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Oral manifestations of Ehlers-Danlos syndrome Type VII: histological examination of a primary tooth

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Abstract

A two-year, 2-month old girl with Ehlers-Danlos syndrome Type VII is described. The patient presented with bleeding after tooth brushing, and exhibited microdontia and yellow discoloration of teeth. She had carious teeth, but did not exhibit periodontal disease, poor wound healing after extraction, radiographic evidences of pulp stones, or malformed roots. Microscopic examination of a decalcified section of an extracted tooth stained with H&E demonstrated some inclusions in the dentin, around which collagen was either missing or scanty, as confirmed by counterstaining with van Gieson's solution. The sections of pulp stained with van Gieson's solution showed an abnormal pattern of fibrous tissue. Furthermore, the radiopacity of the dentin of this patient was significantly higher than that of the control dentin.

Introduction

Ehlers-Danlos (E-D) syndrome is a heterogeneous group of hereditable disorders of connective tissue. At least 11 types are known based on clinical features, mode of inheritance, and defects in collagen biogenesis (McKusick 1986). The principal clinical features common to all E-D syndromes are skin hyperextensibility, joint hypermobility, and skin fragility. Other clinical complications include tendency to bleed, scar, and bruise easily. The range of severity of the conditions varies according to the type (Hollister 1978; Gosney 1987).

Oral manifestations of an unclassified E-D syndrome were described in detail by Barabas and Barabas (1967). These included fragility of the oral mucosa with delayed healing, microdontia, short or malformed roots, large pulp stones and calcification of the pulp, bleeding after tooth brushing, and periodontal disease. Under light microscopy of the teeth, Barabas (1969) found no scalloping at the dentinoenamel junction, vascular inclusions in the dentin, and fibrous degeneration of the pulp. The purpose of this paper is to describe a patient with E-D syndrome Type VII and define the associated dental manifestations.

Materials and Methods

Subject

A Japanese girl, 2 years, 2 months old, was referred by her orthopedist to the Department of Pedodontics, Osaka University Faculty of Dentistry for dental management. The child was the product of a 43-week pregnancy (birth weight 2315 g). Physical examination at birth revealed dislocation of her right hip, swan-neck deformities of the fingers, joint hypermobility, skin fragility, and skin hyperextensibility. Based on these clinical features, she had been diagnosed at 3 months as having Type VII E-D syndrome (Hamada et al. 1986). Her unaffected parents were first cousins, and she had no siblings or other family history of this syndrome. Her mother had taken no medicine during pregnancy.

At three years, her height was 95 cm (90th percentile), and she weighed 11 kg (less than 10th percentile). In addition, she had severe *genu valgus*, making it impossible for her to walk; she had been undergoing orthopedic treatment since age one year, five months for this condition. According to her orthopedist, her hand and wrist radiographs revealed a skeletal age which was equivalent to her chronological age (Hamada et al. 1986).

Clinical Examination

At age 2 years, 2 months, all primary teeth except the upper left second molar had completed eruption. Her first primary tooth had erupted at age 4 months, suggesting early eruption of her primary teeth, less than the third percentile in mean eruption time of the first primary tooth in Japanese children (Yoshida 1986).

Oral examination revealed many carious primary anterior upper teeth, a condition commonly known as nursing bottle caries (Fig 1). The maxillary central and lateral incisors and first primary molars had extensive decay which required pulp therapy, but all lower teeth and upper second molars showed no signs of decay. The primary teeth were slightly yellow, but there was no evidence of enamel dysplasia. Conversely, the gingiva

often bled after tooth brushing, in spite of good oral hygiene. The maxillary right central incisor was extracted because of unsuccessful pulp treatment. There was no unusual bleeding after extraction, and wound healing was normal. When coronal pulp amputation with a slow-speed round bur was performed on the maxillary first molars, pulp tissue in the palatal root was easily separated from the root dentin without the usual procedures necessary to remove the root pulp tissue. The extracted central incisor and pulp tissues from the first molars were examined histologically.

Measurements of the mesiodistal and buccolingual dimensions of the primary teeth crown were made on a study model using a slide caliper, and the crown sizes were compared to the mean value of primary teeth of Japanese children (Sugiyama 1969). Five teeth in the maxilla could not be measured because of marked dental decay.

Microscopic Examination

The extracted primary central incisor was fixed in 10% formalin for 48 hr and hemisected mesiodistally through the midline. One of the two halves was embedded in plastic, and 50 µm thick ground sections were prepared. The ground sections first were examined by transmitted light microscopy, and then radiographs were taken by a contact micrographic device. In order to study the degree of radiopacity of dentin to determine the degree of calcification, an aluminum foil stepwedge was used as the reference norm in the contact microradiographs. The degree of radiopacity was expressed in micron thicknesses of aluminum foil, and the difference with control teeth was statistically analyzed using a *t*-dependent test as described by Abe et al. (1988).

The other half of the extracted tooth was decalcified, embedded in paraffin, and cut serially in 5 µm sections (Abe et al. 1988). The serial decalcified sections were stained with H&E for light microscopic examination. Van Gieson's solution was used to stain the collagen fiber in dentin. Ground sections and decalcified sections of primary maxillary central incisors with and without dental caries from healthy children were prepared as controls and examined as described above.

The pulp tissues from the palatal root dentin of the primary first molars were fixed in 10% formalin for 48 hr, embedded in paraffin and cut in 5 µm sections. The sections were stained with H&E or van Gieson's solution. Normal pulp tissue from a fractured primary incisor was used as a control. The tissue was prepared according to the procedures described above.

Results

Clinical Examination

The mesiodistal and buccolingual dimensions of the patient's teeth fell below one standard deviation (SD) from the mean crown size of primary teeth in Japanese children.

All mandibular premolars and permanent molars were present on lateral radiographs of the mandible, and dental age determined by the method of Moorrees et al. (1963) corresponded to the chronological age. Moreover, these radiographs showed that pulp stones were not present, pulp chambers were normally patent, and roots of the mandibular primary molars were normal (Fig 2).

Microscopic Examination

Transmitted light microscopic examination of the ground section of extracted primary incisor demonstrated that the dentin in the root portion was divided into two parts: an opaque zone near the pulp, where the direction of dentinal tubules was clearly shown; and a transparent zone near the cementum, where we recog-

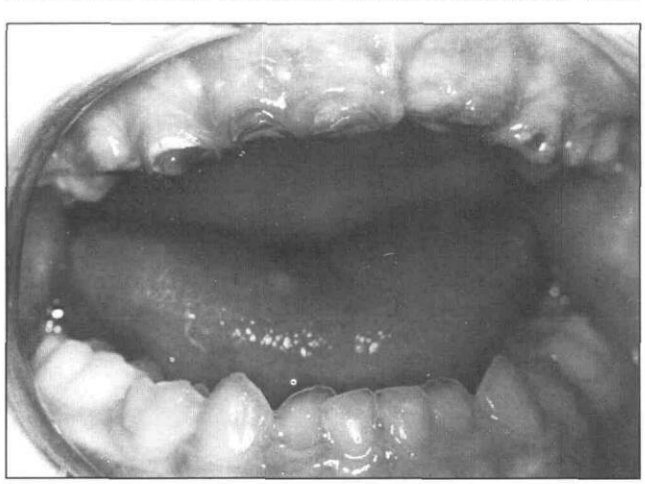

Fig 1. Intraoral view of E-D syndrome patient shows numerous carious lesions in the primary dentition, commonly known as nursing bottle caries.

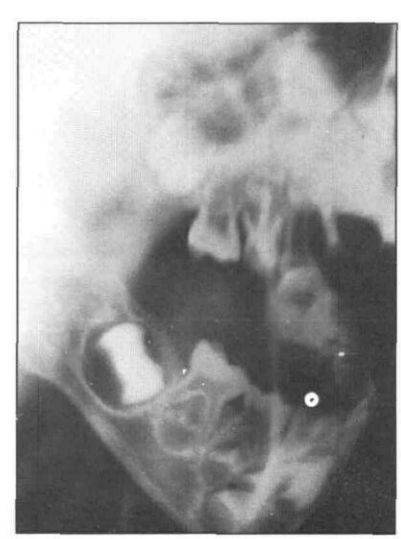

Fig 2. Lateral radiograph of the right mandibular region. Note that the pulp and root show normal appearance, and no evidence of pulp stones.

nized only a few dentinal tubules (Fig 3). Around the boundary between the opaque and transparent zones, tear-drop shaped features were distinguished (Fig. 3, arrows). The crown could not be examined, since it had been destroyed completely by dental decay.

The contact microradiographs showed a row of radiopaque tear-drop shaped spots along the circumpulpal dentin, each surrounded by a radiolucent zone (Fig 4). The difference in radiopacity between 27 sites of dentin from the patient with E-D syndrome and the corresponding sites of control dentin from a healthy child was statistically significant ($P < 0.05$, t-dependent test; Table 1).

Decalcified sections showed several inclusions stained dark with hematoxylin which were surrounded with an area stained mainly with eosin. Highly magnified micrographs further demonstrated that these inclusions appeared fistulous and were surrounded by inner hematoxylin-stained dark areas and outer eosinophilic areas (Fig 5). Around the inclusions the dentinal tubules took an irregular course, and the number of tubules was reduced when compared to that of the control dentin. Furthermore, a laminated calcified matrix with fewer dentinal tubules and multiple cell inclusions was present in dentin adjacent to the pulp. There was no regular predentin zone; however, it might have been removed during the canal treatments. Van Gieson's solution (applied to the decalcified sections) showed that the control dentin from a healthy child stained uniformly red, while the affected dentin from the patient with E-D syndrome stained orange or yellow. In particular, the affected dentin around the inclusions stained yellow.

The sections of pulp of the E-D patient stained with H&E revealed a few minute calcified bodies which were stained with hematoxylin (Fig 6). With van Gieson's solution, the fibers in the pulp tissue from a healthy child were stained red and presented the network pattern. On the other hand, yellow staining was scarcely observed in the pulp tissue from the patient with E-D syndrome, and the fibers which stained red with van Gieson's solution showed a wavy pattern (Fig 7).

Discussion

E-D syndrome Type VII is known to be caused by the deficiency of procollagen peptidase in collagen biogenesis (McKusick 1986; Gosney 1987). The major clinical features are severe joint laxity, congenital hip dislocation, and subluxations at the knees and other large joints. Other clinical signs are short stature, as well as moderate elasticity and bruisability of the skin. Although the patient reported here was not short and the basic defects in collagen biogenesis were not determined, the presence of marked joint hypermobility and the congenital dislocation of the hip, together with various skin symptoms at birth, were considered to be consistent with the diagnosis of E-D syndrome Type VII (Hamada et al. 1986).

The dental findings in our patient were yellow teeth, microdontia, and bleeding after tooth brushing. Easy separation of pulp tissue from the palatal root dentin may demonstrate fragility of pulp tissue. However, as the patient has not experienced tooth fractures by any external force or suffered laceration of oral mucosa upon suturing, it still is unknown whether she has fragility of her oral mucosa and teeth. Moreover, pulp stones and pulp obliteration, the principal dental manifestations described in the previous reports of E-D syndrome (Barabas and Barabas 1967; Hoff 1977; Gosney 1987) were not observed in our patient on ra-

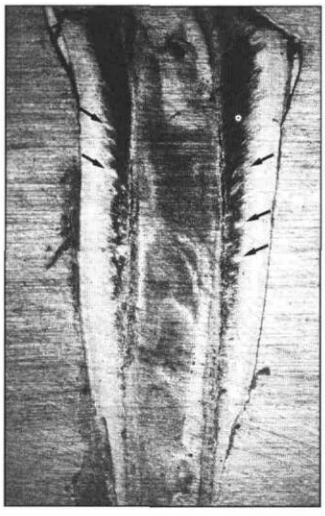

Fig 3. Ground section of the tooth shows many inclusions nearly midway between the pulp and root surface of the dentin (arrow). (Orig. Mag. 4X)

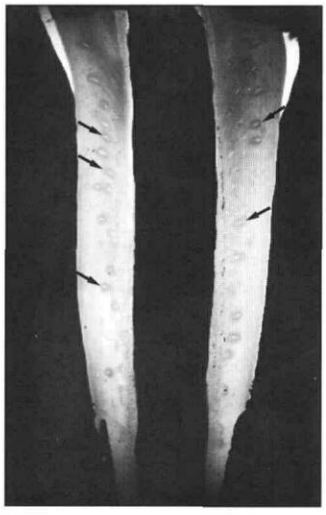

Fig 4. Contact microradiograph shows a row of radiopaque tear-drop shaped spots nearly midway between the pulp and root surface surrounded by a relatively radiolucent zone (arrow). (Orig. Mag. 4X)

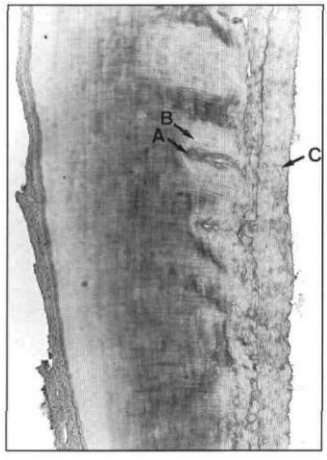

Fig 5. (*right*) H&E section shows that the inclusion appears fistulous and is surrounded with a hematoxylin-stained dark area (arrow A), around which the eosinophilic area is recognized (arrow B). Laminated calcified matrix with few dentinal tubules and many cell inclusions are present close to the pulp (arrow C). (Orig. Mag. 25X)

diographic examination. However, the H&E sections of the pulp from a first primary molar showed a few minute calcified bodies such as Slootweg and Beemer (1987) found in the pulp tissue of a first permanent molar. The etiology of pulp calcification is not yet known. There are no definite associations with pulp irritation, sex, or age of the patient and type of the tooth in the dental arch, although the incidence of pulp calcification appears to increase with age (Shafer et al. 1983). In addition, the incidence of pulp calcification is unexpectedly high when examined histologically (Willman 1934). Therefore, it is difficult to conclude that the pulp calcification in the present case is one of the principal oral manifestations of Type VII E-D syndrome.

Table 1. Degree of Radiopacity in the Deciduous Tooth Dentin.

Tooth	*Gender*	*Subject*	*Degree of Radiopacity (Mean ± SD) * (μm)*
Upper incisor	Female	E-D syndrome Type VII	36.1 ± 4.3**
Upper incisor	Female	Healthy child	22.6 ± 2.4**

* Each data was represented by thickness of aluminium (μm), which is used as the reference norm for X-ray absorption in microradiographic studies.

** Significant difference detected when compared with the control tooth (*t*-dependent test, $P < 0.05$).

There were several inclusions that appeared fistulous in the dentin of this patient. The staining pattern with H&E and findings on the contact microradiograph demonstrated that these inclusions were surrounded by a highly calcified region surrounded by a poorly calcified region. Furthermore, the yellow staining around the inclusion using van Gieson's solution revealed lesser amounts of collagen, or the presence of noncollagenous substances.

A laminated calcified matrix with fewer dentinal tubules and multiple cell inclusions also was found in the dentin adjacent to the pulp in the tooth in this patient. A laminated calcified matrix known as tertiary dentin is found in normal teeth when pathological irritations such as those arising from caries or trauma to the pulp tissues. In the present case, the tooth examined had pulpal inflammations which may have contributed to the development of the laminated calcified matrix. However, the extent of the laminated calcified matrix was unusually thick in the present case, when we examined histologically the tertiary dentin of carious central incisors with pulpal inflammation from normal children. These findings may support the possibility shown in the previous report (Barabas 1969) that the dentin matrix has formed rapidly and, therefore, elements in the pulp are incorporated in the dentin. However, the function of odontoblasts appears to be deficient in the production of collagen within the dentin matrix. The collagen in the pulp tissue of our E-D syndrome patient showed a wavy pattern, which was different from nor-

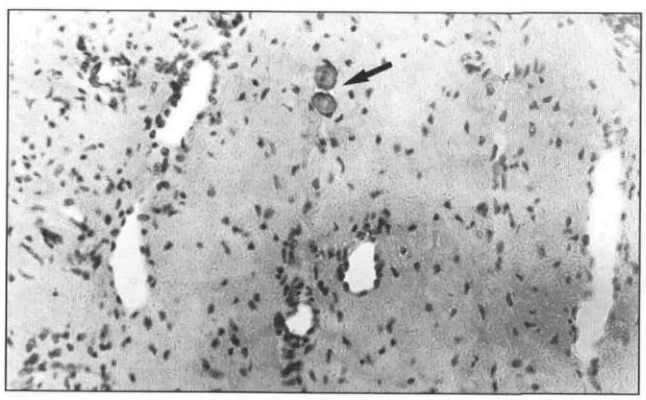

Fig 6. H&E-stained sections of the pulp separated from the palatal root of the first primary molar revealing a few minute calcifying bodies (arrow). (Orig. Mag. 50X)

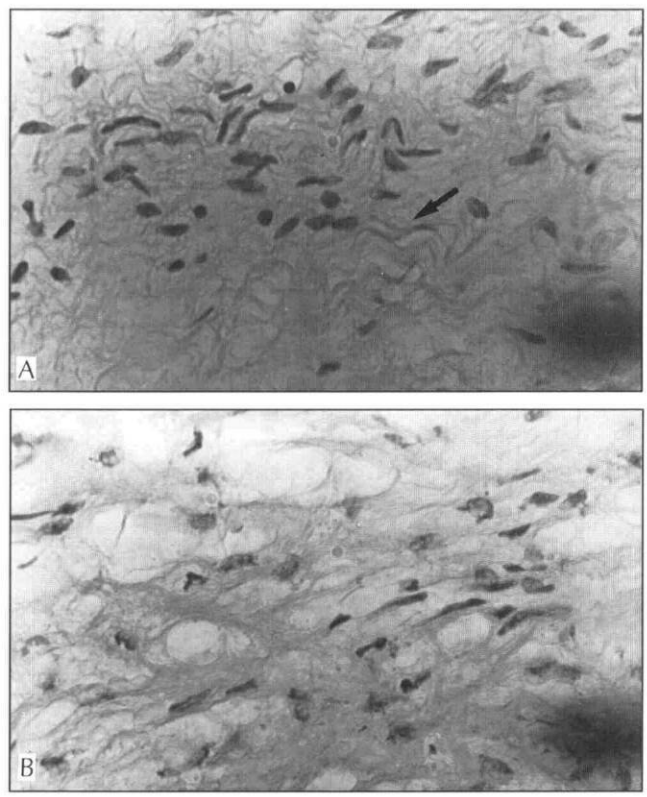

Fig 7. The pulp section from the patient with E-D syndrome (A) and the control pulp section (B) treated with van Gieson's solution. The collagen in the pulp tissue with E-D syndrome was stained red and showed a wavy pattern (arrow), although that in the control pulp tissue showed a network pattern. (Orig. Mag. 100X)

mal pulp tissue characterized by a network structure (Fig 7). This reflects the deficiency in collagen biogenesis of E-D syndrome Type VII.

Other dental manifestations, such as periodontal disease, poor wound healing after tooth extraction, and malformed roots of the deciduous teeth, were not recognized in this patient.

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Most common dental problems

A nationwide survey of dentists found that 58 per cent reported cavities as their most common patient problem. The survey also revealed that nearly two-thirds of dentists (64 per cent) consider periodontal disease the most common oral care problem they will face in the 1990s. Other concerns were preventive care/patient education (34 per cent) and restorative/cosmetic treatment (20 percent).

A Colgate survey of 200 dentists found that excess tartar buildup is the second most common problem that dentists report their patients experience.

According to the survey, almost half of dentists (48 per cent) think the cost of dental care will keep pace with the rate of inflation. Dentists also reported that more than half (62 per cent) of their patients are covered by some form of insurance. That figure has been increasing over the past five years. Two of three dentists surveyed provide dental services on a free or reduced basis for uninsured working poor or indigent patients.

The survey also found that dentists in the western region of the U.S. appear to spend more time on cosmetic care than do dentists in the rest of the country. These dentists also are more likely than those in the rest of the country to report that their patients have sore or bleeding gums.