhood is a rare but confusing disorder. Systemic and diffuse disease do occur but are uncommon. Much more common are local lesions of different types which can be multiple; these are often associated with joint symptoms and the development of joint contractures and tendon contractures due to nodule formation. In such circumstances the condition mimics juvenile chronic polyarthritis (Still's disease). A third, rare variant, sclerodermatous fasciitis, has also been described in one young patient.

Our knowledge of scleroderma has suffered from its definition as a skin disease. The relationship between systemic sclerosis and other forms of diffuse or localized scleroderma is seen at its most confusing in childhood where systemic sclerosis is rare, but localized forms are common. In the opinion of most authorities, patients with localized patches of scleroderma as on the face, scleroderma *en coup de sabre* on the limbs, linear scleroderma *en bande*, and morphea show no abnormalities except those related to the skin and have no systemic manifestations (Christianson and others, 1956). Eisen (1971) states, 'The question of whether localized scleroderma ever progresses into systemic sclerosis remains unanswered although Curtis and Jansen (1958) reported such a progression in six of 106 cases (5.7%) in their series. Tuffanelli, Marmelzat, and Dorsey (1966) have reported three cases in which localized scleroderma with hemiatrophy were associated with systemic lupus erythematosus, systemic sclerosis, or a rheumatoid arthritis-like picture.'

In a rheumatism unit with small experience of purely skin conditions, we have seen a number of children with localized lesions referred because of more widespread symptomatology. This is an account of such cases compared with two examples of other types of scleroderma with onset under the age of 16 years, one having diffuse systemic sclerosis of the classic type (Velayos and Cohen, 1972) and one having sclerodermatous fasciitis with eosinophilia as described by Shulman (1974) and Rodnan and others, (1975).

Diffuse sclerosis

CASE 1

In December 1968 this 13-year-old girl noticed that her fingers were going cold and blue, which was followed by swelling of the hands and stiffness of and difficulty in straightening the fingers. On examination in June 1969, the skin was tight over the fingers, forearms, arms, and feet up to the knees, and in some areas minor pitting was obtained on pressure, indicating oedema. There was loss of extension in the elbows: the wrists and fingers showed loss of movement with early flexor contractures at the proximal interphalangeal joints with some skin scarring over them (Fig. 1). In the flexures of the elbows and on the extensor aspect of both knees, there was marked pigmentation with relative perifollicular depigmentation (Fig. 2). There was no evidence of oesophageal, heart, lung, gut, or kidney involvement. Laboratory investigations at this time showed an ESR of 5 mm/h (Westergren); white blood count $2.9 \times 10^9/l$ ($2900/mm^3$) with normal differential, later normal. The differential sheep cell agglutination titre 1/1; latex negative; LE cells were not seen; antinuclear antibodies (ANA) were negative; smooth muscle antibody was present; the DNA binding capacity was 5.3% (normal 0–10%), and C3 was normal. X-rays of the hands confirmed the contractures, but were otherwise normal. In view of the slight oedema it was decided to treat her with corticosteroids, and prednisone was given from August 1969 to February 1970, initially 40 mg daily for the first 2 weeks and then 20 mg daily. Despite this she became worse, so that in February 1970 penicillamine was added up to 1.5 g daily and, together with smaller doses of prednisone, continued for 6 months, again with no improvement. In August 1970 chlorambucil was started, first at 7 mg, and later between 4 and 6 mg daily, monitored to maintain the white blood count above $3.0 \times 10^9/l$ (3000) and the platelets above $120 \times 10^9/l$ ($120000/mm^3$). Over one year there was considerable loosening of the skin, and

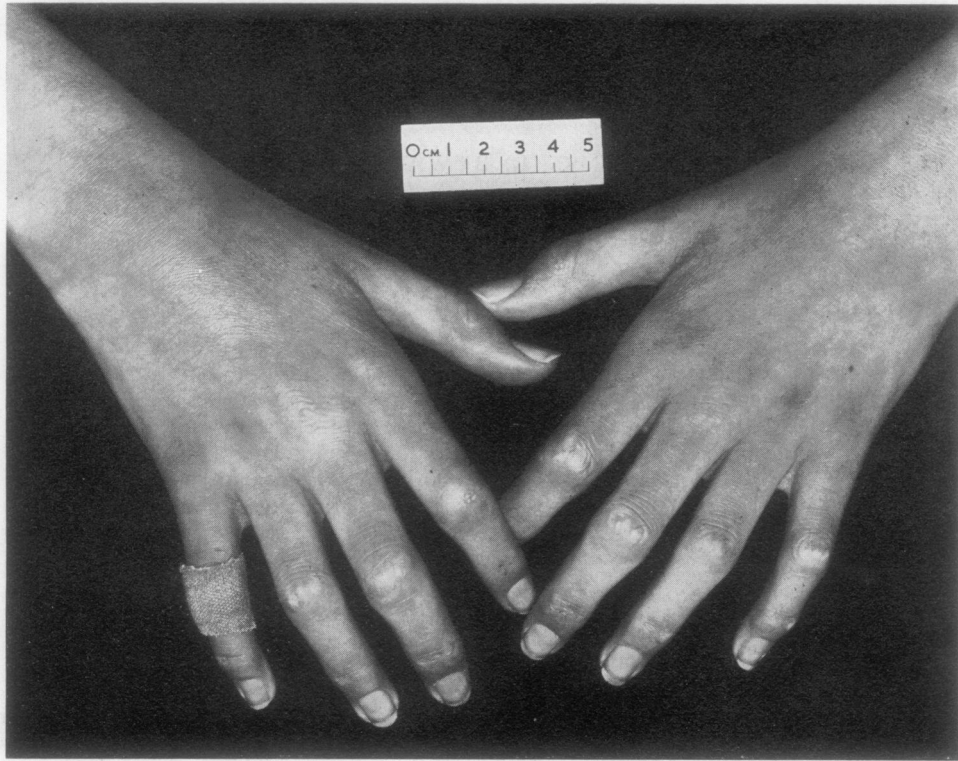


FIG. 1 *Hands of Case 1 showing contractures, scarring, and pigmentation*

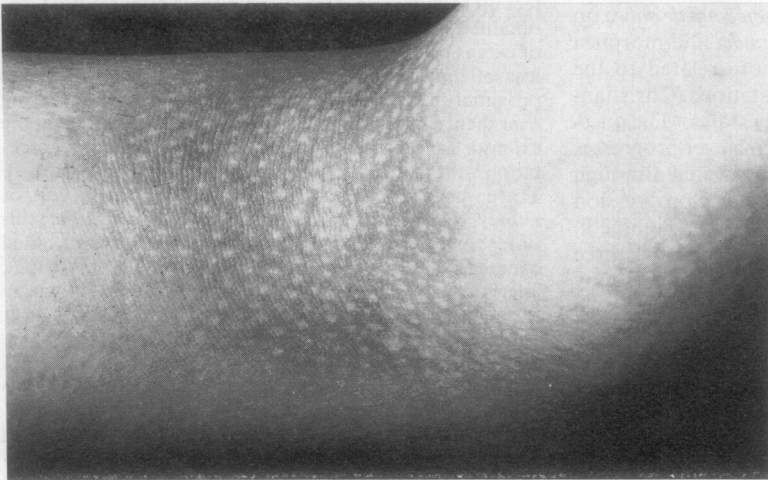


FIG. 2 *Pigmentation with perifollicular depigmentation around the elbow in Case 1*

improvement of the flexion contractures. Improvement has continued over the last 4 years as judged by loosening of the skin and increased range of movement of the joints. No systemic symptoms have developed. Chlorambucil has gradually been withdrawn after 3½ years, as has prednisone, and she has remained well for the past year, with only scarring of the skin of the fingers and some residual contractures of the proximal interphalangeal joints. In

1971 minor changes suggesting erosion were noted on the ulnar styloid processes which had healed by 1973 (Fig. 3).

Localized scleroderma

Multiple focal lesions were seen in 9 patients, either as morphea or of linear type. A further patient had pre-



FIG. 3 Serial x-rays of the ulnar styloid process showing erosions developing over 2 years and subsequently healing in a further 2 years in Case 1

existing Still's disease of classical type with multiple erosions when she developed morphea under observation, not due to local steroid injection (Holt, Marks, and Waddington, 1975). The other 8 patients all had fixed flexion deformities of one or more joints, not accounted for by the local skin lesion. The wrists and elbows were most commonly affected but ankles, feet, and shoulders were also involved. The majority complained of stiffness, rather than joint pain, but soft tissue swelling was occasionally observed in joints. Much more common was widespread tendon nodule formation. ESR was normal in 8 out of 9, rheumatoid factor negative, but ANA was present in 4 without a rise in antibodies to DNA or change in complement. Slightly raised IgG was not unusual (Table).

Table Laboratory parameters in localized scleroderma with joint manifestations

Patient	ESR	DAT	ANA to 1:10	DNA% to 10%	IgG 6.0-16.0 g/l
(Case 2)					
R.D.	6	1:1	1:10	7	10.0
S.C.	9	1:1	1:250	7.7	15.1
B.H.	9	1:1	1:10	4.5	16.4
S.P.	15	1:1	1:10	10.2	18.8
R.K.	4	1:1	1:250	5.9	12.0
(Case 3)					
B.W.	35	1:1	1:1250	7	18.8
M.J.	4	1:1	1:1250	4.9	10.91
E.F.	18	1:1	1:10	6.9	17.44
J.H.	8	1:1	1:10	5.1	11.89
(Case 4)					

C3, electroprecipitin, and extractable nuclear antigen negative in all.

CASE 2

At the age of 10 in 1948, this girl experienced difficulty in closing the left hand, stiffness of the left wrist, followed by stiffness and swelling of the right wrist and loss of extension of the right elbow. With the presenting symptoms of pain and stiffness of the joints, she was initially thought to be suffering from Still's disease. A few months later she noted the appearance of altered skin resembling morphea over the right forearm and later the left forearm (Fig. 4), and then the left breast (Fig. 5) and back of her chest, and an

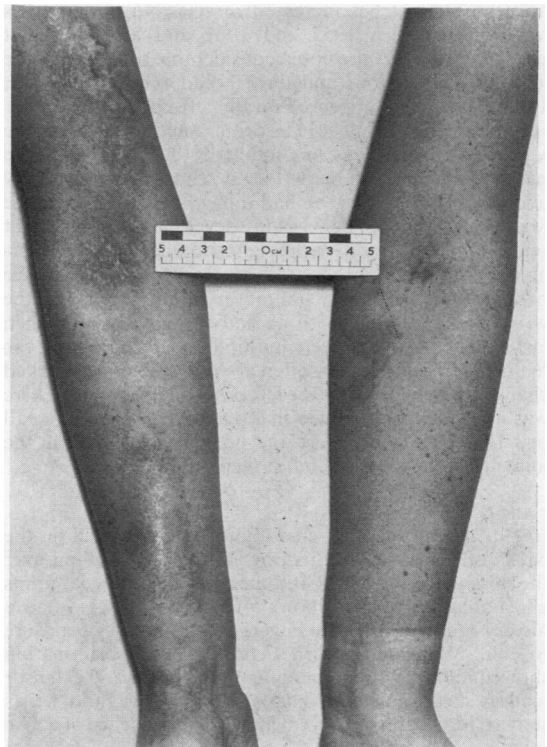


FIG. 4 Extensive patches of morphea have developed along the right forearms, and smaller ones along the left in Case 2

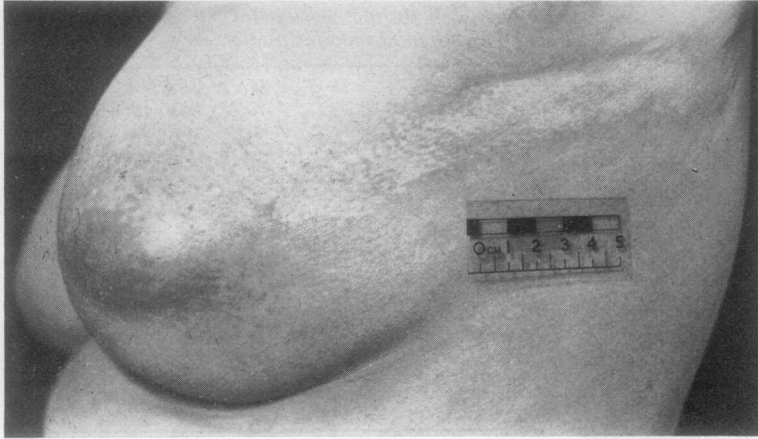


FIG. 5 A single patch of morphea on the breast of Case 2 when aged 13

exacerbation of joint symptoms. Laboratory findings were an ESR of 5 mm/h (Westergren); white blood count $5.2 \times 10^9/l$ ($5200/mm^3$) DAT 1/1. X-rays of the hands were normal. A year later there was an increase in the number and size of the morphea patches affecting both forearms, both breasts, and hands. In 1951 she received a 6-week course of cortisone (100 mg daily) with little effect. In February 1952 Acthar Gel was given (80 mg daily) for 6 weeks, again with no real change in symptoms or signs. In 1955 further morphea patches developed over the medial and lateral sides of the arms and forearms and the thighs, and the old patches increased in size. No new patches appeared between 1955 and 1961 and after her first pregnancy in 1959 she noted considerable softening of the skin over her lesions and these became less obvious. In 1962 a new patch appeared on the left upper arm. In her second pregnancy in 1963 she again noted softening of the sclerodermatous areas but following this pregnancy the patch of morphea on her left leg extended quite markedly and for a few months she had difficulty straightening the leg. In 1967 further new lesions developed over the right upper arm and later over the right shoulder with considerable limitation of the shoulder due to the skin lesion. She has continued to have limitation of movement of the wrists and hands but with no active synovitis, and when last seen in 1975 there were multiple local skin lesions, the majority of which had softened with still quite marked changes, particularly on the left thigh and shoulder. There was no evidence of diffuse changes but she had one small new lesion on her left leg, and no further changes in the joints were detected when last seen in 1975.

CASE 3

In 1964 at the age of 8, small lumps were noticed on the backs of the hands of this boy. There was swelling over the dorsum of the hands and metacarpophalangeal joints and limitation of the elbows and wrists. He also had a history of blueness of the fingers precipitated by exposure to cold. When referred in February 1968, examination showed multiple minute nodules in the flexor and extensor tendon sheaths of both hands. Both elbows and wrists showed limitation of movement without evidence of active synovitis. The skin over the forearms, legs, and feet was tight. Routine laboratory tests showed an ESR of 6 mm/h (Westergren); haemoglobin 11.8 g/dl; white blood count

4.7 (4700) with differential count; neutrophils 36%, eosinophils 9%, lymphocytes 49%, and monocytes 6%. DAT and latex were both negative. Initial testing showed no ANA but subsequently they were noted to be present, with nucleolar staining. X-rays were normal. Biopsy of the skin and a tendon nodule (Figs. 6 & 7) were compatible

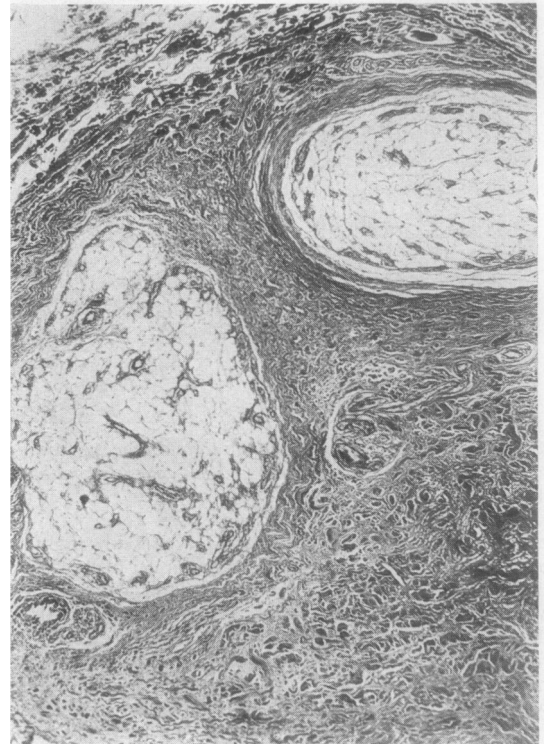


FIG. 6 Skin biopsy showing fat lobules surrounded and compressed by sclerodermatous tissue. Note the marked variation in size and staining of collagen bundles and compression atrophy of skin appendages. (Reticulin staining. $\times 48$)

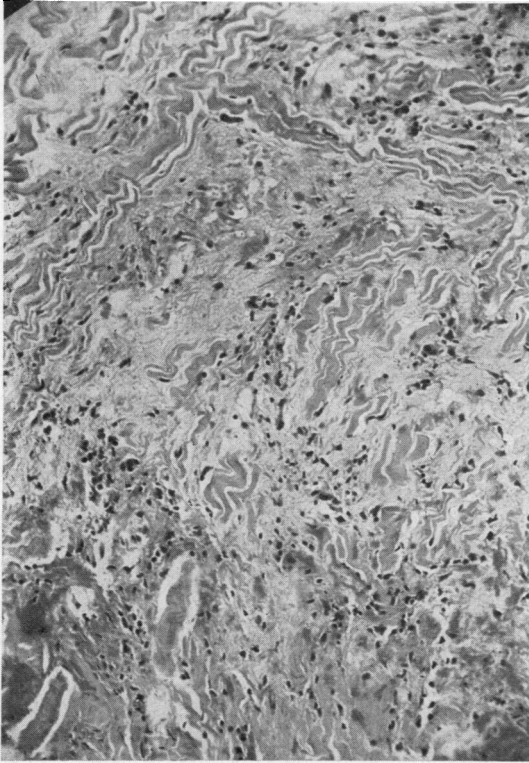


FIG. 7 Tendon nodule in Case 3, showing collagen bundles of variable size, some fibrinoid material round cells, and activated fibroblasts. (H & E. $\times 95$)

with a clinical diagnosis of scleroderma, the latter corresponding to our previous experience of nodules in scleroderma. In 1969 he still had blue fingers in the cold and was clumsy with his hands and stiff in the feet with some residual nodules. The skin was tighter in previously affected areas and was now tight over the nose. Some scarring was noted over metacarpophalangeal joints. By February 1974 he was generally well with some residual nodules and fixed flexion deformities in both elbows, and minor limitation of metacarpo and proximal interphalangeal joints. The skin remained somewhat thick over the fingers and the face but the legs between the ankles and the knees had improved. ESR was 5 mm/h; DAT 1/1; ANA positive; DNA binding capacity 5.9; complement normal. There are no radiological changes. He has remained generally well and functions normally.

CASE 4

This boy started to limp when aged 7 and was later found to have limitation of many joints without synovitis. When referred to us 3 years later, early in 1974, he had extensive minute nodule formation in the extensor tendon sheaths of the hands and feet and an indurated band-like lesion on the right thigh (Figs. 8 & 9), as well as widespread joint limitation. ESR was 11 mm/h; DAT 1/1; ANA negative; DNA binding capacity 5.1%; C3 2.0 g/l (200 mg/100 ml); joint x-rays normal. He was treated initially with physio-

therapy and splintage but, as he showed no real improvement in the limitation of movement and nodules were tending to increase, he was started on penicillamine, working up to 250 mg daily. During the first 12 months of therapy there has been considerable regression in the nodules of the tendon sheaths with little change in the band-like lesion on the right thigh or the joint limitation. Normal growth, however, has continued of the right thigh and leg.

Sclerodermatous fasciitis

CASE 5

In 1965, aged 14 years, this boy complained of pain in the hands and knees and stiffness of the metacarpophalangeal joints, worse on wakening. When admitted after 3 months of symptoms he was noted to have limitation of shoulder, elbow, wrist, metacarpophalangeal, hip, knee, and ankle joints. There was little soft tissue swelling and extensive flexor and extensor tendon involvement in the hands and wrists. There was slight thickening of the skin over the hands and below the knees with some pigmentation. The tendon sheaths showed nodular thickening. At this time the most likely diagnosis was thought to be Still's disease,

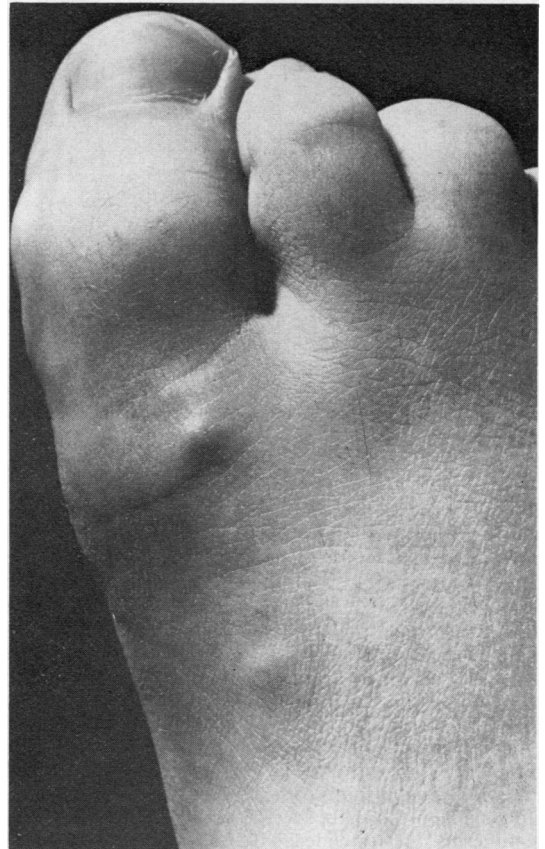


FIG. 8 Nodules along the extensor tendon of the great toe in Case 4

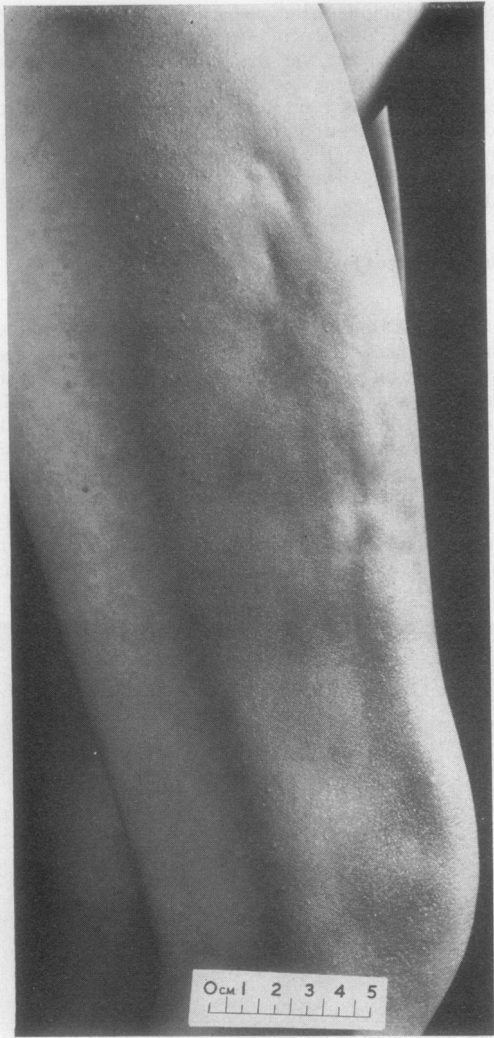


FIG. 9 *Linear lesion on the right thigh in Case 4*

although scleroderma and dermatomyositis were suggested. ESR was 78 mm/h; white blood count 9.7 (9700) (polymorphonuclears 49%, eosinophils 21%, lymphocytes 22%, monocytes 8%); DAT and ANA were negative although gammaglobulins were increased; x-rays were normal. Treatment was started with salicylate and physiotherapy and then ACTH was added for 6 weeks with some benefit, as shown by an immediate improvement in grip strength and palm print contact and a reduction of the ESR from 74 mm/h to 2 mm/h. He was discharged but 5 months later was readmitted because of tightness over the skin of the arms and legs. At that time he still had limitation of many joints with pes planus. The skin changes had become much more severe warranting a diagnosis of scleroderma; they extended to the upper arms and involved the whole of the legs but in a patchy fashion; in some areas there was pitting of the skin on pressure (Fig. 10). No telangiectasia were present. ESR was now raised at 55

mm/h and eosinophilia remained at 17% in a total white count of 6.0 (6000). ANA was still negative; DNA binding capacity 8% (normal); and barium swallow normal.

A 2.5 cm deep biopsy of skin and fascia down to and including muscle showed changes consistent with scleroderma involving deep fascia. The superficial third is shown in (Fig. 11a, b, c, d, e,) and passes from normal epidermis into a layer of collagenous thickening typical of early scleroderma and extending into the fatty layer down to the deep fascia and muscle. The new tissue is cellular and the collagen less refractile and less eosinophilic than normal. Those fibres bordering the fatty areas are separated by areas of more basophil ground substance containing reticulin and in places by fibrinoid. The cells include fibroblasts, plumper and more numerous than usual and a number of lymphocytes. Beneath the fatty layer there is a thick band of new collagenous fascia extending down to the deep fascia surrounding the muscle. This fascial tissue is composed of collagen fibres, less eosinophil and less refractile than normal, basophil in parts, and appearing in places almost homogenous. Elastin fibres are finer than normal. The fibroblast nuclei are plump and proliferating. Through it run bands of normal collagen denser and more birefringent and foci of perivascular cellular infiltration, plasma cells, lymphocytes, histiocytes, and occasional eosinophils. The original deep fascia is normal but accumulated cellular infiltration clothes it superficially. The muscle fibres themselves are normal, apart from some vacuolar change but the bundles are separated by new collagenous tissue, as was also seen superficially, with areas of oedematous fibrinoid change and other areas of intense cellular infiltration, either in oedematous strands or in granulomatous masses. The cells of such collections



FIG. 10 *Pitting of the skin on the leg in Case 5*

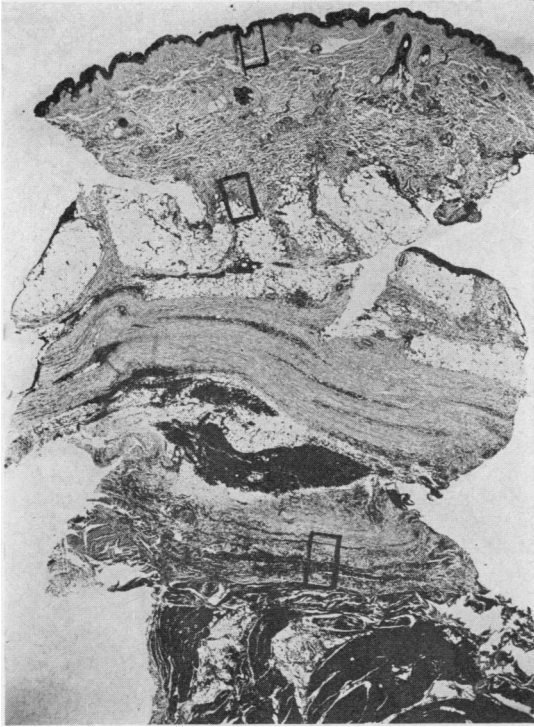


FIG. 11(a)

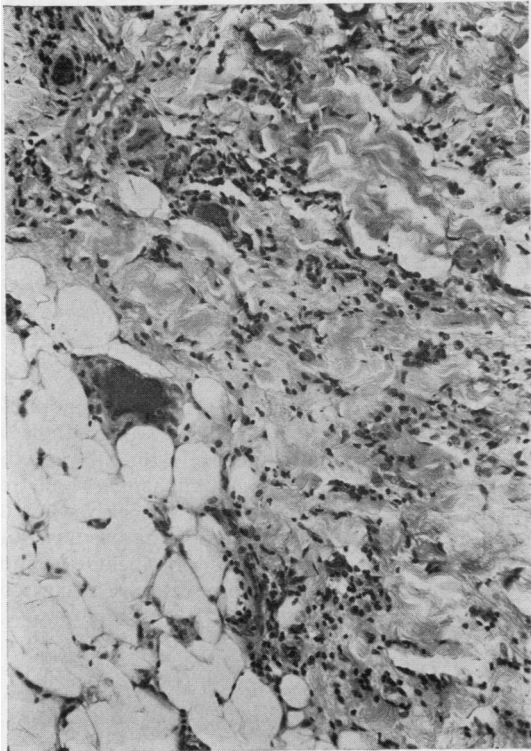


FIG. 11(b)

were, as also more superficially, lymphocytes, plasma cells, histiocytes, fibroblasts, and, occasionally, an eosinophil and mast cell.

He was treated with prednisone 20 mg daily from January 27, 1966, on which the skin oedema subsided but the skin tightened further. As occurred previously with the ACTH, the inflammatory manifestation subsided and the ESR fell from 60 mm/h to 5 mm/h and the grip strength rose. Prednisone was reduced to 5 mg alternate days by 1968. He was reviewed regularly in 1967, 1968, 1969, and 1974. By 1974 he was generally well, and has remained so, working as a spot welder, no longer on prednisone. In the hands there was swan-neck deformities of the proximal interphalangeal joints, ulnar deviation at the metacarpophalangeal joints, and loss of extension of wrists, elbows, and hips. The skin was tightly bound down on the legs. ESR was normal; ANA negative; C3 1.1 g/l (110 mg/100 ml); antibodies to DNA and DNA electroprecipitin tests all negative. X-rays of the hands over the years showed subluxation at the metacarpophalangeal joints.

Discussion

Scleroderma in childhood is not common (Jaffe and Winkelmann, 1961; Medsger and Masi, 1971). Particularly in children, differentiation between focal or diffuse skin syndromes can be difficult (Kass, Hanson, and Patrick, 1966). In this paper we would draw particular attention to the association of

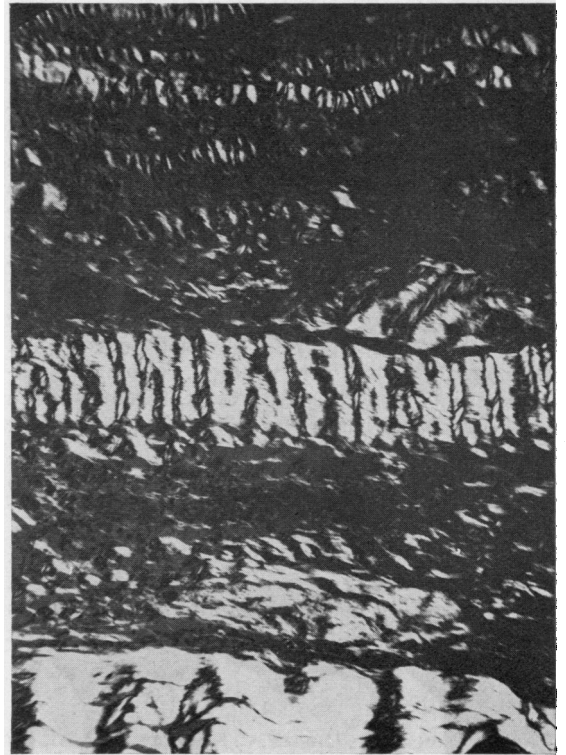


FIG. 11(c)

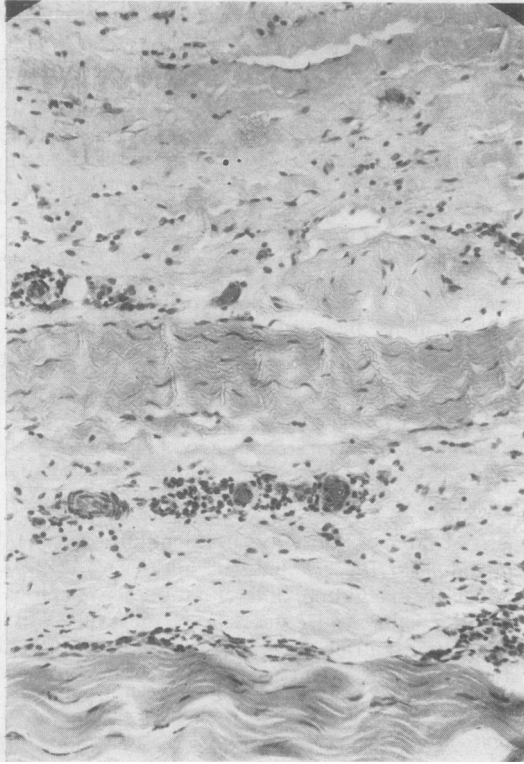


FIG. 11(d)

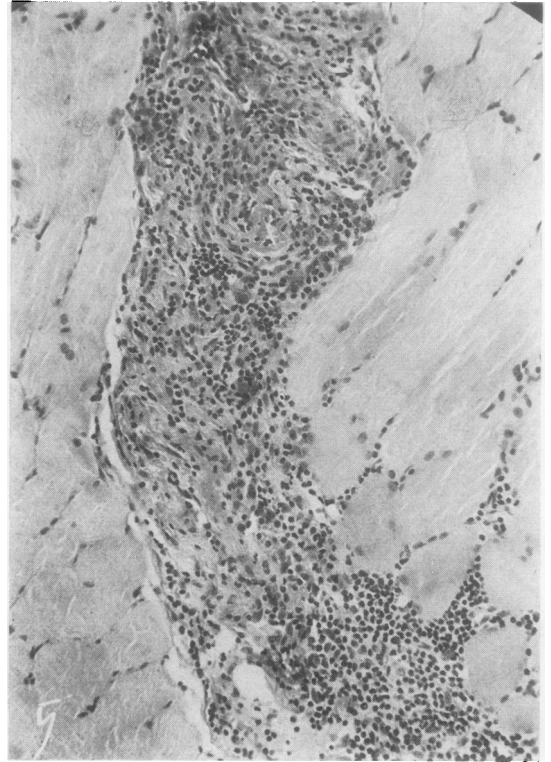


FIG. 11(e)

localized skin lesions with joint and tendon involvement. The manifestations range from arthralgia to soft tissue swelling while contractures, due to tendon involvement, are common. Nodule formation, which histologically does not resemble either rheumatic fever or rheumatoid arthritis, is common in the early stages. This particularly affects the flexor and extensor tendons of the hands and feet. These cases can easily be confused with juvenile chronic polyarthritis (often termed Still's disease). ESR is usually normal and rheumatoid factor test negative, although antinuclear antibodies may be present, together with a mild increase in gammaglobulin. In our experience antibodies to DNA are not excessive nor is C3 low. This is at variance with the findings of Hanson, Drexler, and Kornreich (1973) who reported rheumatoid factor in 7 of 21 children with focal scleroderma, as well as an increase in DNA binding capacity (V. Hanson and others, personal communication, 1974). He also noted the presence of antinuclear antibodies and IgG. Perhaps the most interesting type is that

FIG. 11 Case 5. (a) Skin showing thickening of deep dermis by collagenous tissue spreading down between the fat lobules. The superficial dermis is more normal. Deep to the adipose layers is fascial thickening (see text) and the muscle itself is invaded by plasma cell and lymphocyte collections containing a few eosinophils. (Azan trichromic stain $\times 11$.) (b) Higher power of fatty junction outlined by rectangle in (a). (H & E. $\times 95$.) (c) Showing by polarized light and (d) by normal light the broad bands of original normal fascia and the finer less refringent new collagen. (H & E. $\times 68$.) (e) Muscle showing thickened intramuscular septum with lymphocyte and plasma cell infiltration and including a few eosinophils. (H & E. $\times 95$)

recently described by Shulman (1974) as eosinophilic fasciitis (Rodnan and others, 1975). Our example of this was diagnosed retrospectively on the basis of eosinophilia, hypergammaglobulinaemia, and re-assessment of the histology. It is probably wiser to regard it, as we did, as sclerodermatous fasciitis. Features of this type of scleroderma include eosinophilia, raised ESR, and also some response to corticosteroids.

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