Two first cousins with spondyloepiphyseal dysplasia tarda (X linked recessive form), one also with poikiloderma atrophicum vasculare progressing to lymphocytic lymphoma

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SUMMARY Two male cousins with spondyloepiphyseal dysplasia tarda (X linked recessive form) are described. One presented with a poorly differentiated lymphocytic lymphoma of the skin in areas of poikiloderma atrophicum vasculare which had been present for 10 years.

Case reports

The index patient first presented in 1970 at the age of 15 years with a non-itching eruption of 2 years' duration on his left shoulder, left costal margin, and left thigh. The skin in these areas was dry, scaly, and atrophic, with prominent telangiectasia and a reticulate background of pigmentation. The histology was consistent with the diagnosis of poikiloderma atrophicum vasculare, although there was extension of the lymphohistiocytic infiltrate into the deep dermis. No treatment was advised but he was followed up for one year before defaulting.

In 1977 he returned to hospital with an acute perforation of a duodenal ulcer. Two years later (aged 22 years), pinkish nodules up to 1 cm in diameter were noticed in the original area of poikiloderma on his left shoulder and several infiltrated lesions which were showing signs of ulceration were present on a deeply pigmented patch on his right buttock. Large, firm, mobile lymph nodes were palpable in both groins but there was no hepatosplenomegaly.

Haematological studies showed: haemoglobin 15.8 g/dl, white blood cell count $7.6 \times 10^9/l$ with 50% neutrophils, 41% lymphocytes, 8% monocytes, and 1% eosinophils. Platelet count was $215 \times 10^9/l$ and ESR 6 mm in the first hour. Bone marrow examination was normal and his marrow cells had the normal male karyotype. The following investigations were also normal: blood urea and electrolytes, liver function tests, serum calcium, phosphate,

thyroxine, cholesterol, proteins, immunoglobulins, and components CH50, C3, and C4. Urine contained no abnormal amino-acids. Bilateral ascending lymphangiography demonstrated abnormal pelvic and para-aortic lymph nodes. Biopsy of one of the shoulder nodules showed a dense, mainly lymphocytic, infiltrate extending into the deep dermis. The features were those of a poorly differentiated lymphocytic lymphoma rather than classical mycosis fungoides, with which poikiloderma atrophicum vasculare is more usually associated. Cytochemistry was attempted but the cell yield was too small for this to be helpful.

Histological examination of an excised node and receptor studies suggested simple follicular hyperplasia. Dermatopathic lymphadenopathy was also thought to be responsible for the abnormal intra-abdominal nodes seen on lymphangiography. Investigations did not therefore reveal any definite evidence of a systemic lymphoma.

Diagnosis of the X linked recessive form of spondyloepiphyseal dysplasia tarda was only established at the age of 23 years on the basis of late onset of locomotor symptoms, body proportions, radiographic changes, and pedigree (fig 1).

He was 159 cm tall with a head to pubis measurement of 76 cm and pubis to heel measurement of 83 cm, indicating only slight shortness of stature associated with a short trunk (fig 2). His span was normal at 203 cm. There was some stiffness of the spine, but movements at all other joints except the hips were normal, and these only lacked external rotation. Radiographs illustrated platyspondyly of

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FIG 1 Pedigree of the family.

FIG 2 Index patient aged 23 years: height 159 cm with short trunk, normal limbs, and ulceration of the tumour nodules on the right buttock patch of poikiloderma.

most vertebrae (fig 3) and the femoral heads were flattened and irregular. There was a bifid seventh rib on the left, but no other findings of note.

A male first cousin on the maternal side, now aged 30 years, was similarly affected, with a height of 149.9 cm, head to pubis measurement of 67.3 cm, and pubis to heel measurement of 82.6 cm (fig 4). His short stature was not noted until the age of 10 years and back pain only occurred at 27 years. He lacked some external rotation at the hips, but other joints moved freely. There was no previous history nor sign of any skin disorder. Radiographs confirmed the typical appearance of the vertebrae

(fig 5) and showed some irregularity of the femoral heads with early osteoarthritis (fig 6). There were no significant radiographic findings elsewhere.

FIG 3 Lateral radiograph of spine with flattening and irregularity of vertebral bodies and hump shaped protrusions from superior and inferior surfaces.

FIG 4 First cousin of index patient, aged 30 years: height 149.9 cm with short trunk and normal limbs.

FIG 5 AP and lateral radiographs of spine with platyspondyly and hump shaped protrusions superiorly and inferiorly.

FIG 6 AP radiograph of pelvis with some irregularity of femoral heads and early osteoarthritis.

Two more distant male relatives were thought to be affected with spondyloepiphyseal dysplasia tarda (a great grandfather and a first cousin once removed) but both were dead and there was no confirmatory medical evidence. There was no evidence for skin or skeletal disorders in any other member of the family, nor any other developmental anomalies of note.

Discussion

Poikiloderma is characterised by atrophy, a reticulate variation in pigmentation, and telangiectasia. It may be a local response to skin injury from cold, heat, ionising radiation, or photosensitising chemicals. Rarely it occurs as a manifestation of dermatomyositis, lupus erythematosus, or scleroderma, but

the distribution is then different. Poikiloderma can be the precursor of cutaneous lymphoma and this is usually seen in patients with poikiloderma atrophicum vasculare or the premalignant type of parapsoriasis en plaques. Poikiloderma atrophicum vasculare seldom develops before middle age although 24 of the 122 cases (19.7%) reported by Samman¹ were aged 20 or under at the onset of the disease. The condition is extremely rare, representing only 0.015% of new patients seen at St John's Hospital, London, during 1952 to 1965.²

Poikiloderma or poikiloderma-like eruptions occur at an early age in several inherited conditions.^{3,4} In some of these the resemblance to premalignant poikiloderma is not marked and lymphomatous transformation does not occur, although interestingly congenital telangiectatic erythema (Bloom's syndrome) carries an increased risk of systemic lymphoreticular malignancy. The histological changes may, however, be identical to those of poikiloderma atrophicum vasculare as found in poikiloderma congenitale, the Rothmund-Thomson syndrome.⁵ In these children photosensitivity is often a feature and epitheliomata may develop in later life.

It seems likely that the two men suffer from the X linked recessive form of spondyloepiphyseal dysplasia tarda as described by Maroteaux *et al*,⁶ Langer,⁷ and Bannerman *et al*.⁸ The pedigree is consistent with this pattern of inheritance, and their clinical and radiographical signs are typical. There are several types of spondyloepiphyseal dysplasia but as a group they are rare, with a likely prevalence of around 7.7 per million (R Wynne-Davies, unpublished data). The X linked recessive form is probably the most frequently diagnosed.

To our knowledge skin changes have not previously been reported in this condition, but it is felt that the rarity of the two disorders would make their coincidental appearance in the same patient extremely unlikely.

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