A case of mosaic Ehlers–Danlos syndrome

Edwina Lamrock,1 Edward Wills2 and Gayle Fischer3

1Department of Dermatology, Royal North Shore Hospital, St Leonards, 2Department of Anatomical Pathology, Concord Repatriation Hospital, Concord, and 3Sydney Medical School, University of Sydney, Department of Dermatology, Royal North Shore Hospital, St Leonards, New South Wales, Australia

ABSTRACT
Ehlers–Danlos syndrome (EDS) is a group of inherited connective tissue disorders. The clinical manifestations are heterogeneous and usually generalised. We present a case of mosaic EDS, an extremely rare variant. Our patient presented with a single localised patch of EDS affecting her upper left thigh.

Key words: connective tissue disorder, Ehlers–Danlos syndrome, mosaic.

INTRODUCTION
Ehlers–Danlos syndrome (EDS) is a heterogeneous group of inherited disorders of connective tissue, the hallmarks being hyperextensible skin, hypermobility of the joints and fragility of skin and blood vessels. It is classified into subtypes I–VIII and X, with some overlap of the subtypes. It is considered to be a generalised disease. We present an extremely rare presentation of mosaic EDS.

CASE REPORT
A 27-year-old woman of English origin, presented with a darkened patch of skin in the inside surface of her upper left thigh and pubic area. Her mother had first noticed this darkened area of skin when she was 18 months old. At that time the lesion was small, approximately a few centimetres in length and width. The area remained stable for many years, seemingly growing in proportion to total body growth. Approximately 3 years prior to presentation the patient noticed that the area was increasing in size and darkening in colour. She also noticed that the involved skin had become wrinkly in texture, velvety to the touch and very distensible when stretched with normal elastic recoil. At the time of presentation the lesion measured 10 × 10 cm. Noticeably, there was an absence of hair, including pubic hair, in the affected skin (Fig. 1).

The patient also had one café-au-lait macule on her left leg. The rest of her skin appeared unaffected. There was no hypermobility on joint examination, or abnormal scarring. After presentation the patient developed digestive problems, including malabsorption, which worsened during last 12 months before the time of writing and are currently being investigated.

A histological examination showed loose connective tissue in the upper dermis with increased numbers of interstitial spindle cells, small vessels and lymphatic vessels. The elastic fibres present were thin but the elastic fibres in the reticular dermis were intact and coarser. There was no increased mucin in the upper dermis (Fig. 2). Electron microscopy showed transversely sectioned collagen fibrils in the reticular dermis, which varied considerably in width and shape, with scattered large irregular ‘collagen flowers’ (Fig. 3). A normal banding pattern was evident in longitudinal sections of collagen fibrils. Consultation with a geneticist indicated that it was highly unlikely that there was any gonadal involvement and that the gastrointestinal symptoms were unrelated to her skin abnormalities. A diagnosis of mosaic EDS was made.

DISCUSSION
EDS is characterised by skin hyperextensibility, atrophic scarring, generalised tissue fragility and joint hypermobility. It is a genetically heterogeneous condition. The primary defect involves collagen synthesis and metabolism, particularly the genes encoding fibrillar proteins or collagen-processing enzymes.1 Fibrillar collagens or collagen-modifying enzyme mutations have been identified in most forms of EDS.2

Abbreviation:

<table>
<thead>
<tr>
<th>EDS</th>
<th>Ehlers–Danlos syndrome</th>
</tr>
</thead>
</table>

Correspondence: Dr Edwina Lamrock, Department of Dermatology, Royal North Shore Hospital, Reserve Road, St Leonards, NSW 2065, Australia. Email: elamrock@gmail.com

Edwina Lamrock, B.Med (Distinction). Edward Wills, MD FRCPA. Gayle Fischer, MBBS MD FACD.

The authors do not have any conflict of interest disclosures related to this work.

Submitted 3 October 2011; accepted 20 November 2011.
Genetic mosaicism describes an individual who displays two or more cell populations with distinct genotypes originating from a homogenous zygote. A somatic mutation is a genetic change that occurs after fertilisation (post-zygotic) and does not involve gonadal (germline) cells. Our patient displays mosaic EDS with the post-zygotic mutation occurring in somatic, not gonadal cells.

Our patient displays clinical features of the classical subtype of EDS, particularly soft, velvety, hyperextensible skin. The altered pigmentation of the affected area may be reflective of the bruised appearance of the skin seen in this subtype. The absence of other features also makes the classical subtype of EDS more likely. The differential diagnosis in this case would be cutis laxa; however in our patient the affected skin had normal elastic recoil, making this diagnosis highly unlikely.

A review of the literature revealed two previously reported cases of localised EDS. Cullen (1979) described a 34-year-old Scandinavian woman who first noticed multiple small nodules involving the skin of her left shoulder. She presented to the dermatologist at the age of 26, by which time she had developed hyperextensibility of the same area. There were no scars or abnormalities in pigmentation. There was no increased mobility of her joints and no family history of EDS. A biopsy of this site healed normally. A histological examination showed increased concentration...
of elastic fibres in the deep dermis with a relative decrease in the amount of collagen fibres. The second case by Krieg et al. (1984) describes a 19-year-old German woman who noticed elastic, soft, hyperextensible skin over her proximal right thigh at the age of 14. This increased in size over a few years then stabilised. On presentation to a dermatologist the skin was soft and hyperelastic, the area measuring 41 × 15 cm. A scar in the area was slightly dehiscent and reddened. A histological examination showed increased numbers of broadened elastic fibres in the affected dermis. Collagen fibres were unremarkable.4

In all three cases of localised EDS the patient was female, with no family history of EDS and no joint hypermobility. One of the three patients had a mildly abnormal scar. One of the patients did experience a spontaneous rupture of a pulmonary bleb, leading to a small pneumothorax. The other two patients had no evidence of any other organ involvement except the skin. Our patient was the only one to have noticed skin changes in childhood. All three patients experienced a period of growth of the affected area and then subsequent stabilisation. The common histological finding was that of broadened elastic fibres, increasing in proportion to the collagen fibres.

The partial expression of genodermatosis through mosaicism is well reported. This case emphasises the fact that, although EDS is considered a generalised disease, very rarely, localised involvement may occur.

### REFERENCES