cases it should be possible to control the dermatitis until the fractures are healed and thereafter extract the foreign material.

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Serum Aminoterminal Propeptide of Type III Procollagen in Progressive Systemic Sclerosis and Localized Scleroderma

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Sera from 31 patients with progressive systemic sclerosis (PSS), 5 patients with widespread localized scleroderma (LS), and 3 patients with lichen sclerosus et atrophicus were analyzed for aminoterminal propeptide of type III procollagen (PIIINP) using a radioimmunoassay based on human propeptide. Thirty-eight per cent of the patients with PSS had levels above normal range, including all of the 3 patients with diffuse scleroderma. The same applies to 4 of 5 patients with widespread localized LS, while PIIINP in all 3 patients with lichen sclerosus et atrophicus were within normal levels. In patients with acrosclerosis, elevated PIIINP seems to be correlated to rapid progression and extension of lesions. A significant increase in PIIINP was found in a patient following discontinuation of prednisone and cyclophosphamide, while the present investigation did not allow judgement of effects of treatment with either penicillamine or cyclosporin A. (Accepted August 10, 1988.)

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Progressive systemic sclerosis (PSS) or scleroderma is characterized by fibrosis of the skin and internal organs. Localized scleroderma (LS) shows similar findings, only restricted to involved areas of the skin, which in some cases, however, may be large. LS may even occur in a generalized fashion. The two diseases are indistinguishable histologically. Although the pathogenesis is unclear, as suggested by histopathology, the collagen content of involved skin is increased per surface area (1). The accumulation seems to arise from an increased synthesis as opposed to a decreased degradative role (2). A disturbed control of collagen synthesis has been found in fibroblasts from patients with PSS leading to the overproduction of collagen types I and III (3, 4).

Recently, a radioimmunoassay for the aminopropeptide of type III procollagen (PIIINP) has been used to monitor fibrogenesis in liver diseases (5, 6), and in 1986 Krieg et al. (7) used this assay in patients with PSS and found that 41 per cent of patients had values above the normal range. Risteli et al. (8) have improved the method using a new rapid equilibrium type of radioimmunoassay based on human propeptide in contrast to earlier methods, which used bovin propeptide. We report on the use of this new assay in patients with PSS as well as in patients with LS. We also studied three patients with lichen sclerosus et atrophicus.

PATIENTS AND METHOD

Sera were collected from 31 patients with PSS, three of which had diffuse scleroderma, in which fibrosis starts at the trunk. Sera were also collected from five patients with widespread LS (morphoea) and from 3 patients with lichen sclerosus et atrophicus of the skin. One of the patients with diffuse scleroderma, ten with acrosclerosis, four with LS, and all three with lichen sclerosus et atrophicus were studied in a period without treatment, while all other patients were in systemic treatment. One patient was investigated while she received prednisone and cyclophosphamide, another received cyclosporin A, while all other patients on systemic treatment were on penicillamine given in dosages from 250 mg to 750 mg per day, in general 750 mg per day.

Eleven patients had serial samples collected with various intervals during a period from 2 to 8 months. All patients were studied with serum creatinine, alkaline phosphatases, and liver enzymes. Patients with suspected kidney involvement were also investigated with creatinine clearance. Other internal manifestations were diagnosed by lung X-ray, lung function tests, and studies on esophageal motility. Liver biopsies were not performed. All patients fulfilled the ARA critera for PSS (9).

Serum PIIINP levels were measured by the radioimmunoassay based upon the human propeptide (8) using the now commercially available kit from FARMOS Diagnostica, Oulunsalo, Finland. The reference range based upon healthy Finnish blood donors (n=88) is 1.7–4.2 μg/l, similar results on healthy Danish controls were 2.3–4.6 μg/l (n=39). The 95% specific cut-off levels were 2.1–4.3 μg/l. Until the analyses could be performed all sera were stored at −20°C.

RESULTS

Twelve patients with PSS (38 per cent) had PIIINP values above the upper reference level (Fig. 1). This included all 3 patients with diffuse scleroderma and 6 of 7 of a subgroup of patients with acrosclerosis and a rapid progression of disease, all having lesions above the wrists. Four of 5 patients with widespread LS had increased PIIINP, while all 3 patients with lichen sclerosus et atrophicus were with values within normal limits. The difference between our patients with scleroderma, PSS as well as widespread LS and controls was significant (p<0.01). In general, non-treated patients had higher PIIINP-levels than treated (p=0.01).

The results of serial investigations can be seen in Fig. 2. The only patient with a quantitatively distinct difference between treatment values and non-treatment levels was a patient with severe acrosclerosis treated with 25 mg prednisone and 100 mg cyclophosphamide daily. During treatment, PIIINP was 1.6 and 1.4 μg/l, after discontinuation of the

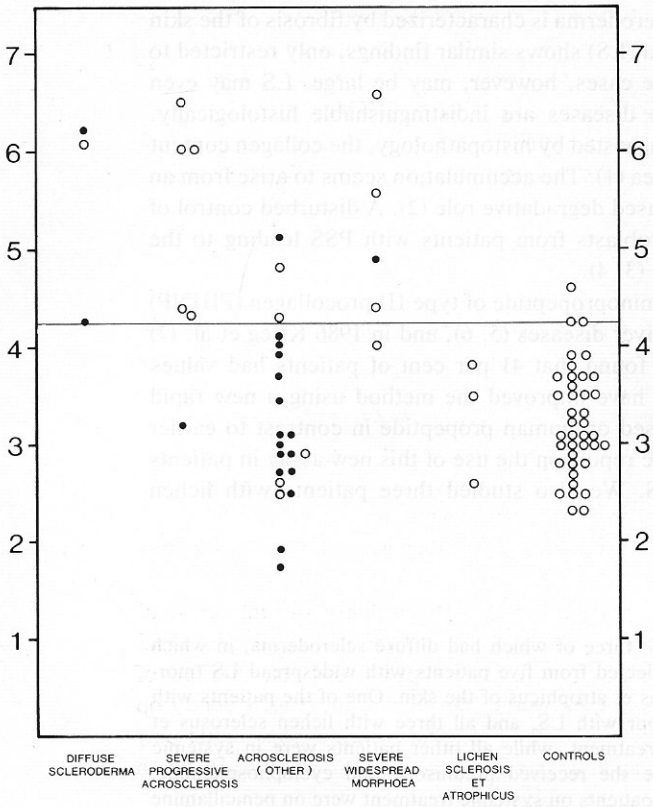

Fig. 1. Serum PIIINP levels in scleroderma patients and patients with lichen sclerosus et atrophicus. Scleroderma has been subgrouped into diffuse scleroderma, acrosclerosis, and among these a further subgroup with rapid progression with high clinical activity, and patients with localized scleroderma with widespread lesions. Circles represent patients studied before or after discontinuation of treatment. Spots represent patients on systemic treatment, in most cases with penicillamine. All values are μg/l. The line represents our upper reference level.

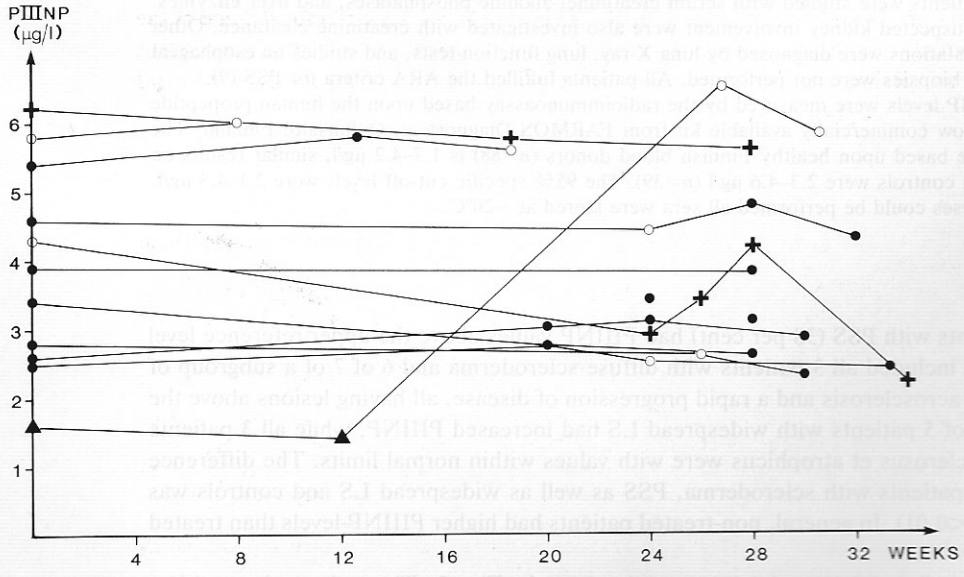

Fig. 2. Serial serum PIIINP levels from 11 scleroderma patients followed with intervals during a period from 2 to 8 months. Circles represent samples taken during periods without systemic treatment. Spots represent samples taken during treatment with penicillamine, triangles during treatment with prednisone and cyclophosphamide, and crosses during cyclosporin A.

drugs the levels rose to 6.5 and 5.8 μg/l. It should, however, be emphasized that in the majority of the patients treated with penicillamine, no treatment values normally were investigated after only a four-week discontinuation period, and that in a patient with acrosclerosis, investigated more than a year after penicillamine, PIIINP was 6.6 μg/l.

Two patients with an increased or borderline PIIINP (5.1 and 4.3 μg/l) had marginal pathological alkaline phosphatases. All patients had normal kidney function as judged by creatine clearance and/or creatine in serum.

DISCUSSION

The results of the present investigation are in accordance with the data of Krieg et al. (7). Increased PIIINP values were found in 38% of patients with PSS and in 4 of 5 patients with widespread LS. High values were found in all of the 3 patients with diffuse scleroderma and in 6 of 7 patients with acrosclerosis above the wrists and characterized by a rapid and progressive development of their disease. This agrees with observations of increased production of type III collagen in cultured fibroblasts from scleroderma patients (3, 4) and possibly reflects the increased collagen biosynthesis in our patients. The results of out study indicate that PIIINP may be utilized for evaluation of disease activity in scleroderma.

It is not possible from the present data to evaluate with certainty the influence of penicillamine on PSS as the majority of patients investigated with and without the drug had been without medication for only 4 weeks. It should also be kept in mind that an effect of penicillamine on collagenolysis and cross-linking would hardly present itself directly on PIIINP. The data from our patient treated with prednisone and cyclophosphamide may indicate that this combination therapy had an effect on fibrogenesis in the patient. Our data on cyclosporin A are too limited to allow any conclusions.

PSS patients with liver fibrosis may have increased PIIINP vaules for other reasons than due to their scleroderma. Increased PIIINP has been found in a great number of liver diseases with fibrosis and/or cirrhosis (5, 6, 10). This may be a restriction for the use of the test in individual patients, but seems to have had no influence on the results of the present study. It is our opinion that PIIINP may be utilized as a marker of fibrogenesis in PSS and therefore could be of prognostic value.

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Multiple Eccrine Poromas Arising in Chronic Radiation Dermatitis

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A 70-year-old white man developed 7 eccrine poromas in an area of chronic radiation dermatitis of his right lower extremity over a period of 37 years. To our knowledge, multiple eccrine poromas unequivocally linked to chronic X-ray damage are hitherto unreported. (Accepted June 22, 1988.)

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Eccrine poroma (1) is a not infrequent benign appendage tumour of the skin, which originates from the acrosyringium and usually arises as a single lesion in the glossy acral regions of middle-aged to elderly persons (2, 3). There are only two reports of solitary poromas in chronic radiation dermatitis contained in the literature, both of them localized on fingers (4, 5). Since these regions represent predilection sites of poromas, the relevance of X-ray damage as a causative factor remains doubtful.

Here, we describe for the first time a case of multiple eccrine poromas confined to a region of chronic radiation dermatitis of the hairy skin suggesting a causative role of ionising radiation in the genesis of this skin tumour.

REPORT OF A CASE

The patient, a now 70-year-old white man, received X-ray therapy for the first time at the age of 9 years for chronic osteomyelitis of his right tibia. Approximately 30 years later, he developed chronic eczema of his right lower leg and according to prevalent therapeutic concepts, received at least two series of superficial X-ray therapy (1959, 1960). No data are available on type and dose of X-rays administered.

At 43 years, a reddish firm nodule was first noted on his right calf, which was left untreated until he presented again in 1973 with now clearly visible signs of chronic X-ray damage of his lower leg. The tumour—by then more than 5 cm in diameter—was excised and proved an eccrine poroma in histology. After excision, a total of 3000 rads X-ray therapy was given for incomplete removal. During the subsequent years, five more tumours of similar appearance, ranging from pea size to several centimeters in diameter, arose at various sites within the X-ray damaged region (ankle, lateral margin of the foot, calf). They were all excised and proved as eccrine poromas. At the same time, the patient continued to suffer from chronic eczema of his right lower leg and also developed a moderate lymphedema with verrucous hyperplasia and a tendency for very slow-healing trophic ulcers.

In October 1987, the patient was again admitted. His right lower leg in its entire circumference and length from knee to ankle displayed the clinical signs of X-ray damage, i.e. atrophy of skin and subcutaneous tissue, patchy hyper- and hypopigmentation and two punched out coin-sized trophic ulcers. In addition, the skin was focally indurated and eczematous. At the medial aspect of his right calf a red,