Oral Manifestations of Ehlers-Danlos Syndrome

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Abstract

Ehlers-Danlos syndrome is a rare hereditary disease of the connective tissue which can present oral manifestations. A brief history of the disease is presented along with the epidemiology and characteristics of the 8 main phenotypes of the syndrome. The article also describes the case of a 12-year-old patient presenting with hypermobility of the temporo-mandibular joint and capillary fragility, and highlights the precautions to take when treating patients with this syndrome.

MeSH Key Words: *case report; dental care for chronically ill; Ehlers-Danlos syndrome*

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Ehlers-Danlos syndrome (EDS) is a hereditary collagen disease presenting primarily as dermatological and joint disorders. The first description of the syndrome in the literature was of a young Spaniard who was able to stretch the skin overlying his right pectoral muscle over to the left angle of his mandible.[1] In 1901, Ehlers described the condition as a hyperelasticity of the skin and a strong tendency to bruising. In 1908, Danlos introduced the idea that the condition represented a pseudo-tumour of a molluscoid or fibrous type. It was not until 1934 that Pommeau-Delille and Soussie described the condition as Ehlers-Danlos syndrome. Other evocative terms such as ,Äúelastic man,Äù (or woman) or ,ÄúIndia rubber man,Äù have been used.

Several articles describe the skin and joint problems linked to EDS, but very few describe the oral manifestations of the condition.[2-4] The purpose of this article is to review current knowledge about the syndrome, to present the case of a 12-year-old affected by hypermobility of the temporo-mandibular joint (TMJ) as well as vascular manifestations inherent to the syndrome, and the precautions to take when providing dental treatment for EDS patients.

Epidemiology and Diagnosis

The prevalence of the condition varies between 1:10,000[5] and 1:150,000[6] depending on the author. The diagnosis of EDS depends primarily on clinical findings and family history, as it is an autosomal dominant hereditary disorder which presents in several ways (see **Table 1**, Classification of Ehlers-Danlos syndrome, http://www.cda-adc.ca/jcda/vol-67/issue-6/330.html). Only 4 types of EDS, namely types IV, VI, VII[6] and X[5] can be confirmed by biochemical and molecular tests. Since humans possess 19 types of collagen, it is especially difficult to establish a precise diagnosis.[7] Even when there is a bleeding disorder associated with the syndrome, blood analyses are not diagnostically useful, in that no correlation has been made between the findings of such tests and the various types of EDS.

The differential diagnosis of EDS includes Marfan,Äôs syndrome, generalized familial joint hypermobility synd rome, cutis laxa, pseudoxanthoma elasticum and Larsen,Äôs syndrome.

Characteristics of EDS

The classic signs of EDS are joint hypermobility; hyperelasticity of skin, which is soft, thin and fragile; the presence of dystrophic scars; and a tendency to excessive bleeding manifested by bruises, ecchymoses and hematomas. At least 15 phenotypes of the syndromes have been catalogued to date, with 2 having recently been reclassified.[5,8] We present a description of the first 8 of these phenotypes, but recommend that you read the works of Pope[1] and Gorlin[5] for further information.

Type I

In type I the skin is hyperelastic. Bony prominences such as the forehead, chin, elbows, knees and ankles are constantly lacerated. Given the limited healing power of the skin with this condition, pigmented and atrophic scars (,Äúcigarette paper scar,Äù) are frequently found in these areas and they are accompanied at times by fibrous nodules caused by the fibrous transformation of subcutaneous hematomas.

The patient usually has a mesomorphic appearance with hands and feet being slightly larger than average. Along with a generalized hypermobility of the joints there is usually an abnormal bleeding tendency. Occasionally the syndrome is accompanied by mitral valve prolapse.
Over half of pregnant women with the condition give birth prematurely, following rupture of the fetal membranes.

Type II

Similar to type I, this form is less severe clinically. The scarring is less common, bleeding tendency is less pronounced and nodules are much smaller or totally absent. However, joint hypermobility is similar to that observed in type I and premature births are also a feature of type II, even if they are less common.

Type III

The patient with type III is usually tall and thin, as in Marfan‚Äôs syndrome. The dominant features of this variation are joint hypermobility and hyperelasticity of the skin, which often feels velvety. Bruises and dystrophic scars are rarely observed.

Type IV

Type IV is characterized by a marked fragility of the vascular system. The individual is usually smaller than average. The skin of the hands and of the back appears to age prematurely (acrogeria). The eyes are widely spaced, the nose is narrow, the ear lobes are atrophied and the hair is thin. Aneurysms of the large and medium-sized arteries (axillary, femoral and carotid) are common. Frequently scar tissue appears to be hemorrhagic. Rupture of internal organs is common even at a young age, and perforation of the intestinal tract can be a problem.[9] Joint hypermobility is usually limited to the small articulations of the hand, with acro-osteolysis of the distal phalanges. Mitral valve prolapse can also be present.
Rupture of arteries and hollow organs such as the uterus and the intestine[7,9-11] explains the high mortality rate (51% before age 40). Type IV is consequently, the most serious form of EDS.

Type V

Women are only carriers of this rare form, similar to types I and II, because transmission is associated with the X chromosome.

Type VI

This form resembles type I except for an ocular involvement with detached retina being a common feature. Severe scoliosis and vascular rupture are also features.

Type VII

This is a rare phenotype characterized by joint hypermobility, bilateral dislocation of the hips and a small stature.

Type VIII

First described by Stewart and others in 1977,[12] type VIII is characterized by generalized early-onset periodontitis and by large patches of scar tissue on the shins, similar to diabetic ulcers or varicose veins. The periodontal problems appear at puberty and usually lead to loss of the teeth before age 30. Biesecker and others[13] describe a case of a man who became edentulous at age 16 as a result of severe periodontitis. Hoffman and others[14] describe a case of EDS type VIII where a girl required splinting to treat mobile teeth. Type I (Hoffman[14]) and type III (Lapi√®re and Nusgens[15]) anomalies of collagen have been linked to EDS type VIII.
Hyperelasticity of the skin and hypermobility of the joints are moderate in this phenotype. The facies can resemble that described in type IV ‚Äî hypertelorism, widening of the root of the nose, a narrow curved nose, narrow face and scarring on the forehead and chin.

Clinical Manifestations of EDS

Oral examination can help diagnose EDS (see **Table 2,** Clinical manifestations of Ehler-Danlos syndrome, www.cda-adc.ca/jcda/vol-67/issue-6/330.html).

Extraoral

The extraoral manifestations of EDS are the presence of scarring on the chin and forehead, a history of repeated luxations of the TMJ, epicanthus, hypertelorism, a narrow curved nose, sparse hair and hyperelasticity of the skin.

Intraoral

The classic intraoral signs of EDS can point to the eventual diagnosis of the condition.

Mucosa

As fragile as the skin, the mucosa tears easily when touched by instruments. Sutures do not hold.[16]

Periodontal Tissues

The fragility of the gingiva can be detected following treatments such as prophylaxis, periodontal surgery or extraction. Hemorrhage may be difficult to control during surgical procedures. Early-onset generalized periodontitis is one of the most significant oral manifestations of the syndrome.[1,17] This can lead to the premature loss of deciduous and permanent teeth.[16,18]

The Teeth

Hypoplasia of the enamel is commonly seen.[10] Premolar and molar teeth can present with deep fissures and long cusps. The teeth seem to be fragile and microdontia is sometimes present. Radiographic examination often reveals pulp stones and roots that are short and deformed. Microscopic-level anomalies of the various dental tissues are described in detail by Barabas[11] and Pope.[1] One case of type III EDS with multiple supernumerary teeth has been reported in the literature.[19]

The Tongue

The tongue is very supple. Approximately 50% of those with the syndrome can touch the end of their nose with their tongue (Gorlin‚Äôs sign), compared to 8-10% of the population.[5]

The Palate

The palate is commonly vaulted.[16,20]

Case History

Intermittent swelling of the face brought the 12-year-old patient, who described having a generalized hypermobility of the joints, to consult the dental clinic at Laval University. The history revealed intermittent luxations of the TMJ, the frequency of which had risen from monthly to weekly in a very short time span (6 months) (**Fig. 1**). Pain, which arises 24 hours before a luxation, precedes the bilateral swelling of the face and bleeding in the 2 cheeks (**Fig. 2**). These episodes last from 30 seconds to 2 minutes and the residual pain lasts up to 12 hours. The patient can relieve the pain by continually applying ice during these episodes for periods of up to 2 hours.

Clinical Examination

The clinical exam revealed a normal abdomen and the presence of 2 bruises on the inner bony prominences of the left and right ankle. No hyperelasticity of the skin, post-traumatic hyperpigmentation or fibrous nodules were detected.

The examination of the musculo-skeletal system revealed scoliosis, but without evidence of the *genu recurvatum*, kyphosis, flat feet or thoracic asymmetry seen in some types of EDS. The patient was able to adopt some unusual postures on request (**Fig. 3**). We noted hyperextension and hyperabduction of the fingers (**Fig. 4**), as well as a marked hypermobility of the elbows, feet and toes. The examination of the extremities revealed nothing unusual and no evidence of arachnodactyly.

Cardio-pulmonary auscultation was normal, with no evidence of mitral valve prolapse. The peripheral pulse was also normal. Neurological examination revealed diminished reflexes, with the exception of the triceps reflex.

In the examination of the head and neck, the sclera were slightly blue and the pinna of the ear was prominent. The patient could touch the end of her nose with her tongue. The skin gave the signs of capillary fragility resulting from the constant application of an ice pack. The neck was normal.

There was bilateral clicking of the TMJ at the end of opening, with no pain to palpation. The maximum opening of 58 mm exceeds the normal opening of between 35 and 45 mm. Palpation of the left masseter caused pain.

Oral examination revealed a late mixed dentition with 2 retained primary second molars. The molar relationship was Class II.

Radiological Examination

A panoramic radiograph (**Fig. 5**) revealed the congenital absence of the 2 maxillary second bicuspids. There was no other anomaly evident.

Special Tests and Consultations

Blood, electrolyte and liver function tests were normal. Coagulation values were normal with a bleeding time of 5.3 minutes (normal for a female is < 7 minutes), a Quick time of 9.2 (normal between 12 and 15

seconds, but no problem if below), an International Normalized Ratio (INR) of 1.04 (normal is 1). Thrombin time was also normal; however, the cephalin time was at the upper limit of the normal range (32.3, where the normal is 28 seconds).
Results of consultations in ophthalmology and cardiology eliminated the possibility of detached retina or mitral valve prolapse. The genetics and rheumatology consults confirmed a diagnosis of EDS type II or III. The definitive diagnosis is probably type III. The bleeding tendency suggests type II; however, the absence of hyper elasticity of the skin points away from this diagnosis. The bleeding tendency, the joint hypermobility and the ability to touch the nose with the tongue suggests type VIII; however, the young age of the patient doesn,Äôt allow for severe periodontal involvement. This usually manifests itself following puberty.
As a preventive measure we advised the patient to limit her mandibular movements in order to avoid the risk of luxation or subluxation. Surgery of the TMJ is only contemplated as a last resort to correct luxation or subluxation. It is not done to reposition the meniscus.

Clinical Precautions for the Dentist

The presence of mitral valve prolapse generally indicates that prophylactic antibiotics are indicated for relevant procedures.[20] Dental visits of short duration are preferable in order to avoid causing iatrogenic problems in the TMJs. Inferior alveolar nerve blocks should be given with great care to avoid causing hematoma.[20,23]
Forces used in orthodontic treatment should be lighter than usual, given the fragility of the periodontal ligament. The teeth move rapidly with well-controlled forces, and root resorption does not seem to be a major problem.[8] Because relapse is frequent, a longer period of retention is necessary.[8] The buccal mucosa is vulnerable to damage from orthodontic appliances.[24]
Ideally, dental and maxillofacial surgery should be avoided. It is imperative to test blood coagulation values before proceeding with surgery. Sutures, which do not hold well, should be covered with acrylic dressings.[20]

Conclusions

Oral examination can be instrumental in establishing a diagnosis of EDS. The presence of the classic signs of the syndrome should prompt the clinician to arrange dermatology, genetics, rheumatology, cardiology and ophthalmology consults to confirm and type the diagnosis of EDS. The dentist should perform treatment observing precautions appropriate to this condition.

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CDA Resource Centre

Do you have questions about the oral manifestations of Ehlers-Danlos syndrome? The CDA Resource Centre can provide the information you need. Contact us at tel.: **1-800-267-6354** or **(613) 523-1770**, ext. 2223; fax: **(613) 523-6574**; e-mail: **info@cda-adc.ca**.