Clinical Features of Ehlers-Danlos Syndrome Type VII in Chromosome 6q Deletion

Sir,

The Ehlers-Danlos syndromes are a group of connective tissue disorders with 10 classical subtypes. Their major clinical findings are skin fragility, skin hyperextensibility and joint hypermobility (1–2).

CASE REPORT

A 26-year-old man was referred to our department with a 4-month history of spontaneous skin lesions on both shins.

The patient, who was born to healthy non-consanguineous parents after an uncomplicated gestation, was affected by a chromosome 6q deletion. Major facts in his past medical history were a bilateral congenital hip dislocation, severe myopia and mild mental retardation.

Physical examination revealed short stature, pectum carinatum, long and disproportionate arms, kyphoscoliosis, bilateral genum varum, muscle hypotonia and marked general joint hypermobility, resulting in an unstable gait. His head presented a central forehead fissure, small globes, ocular hypertelorism, pointed palate, small mouth, micrognathia and rotated ears (Fig. 1). The patient's teeth were normal and there was no periodontal disease. The skin of both of his shins was fragile and showed ecchymoses, erosions and ulcers. Superficial varicose veins were also present. Located at the extensor sites of both knees and elbows, the patient had grey, "cigarette paper" scars, with wrinkling and atrophy of the surface. They had a velvety texture and, characteristically, they were easily stretched, returning to their original form on release.

Chromosome 6q deletion was confirmed from G-banding pattern preparation.

All initial analyses, including copper serum levels and thyroid hormones, were within normal limits. Either abdominal or cardiac ultrasound studies showed any pathological findings. An ophthalmological examination excluded keratoconus and intraocular haemorrhage.

Skin biopsies from the involved areas of the shin and the knee showed an atrophic epidermis with basal hyperpigmentation. Located in the upper dermis there were oedematous, broken, collagen fibres. Hemosiderin deposits, mainly perivascular, were present at the reticular dermis. The orcein staining showed an increase in the amount of elastic fibres, which were seen best in the dermo-hypodermal union and the hypodermis. An important increase in flocculent material, representing degraded collagen or collagen precursors, was observed on electron microscopy.

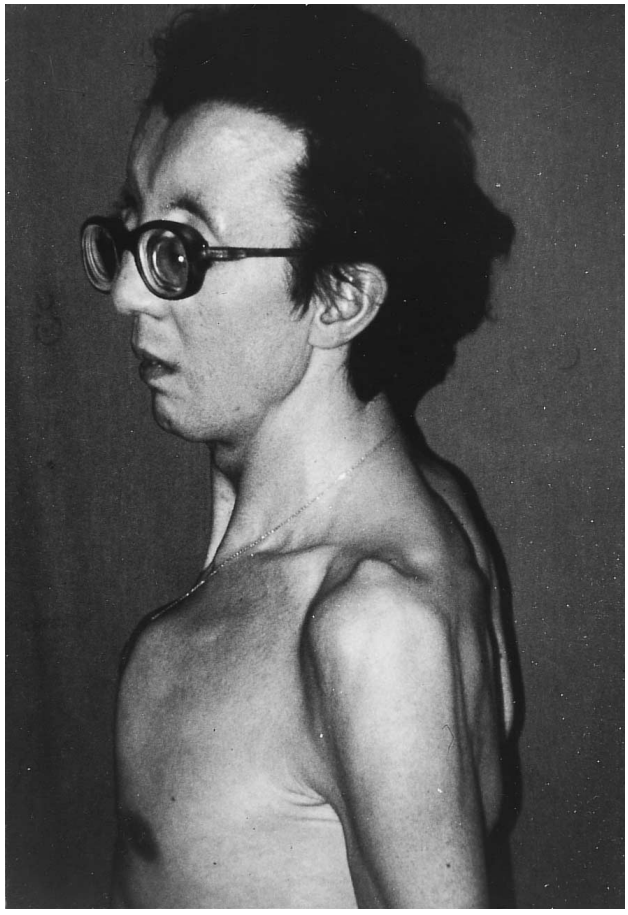

Fig. 1. Clinical features of the patient with facial dysmorphy and pectum carinatum.

DISCUSSION

Bilateral congenital hip dislocation and marked generalized joint hypermobility are considered the major diagnostic criteria of classical Ehlers-Danlos syndrome type VII (2). Other minor features of this clinical form, also known as the arthrochalasia type, are tissue fragility, easy bruising, muscle hypotonia, kyphoscoliosis and short stature (2). It is interesting to note that atrophic and pigmented scars, although rare, can be seen, especially in adults (1). Thus, the patient described here presents both major and minor clinical features of the Ehlers-Danlos syndrome type VII, more precisely, type VII-B (MIM: 225410) (3).

Dockery et al. reported for the first time a patient with clinical features of Ehlers-Danlos type I and IV syndromes and a balanced translocation t(9;17) (4). More recently, Scarbrough et al. reported another patient with clinical characteristics of Ehlers-Danlos syndrome type II and an unbalanced translocation t(6;13) (5). Several papers have also appeared presenting cases of cutaneous and/or joint laxity in patients with chromosome 6q deletions and without any other findings resembling Ehlers-Danlos syndromes (6). To our knowledge a patient with clinical features of Ehlers-Danlos syndrome type VII and a chromosome 6q deletion has not previously been reported.

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Ultrasonic Measurement of Skin Thickness in Patients with Systemic Sclerosis

Sir,

Clinical evaluation of the thickness, texture and fixation of the skin, and the extent of dermal changes is necessary for the estimation of the progression and remission of systemic sclerosis (SSc) (1). Such observations may carry important prognostic information (2, 3). Measuring skin thickness by means of high-frequency ultrasound may represent a useful objective and non-invasive method (4), the results of which seems to correlate with clinical and radiographic evaluations (5, 6). Several ultrasound studies showed clinically involved skin of patients with SSc to be thicker than the skin of normal persons (6–9).

We have studied 20 Danish Caucasian female outpatients with SSc according to the classification criteria of the American College of Rheumatology (10) and 20 healthy age-matched women by means of ultrasound determination of skin thickness and clinical skin scoring. The patients had a mean age of 67.6 years (range 43–83 years) and a mean disease duration of 17.5 years (range 4–36 years). The disease activity and the medication (including or exclusive of penicillamine) of the patients was stable. Four patients had diffuse SSc and the remainder had limited SSc.

Ultrasonography was performed by means of a 20 MHz ultrasound scanner (Dermascan, Cortex Technology, Hadsund, Denmark). Combined A- and B-mode scanning was used to measure the skin thickness, which was defined as the distance between the dermal-epidermal junction and the dermal-subcutaneous interphase. Measurements were performed 3 times by 3 different observers, the result being the mean of these 9 measurements. All measurements were performed in the afternoon in 5 sites:

- region 1: mid portion of the right dorsal 3rd proximal phalanx;
- region 2: dorsal area between 2nd and 3rd right metacarpophalangeal joint;
- region 3: the dorsal aspect of the right forearm, 2 cm above the wrist;
- region 4: the middle of the dorsal aspect of the right forearm;
- region 5: the area of the manubrium of the sternum.

Two experienced observers estimated the skin scores of the 5 regions mentioned using a modified Rodnan score (6): score 0: normal skin; 1: thickened skin; 2: thickened skin which could not be pinched; 3: thickened and immobile skin.

The mean result of the 2 observers was the final skin score, which was compared with the other measurements.

The skin of the digital regions of the SSc patients was significantly thicker than that of the controls. In the 5 regions the values obtained in patients and controls were, respectively (mean $\pm$ +SD), 1.49 ± 0.34 mm vs. 1.22 ± 0.31 mm ($p < 0.001$), 1.25 ± 0.32 mm vs. 1.00 ± 0.19 mm ($p < 0.001$), 1.20 ± 0.37 mm vs. 1.08 ± 0.22 mm ($p > 0.05$), 1.09 ± 0.35 mm vs. 1.06 ± 0.26 mm ($p > 0.05$), and 1.07 ± 0.27 mm vs. 1.11 ± 0.26 mm ($p > 0.05$). In the patients the skin thickness increased with an increasingly distal location of the regions studied. The skin of the fingers of the controls was also thicker than that of the other regions measured, but the trend of progressive thickening of the skin with an increasingly distal location of the regions studied was not found in the controls. ANOVA was performed in order to identify the contributions to the variation of the skin thickness caused by the skin regions and by the skin scores. The contribution of the regions was significant ($p = 0.03$), but not of the skin scores ($p = 0.68$). Hence, the significant overall correlation found between skin thickness and skin scores (rho $= 0.36$, $p < 0.001$) was explained by inherent properties of the regions, unrelated to the skin scores. A significant relationship between the skin thickness and the skin scores was found only for the proximal phalanx region (rho $= 0.56$, $p = 0.01$). An inverse relationship between the skin thickness and the disease duration was found in the proximal phalanx region (rho $= -0.49$, $p = 0.03$), but not in the other regions studied. The skin thickness was unrelated to the age of the patients and the controls.

The present study shows poor correlation between the skin thickness estimated by ultrasonography and the skin score in most of the skin regions examined, probably because the 2 methods measure different properties of the skin. The skin score is dependent, not only on the thickness of the skin, but also on its texture and its fixation, while, in this study, the ultrasonography merely measured the thickness of the skin. The present study confirms previous findings of increased thickness of involved skin of the patients with SSc (6–9). However, the thickness of clinically uninvolved skin was not increased, contrary to the findings in a previous Japanese study (9). The skin of our Danish controls was sonographically thicker than the skin of the Japanese controls, the differences being significant for the forearm and for the area between the knuckles. In the Danish controls the skin of the fingers was thicker than the skin of the other regions studied, the opposite being true for the Japanese controls. The skin thickness of the Danish controls was similar to that found in other studies of Caucasian control persons (5, 6). These findings indicate that skin thickness may vary with ethnic background. The inverse correlation between skin thickness and disease duration is explained by the wide variation in the disease duration in the present, as well as in the Swedish study (6), because the skin of