Ehlers-Danlos Syndrome Type VIII
- A Case Report -
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Ehlers-Danlos syndrome (EDS) is a genetically heterogeneous connective tissue disorder which is comprised of more than 10 phenotypes including EDS-VIII (periodontitis type), which is characterized by chronically inflamed pretibial lesions and severe periodontitis. We describe a 26-year-old female with a long-standing history of abnormal scarring tissues, presenting with pretibial waxy violaceous plaques for more than 20 years. Premature loss of permanent teeth is also noted. Combining the clinical manifestations and laboratory examinations, we conclude this is a rare case of Ehlers-Danlos syndrome type VIII. There is no specific treatment currently. (Dermatol Sinica 24: 150-154, 2006)

Key words: Ehlers-Danlos syndrome, Ehlers-Danlos syndrome type VIII, Periodontitis


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INTRODUCTION

Ehlers-Danlos syndrome (EDS) was first recorded in 1657 by an Amsterdam surgeon named Job Jansoon van Meekren. After Ehlers and Danlos published their observations in 1901 and 1908 respectively, the term of Ehlers-Danlos syndrome was adopted. This spectrum of disorder is phenotypically diverse and the main affected sites are skin, joints, and tissues/organs rich in connective tissue. Presently, more than 10 phenotypes including a rare type, EDS-VIII, are discriminated.

We herein report a case of EDS associated with severe periodontitis, which reminds us of the variable spectrum of EDS and the importance of routine dental evaluation in clinical practice.

CASE REPORT

A 26-year-old female complained of poor wound healing and purplish-gray discoloration on bilateral shins for about 20 years. No history of prenatal abnormality or familial genetic disorder was traced. She was born at a gestational age 39 weeks, birth weight was 3150 gm without premature membrane rupture. Her parents are not consanguineous. Since she was 6-year-old, she was noticed that she had slower wound healing process whenever she had been injured. The repeated minor trauma over her bilateral shins resulted in large areas of purplish to grayish discoloration. In addition, her abnormal dental history could be traced back 12 years as her teeth were generally loosened and her gums would easily bleed. Severe periodontitis was then diagnosed. Frequent gingival swelling and inflammation occurred albeit numerous dental procedures were performed. Because extensive periodontal destruction persisted, 15 teeth were extracted and a removable partial denture was fabricated in a medical center 4 years earlier.

Physical examination revealed a normal developed female, 163 cm in height and 65 kg in weight. She could reach the tip of her nose using her tongue (positive Gorlin sign). No visible vascular streaks were found over her chest and abdominal area. A "cigarette paper-like" scar was found over her right dorsum of hand. Wrinkling and premature aging appearance of palms and soles were also noticed. Keloidal scars were found over her bilateral elbow and knee joint regions. Two mild tender symmetric well-defined slaty discolored plaques about 25cm X 15cm in size, warm on palpation, were noted over bilateral shins and extended to lower parts of calves. Hyperextensibility of bilateral elbow joints (>10) was the only detectable joint abnormality. No specific neurological defect was detected.

During oral examination, only 14 teeth remained. Extensive root exposure with gingival recession and lack of normal scalloping of the dentinoenamel junction were noted. Diffuse brownish discoloration of upper and lower dentition was obvious and cervical portions were stained most intensely. Of note, there were two ill-defined bruising-colored macules with irregular contour on the floor of her mouth. The residual alveolar ridges were like a knife edge and gross bone loss of residual ridges were revealed using a Panoramic view. Radiograph also showed short roots and characteristic pulp stones in the teeth.

Series of laboratory tests included CBC, PT, PTT, and platelet count were performed and the results were all within normal range. The titers of ANA, ANCA, anti-Scl-70, and rheumatoid factor showed negative. Chest X-ray revealed no abnormality in heart size, aortic root diameter, or aortic contour. Echocardiography showed no aortic anomaly. Intra- and extra-cranial vascular systems were obtained with a negative finding.

Skin biopsy was done at the margin of the discolored plaque over right shin. Pathological pictures revealed mild hyperkeratosis, irregular acanthosis of epidermis. The thickness of dermis was slightly reduced. Spotted hemosiderin deposits and RBC extravasation were found over perivascular area in mid-reticular dermis. Verhoeff-van Gieson stain showed elastic fibers were only slightly increased without fragmentation.

Under electron microscopy examination, we can find the collagen contour shows irregu-
larity in cross section and the size of each collagen bundle is not even (Fig. 4). Amorphous depositions within collagen bundles were found in some areas.

The patient was then treated with topical antibiotics. Dentistry and rehabilitation OPD follow up for denture and skin guards design were suggested.

**DISCUSSION**

Ehlers-Danlos syndrome is a group of heterogeneous inherited connective tissue disorders. The estimated prevalence of all types is about 1 in 5,000. The main clinical presentations are variable joint hypermobility, skin hyperextensibility, and tissue or organ fragility. In 1997 Beighton et al. revised the past classification based on each distinctive clinical manifestations. EDS-VIII was attributed to periodontitis type due to its characteristic clinical manifestation of early destructive periodontitis.

In our case, poor wound healing, ease of bruising, abnormal "cigarette-paper scars" formed over her right hand, keloidal scars over bilateral knees, and the positive "Gorlin sign" accompanied with bilateral hyperextensive elbow joints can make the diagnoses of EDS. Distinctively, there were chronic inflamed, hemosideric discoloration plaques on bilateral shins and calves. Vascular involvement was excluded by examinations including chest X-ray, echocardiography, intra- and extra-cranial vascular SonoCT. Severe destructive periodontitis with marked gingival recession and alveolar bone resorption were noted. The two ill-defined bruising-colored macules on the month floor may be signs of fragile mucosa with RBC extravasation and hemosiderin deposition just like the lesions over bilateral shins. Laboratory tests including coagulation tests were all within normal range. Based upon above features, we conclude this was a case of EDS type VIII.

Since McKusick first described a family with severe periodontal disease combined with characteristic scarring on shins in 1972, EDS-VIII is of interest due to its peculiar clinical manifestations. It is a rare type of EDS and less than 50 cases have been published. Heritage was considered to be autosomal dominant but some patients were diagnosed without any evidence of familial history. Due to the lack of any definite biochemical or genetic marker, the diagnosis of EDS-VIII is based on clinical grounds and was discriminated by the present-
Ehlers-Danlos syndrome involving severe early-onset periodontitis and characteristic pretibial lesions. However, in 2003, Rahman et al. was the first to find a candidate gene defect on chromosome 12q13 in a Swedish family. This article confirmed that EDS-VIII is a separate entity and heterogeneous genetic defect was suggested.

The clinical manifestations in EDS-VIII patients vary, in addition to the consistent presentation of severe juvenile periodontitis, with different degrees of skin hyperextensibility, fragility and scarring; minimal-to-moderate joint hypermobility (usually limited to the digits); and normal or slightly increased tendency to bruising on mild trauma. In addition, chronically inflamed plaques which resemble necrobiosis lipoidica on shins are often present.

Although histopathology is considered to be non-diagnostic for most EDS patients, in some reported cases the skin thickness are reduced and show increased amount of elastic fibers. In our case, mild thinning of dermis is noted and elastic fibers increase slightly. The appearance of the elastic fibers is normal and confirm by Verhoeff-van Gieson stain. Perivascular deposits of hemosiderin granules and RBC extravasation are consistent with clinical finding of slaty discolored plaques over shins.

The electron microscopy examination of EDS was characteristic but not specific. The variable collagen diameters and irregular collagen surface were the most frequent findings. In 1991, Hoffman et al. performed electron microscopy study of an extensor tendon of an EDS-VIII patient. They discovered marked varied collagen diameters in cross section and presence of amorphous deposits with peripheral insertion of collagen fibers. They also found the surface of the collagen fibers were irregular and granular. Also in 1993, Dyne et al. disclosed irregularity of the collagen fibers of an EDS-VIII child. Our case also shows marked variation in the collagen diameter and the irregularity of the collagen border. Also, amorphous materials are found in some areas (data not shown).

Oral manifestations of EDS include fragile mucosa, gums bleeding easily, periodontitis

![Fig. 3](image)

(a) Spotted hemosiderin deposits were found over perivascular area in mid-reticular dermis. (H & E, 400X) (b) Verhoeff-van Gieson stain showed elastic fibers were only slightly increased without fragmentation. (400X, gray to black in color)

![Fig. 4](image)

Electron microscopy of reticular dermis of the patient shows variable diameters of collagen bundles and irregular contours (arrows) in cross section. (60,000X) Left upper corner shows normal collagen bundles with regular contours (60,000X).
with early loss of teeth, teeth with high cusps, deformed roots, and large pulp stones.\textsuperscript{1, 6, 10, 14, 15} Although these symptoms/signs are not specific to EDS, we must consider EDS as a differential diagnosis when such oral conditions are met.

Because EDS is a disorder caused by heterogeneous genetic defects, no specific treatment is currently available. Patients must be taught to avoid any trauma to the skin, use of skin guards and avoidance of contact sports may help.\textsuperscript{16}

To our knowledge, this is the first case of EDS type VIII reported in Taiwan. We would like to present this case and remind clinical dermatologists to include Ehlers-Danlos syndrome as a differential diagnosis when a patient has abnormal scarring or severe periodontitis at an early age.

REFERENCES