Enlarged Hair Follicles in Patients with Ehlers-Danlos Syndrome

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Sir,

Ehlers-Danlos syndrome (EDS) is a rare connective tissue disease manifested clinically as joint hypermobility, skin hyperextensibility, poor wound healing with abnormal scarring and bruising due to blood vessel fragility (1). The diagnosis of EDS is based on a scoring system that requires a time-consuming examination (2, 3). Recently attempts have been made to find additional minor criteria that may contribute to the diagnosis of EDS (3, 4).

We have observed that the hair follicles of the skin in patients with EDS are macroscopically more prominent than those of healthy subjects (Fig. 1A, B). To verify this finding the size of the hair follicles in patients with EDS was measured by skin ultrasonography. Ultrasonography is an established method for non-invasive investigation of the skin, and the images clearly show the epidermal entrance echo, the dermis and the hair follicles (5, 6).

PATIENTS AND METHODS

Fourteen patients with EDS (1 man, 13 women; age range 15–51 years, median 34) and 14 age-matched healthy controls (14 women; age range 16–47 years, median 33) were scanned by means of a 20 MHz probe (Cortex Technology, Hadsund, Denmark) as described previously (6). Sun-protected buttock skin was chosen to eliminate the possible influence of solar elastosis, which may confound the ultrasound image (6).

The diagnosis of EDS was made according to the nosology established recently (1, 2). Skin extensibility, joint hypermobility, tendency to bruising, scarring, and a family history of hypermobility were estimated. Clinical scoring of the patients' symptoms revealed a median Holzberg score of 9 (range 7–13) (Table I). The healthy volunteers were also examined to eliminate evidence of hypermobility and EDS (median score 1, range 0–2).

In order to measure the shape of the follicles two B-mode (two-dimensional) images of buttock skin were obtained in each investigated person. One well-imaged hair follicle was chosen for analysis in each ultrasound image. The width of the follicle was determined at two horizontal levels: 1) at the epidermal entrance echo – superficial follicle diameter and 2) in the dermis, 0.30 mm below the epidermal entrance echo – deep follicle diameter. These measurements were performed in both buttock images, and averaged. Student's *t*-test was used to analyse the data. The chosen level of significance was $p<0.05$.

RESULTS

In healthy volunteers the superficial and deep diameters of the hair follicles were not significantly different (Fig. 1C). The superficial follicle diameter was almost identical in the patients with EDS and in the healthy controls (0.45 ± 0.06 mm and 0.42 ± 0.04 mm, respectively). In contrast, the mean deep follicle diameter was significantly enlarged in the patients with EDS compared with that of the controls (0.85 ± 0.14 mm and 0.62 ± 0.08 mm, respectively; $p<0.001$) (Fig. 1D).

DISCUSSION

The defects of the collagen previously reported in EDS account for the increased extensibility of the skin (1, 2). It is possible that the altered skin structure results in increased pliability of the skin which may allow the hair follicles to expand.

To our knowledge only one study of skin sonography in a group of patients with EDS has been reported previously. Iurassich et al. (4) evaluated phalangeal joints, extensor tendons and skin, and a widening of the intra-articular space was shown. Moreover, the skin thickness and echogenicity were found to be reduced in

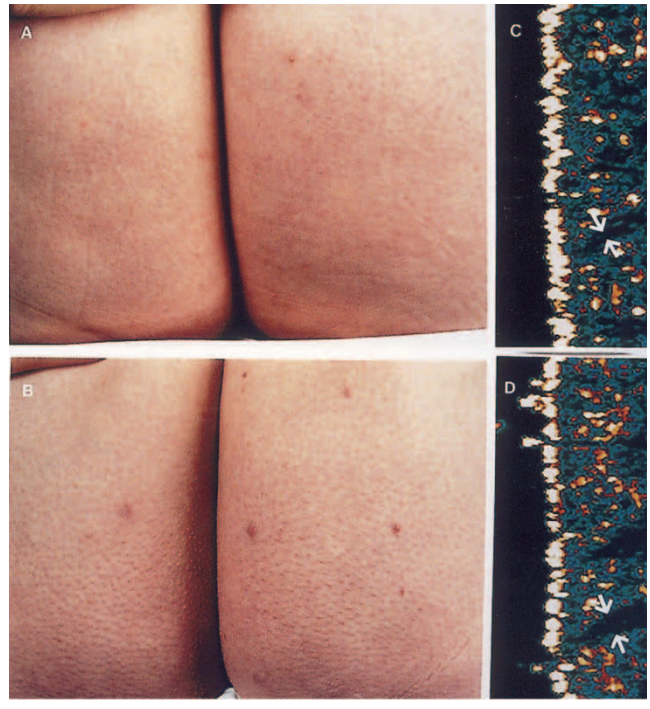

Fig. 1. Skin of a healthy volunteer (A) and of a patient with Ehlers-Danlos syndrome (B). Ultrasound images of the buttock skin: (C) healthy volunteer; (D) Ehlers-Danlos patient. Note the increased size of the hair follicles both macroscopically and in the ultrasound image of the skin of a patient with Ehlers-Danlos syndrome.

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Table I. *Clinical description of the patient group**

Patients	Dorsiflex [0–1]	Opp [0–1]	Hyperext Elbow [0–1]	Hyperext Knee [0–1]	Fw flexion [0–1]	Skin ext [0–5]	Wr scarring [0–4]	Bruising [0–5]	Total score [0–19]
34 F	1	1	0	1	1	2	0	2 (2)	8 (2)
39 F	1	1	1	1	1 (1)	1	0	2	8 (1)
34 F	1	1	1	1	1	1	0	1	7
26 F	1	1	1	1	1 (1)	2	0	1	8 (1)
41 F	1	1	1	1	1	2	0	2 (2)	9 (2)
24 F	1 (1)	1	1	1	1 (1)	3	0	2	10 (2)
34 F	1	1	1	1	1	2	0	2	9
51 F	1	1	1	1	1	4	2	2	13
40 F	1	1	1	1	1	2	0	2	9
15 M	1	1	1	1	1	4	2	2	13
40 F	1	1	0	1	1 (1)	2	1	2	9 (1)
17 F	1 (1)	1 (1)	1	1	0	1	1	2	8 (2)
38 F	1	1	1	1	1 (1)	1	0	1	7 (1)
19 F	0	1	1	1	1	2	0	1	7

*Scoring system by Holzberg et al. (2). Range of scores given in square brackets. Age-matched controls scored 0 except in cases specified in parentheses.
Dorsiflex, dorsiflexion of the fifth finger $>90^{\circ}$ with forearm flat on the table; Opp, passive opposition of thumb to the flexor side of the forearm; Hyperext, hyperextension of elbow and knee >10 degrees; Fw flexion, forward flexion of trunk so that palms of hand rest easily on the floor; Skin ext, skin extensibility – skin of the ventral left forearm lifted midway between the elbow and wrist; Wr scarring, cigarette paper wrinkled scarring.

the patients with EDS. This finding is compatible with our data, as the hair follicles present as low echogenic structures in the dermis. Iurassich et al. (4) used an ultrasound probe with a lower frequency. Consequently a detailed observation of the skin structures was difficult to achieve.

Enlargement of the skin follicles has previously been described only in the affected skin of patients with hidradenitis suppurativa (5). It has been suggested that the alterations of the mechanical properties of the skin were responsible for the change of the shape of the hair follicles. The decrease in skin echogenicity in the patients with EDS may reflect the altered collagen fibre structure (more loosely packed). The alterations in collagen structure have previously been shown in the connective tissue of the photo-aged skin, where decrease of echogenicity has also been observed (6).

The present investigation describes structural changes in skin in patients with EDS, which may be a useful diagnostic clue for this complex disease. It will be interesting to see whether follicle shape is altered in related diseases of connective tissue, such as hypermobility syndrome.

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REFERENCES

1. Beighton P, De Paepe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. Am J Med Genet 1998; 77: 31–37.
2. Holzberg M, Hewan-Lowe KO, Olansky AJ. The Ehlers-Danlos syndrome: recognition, characterisation, and importance of a milder variant of the classic form. J Am Acad Dermatol 1988; 19: 656–666.
3. De Felice C, Toti P, Di Maggio G, Parrini S, Bagnoli F. Absence of the inferior labial and lingual frenula in Ehlers-Danlos syndrome. Lancet 2001; 357: 1500–1501.
4. Iurassich S, Rocco D, Aurilia A. Type III Ehlers-Danlos syndrome: correlations among clinical signs, ultrasound, and histologic findings in the study of 35 cases. Int J Dermatol 2001; 40: 175–178.
5. Jemec GBE, Gniadecka M. Ultrasound examination of hair follicles in hidradenitis suppurativa. Arch Dermatol 1997; 133: 967–970.
6. Gniadecka M, Jemec GBE. Quantitative evaluation of chronological aging and photoaging in vivo: studies on skin echogenicity and thickness. Br J Dermatol 1998; 139: 815–821.