A rare case of ehler-danlos syndrome

A RARE CASE OF EHLER-DANLOS SYNDROME WITH LITERATURE REVIEW

ABSTRACT

The Ehlers-Danlos syndrome comprises of a group of generalized connective tissue disorders which is characterized by fragile skin, skin hyperextensibility, and joint hypermobility. More than 10 types of Ehlers-Danlos syndrome have been identified based on genetic and biochemical studies [1] . In the majority of patients with molecularly characterized as classic Ehlers-Danlos syndrome (type I and type II), the disease is caused by a mutation leading to a non-functional COL5A1 allele and resulting in haplo-insufficiency of type V collagen [2] . Most mutations identified so far result in a reduced amount of the type V collagen in the connective tissues available for collagen fibrillogenesis. Inter and intra-familial phenotypic variability is observed, but no specific genotype-phenotype correlations have been observed. No specific treatment protocol for the underlying defect is presently available for Ehlers-Danlos syndrome. However there are a series of preventive guidelines applicable [2] . Periodontal disorders, increased bleeding tendency, delayed eruption of teeth and joint subluxation are few concerns during dental management of such patients.

This case report discussess the features of classic ehler danlos syndrome presented in a 7 year old female patient and reviews the recent literature.

Key words: Ehler-Danlose Syndrome, Classic Type.

EHLER-DANLOS SYNDROME: A CASE REPORT

INTRODUCTION

The Classic Ehlers-Danlos syndrome is a heritable connective tissue disorder characterized by skin hyperextensibility, fragile and soft skin, delayed wound healing with formation of atrophic scars, easy bruising, and generalized hypermobility of joint. It comprises Ehlers- Danlos syndrome type I and Ehlers-Danlos syndrome type II, but it is now apparent that these form a continuum of similar clinical findings and differ only in phenotypic severity [2] . Presented here is a rare case of a 7 year old girl with features of Classical Ehler Danlos Syndrome.

CASE REPORT

A 7 year old female patient reported with her parents to the department of oral medicine & radiology concerned about a decayed tooth in the lower right back jaw region.

A thorough review of the family history indicated that she was the first and the only child of her parents who had married consanguineously. On further investigation the parents reported that child had an unremarkable prenatal course of development and birth. She had no significant illnesses or hospitalizations as reported . She had normal course of development .

Her medical history did reveal prolonged epistaxis occasionally . Opthalmic assessment was done at the age of 2 years and she was diagnosed with astigmatism for both the eyes. On a re-evaluation a week ago she was also diagnosed with hypermetropia.

The patient’s dental history was, according to her parents, uneventful, although she had never had routine professional care. Tooth eruption and

exfoliation had occurred without difficulty. She reported brushing her teeth twice daily.

Physical examination revealed a thin white female kid with translucent skin with blue sclera and dark circles around her eyes. There was hyperextensibility of her fingers in both hands and legs, elbows and knees with bilateral shoulder subluxation. Her height was 125 cm and weighed 19. 20 kgs., afibrile at the time of presentation. Laboratory examination for the patient revealed normal CBC, platelets, PT, and PTT; however, her bleeding time was found to be greater than 16 mm.

Oral examination revealed early mixed dentition with a Class I relationship of her first permanent molars and primary canines. Severe crowding of incisors and she had a posterior crossbite on her right side was present. Dentinal caries was present with respect to lower right deciduous molar. There was generalized gingivitis with fair oral hygiene.

A provisional diagnosis of Ehler Danlos syndrome was made based on the clinical finding and the patient was sent to the genetic center at the Indira Gandhi Institute Of Child Health. Upon genetic analysis it was found that she had pathogenic variant of COL51A gene. On basis of the genetic analysis and clinical features a confirmed diagnosis of Ehler Danlos Syndrome was made.

The parents were referred to a genetic counselor to explain regarding the condition and the possibility of the condition repeating in the next offspring.

The patients’ dental treatment was performed at the pediatric department which was uneventful.

The patient is placed under regular recall at the dental hospital and was referred to the clinical pediatrician for subsequent care and review.

DISCUSSION

The Classic Ehlers-Danlos syndrome (EDS) is a heritable connective tissue disorder which is characterized mainly by hyperextensibility of skin , abnormal wound healing, and joint hypermobility.

After the description of typical hyperelastic skin by Van Meekeren and hypermobility of joints , in addition, by Knoop , Ehler first noticed easy bruisability of the skin. Danlos drew attention to peculiar cigarette paper scar & multiple pseudotumor formation of the skin [3] .

Prevalence : EDS truely is a rare disease, affecting just one in a million people worldwide. There are many subtle forms of the condition, leading to missed diagnosis or misclassification. Therefore, the incidence rates stated are skewed. The statistics for ED syndrome in India per se has hardly been noted, most of the authors referencing to world wide statistics.

Pathophysiology : There are three different mechanisms by which the EDS traits are produced [6] . The first of these features is a deficiency of the collagen-producing enzymes, such as lysyl-hydroxylase and pro-collagen peptidase. The second is the dominant-negative effect of the mutant collagen α-chains [6] . The third is haplo-insufficiency of COL5A1 gene that encodes the proalpha1(V) chain of the type V collagen. The term haplo-insuffiency refers to the presence of a single functional copy of any particular

gene within diploid organisms, with the other homologous allele (which is supposed to be a functioning duplicate gene) inactivated [12] .

The diagnosis of EDS, classic type is generally established by clinical examination and family history. The diagnostic criteria were developed by a medical advisory group in a conference held at Ville franche in 1997 [2] . The combination of threemajor diagnostic criteriais highly specific for the presence of the condition [2] :

1. Skin hyperextensibility: Skin hyperextensibility should be tested at a neutral site (the one not subjected to mechanical forces or scarring), such as volar surface of the forearm. It is measured by pulling up the skin until any resistance is felt. In young children, hyperextensibility of skin is difficult to assess because of abundant subcutaneous fat.
2. Widened atrophic scar formation (manifestation of tissue fragility).
3. Joint hypermobility: Joint hypermobility depends upon age, gender, family and ethnic backgrounds. Joint hypermobility in classic EDS is generalized, affecting both the large and the small joints and can range in severity from mild to severe [2] . It is usually noted when a child starts walking [6] .
4. A positive family history [2] .

TheMinor diagnostic criteriawere also established, and the presence of one or more of these minor criteria contributes to the diagnosis of classic EDS, though not sufficient to establish the diagnosis [2] :

1. Smoothness of skin, velvety texture.

2. Molluscoid pseudotumors (fleshy, heaped-up lesions associated with scars formation over pressure points such as the elbows and knees).
3. Subcutaneous spheroids (small, hard cyst-like nodules, freely moveable in the sub-cutis over the bony prominences of the legs and arms, which have an outer calcified layer with a translucent core on the radiograph).
4. Complications of hypermobility of joint(e. g.: sprains, dislocations or subluxations, and pes- planus).
5. Muscle hypotonia with delayed gross motor development.
6. Easy bruisability.
7. Manifestations of tissue hyperextensibility and fragility (e. g.: hiatal hernia, anal prolapse in childhood, and cervical insufficiency).
8. Surgical complications including postoperative hernias [2] .

Differential diagnosis of the other EDS-subtypes:

1. EDS hyper-mobility type (EDS type III)

2. Familial joint hyper-mobility syndrome

3. EDS vascular type (EDS type IV)

Differential diagnosis including other heritable connective tissue disorders [2] :

1. Marfan- Syndrome
2. Cutis- Laxa Syndromes
3. Loeys-Dietz Syndrome

The discussed case presented with smooth velvety skin, skin hyper-extensibility , joint hyper-mobility, with history of easy bruising and epistaxis,

muscle hypotonia , features suggestive of a clinical diagnosis of the classical ehler danlos syndrome.

Clinical Management: There are not many treatment options available, yet the optimal management of EDS patients through a series of lifestyle modifications is recommended, such as by minimizing skin trauma brought about during trauma or excessive exposure to the sun, as well as a regular exercise regimen in order to strengthen muscles tone , which in turn decreases the risk of joint injury (such as the previously discussed spontaneous dislocation). Patients with the vascular and the ocular forms of EDS should avoid dangerous contact sports, such as martial arts and football etc. There is even anecdotal mention that increase in the intracranial pressure resulting from Valsalva effect can be problematic, especially with the vascular and the ocular forms; patients may be advised to refrain from such activities as playing musical instruments (trumpet, trombone) as well as activities that require constant squatting or bearing down.

The limited treatment choices available for EDS patients' are unsatisfactory, with most care being supportive in nature. Patients requiring surgical interventions should be treated with the utmost of caution due to enhanced problems of bleeding from spontaneous vascular rupture, scar formation, and potential compromises in airway maintenance. Surgical re-excision of the scars and keloids might provide for some cosmetic benefit, although this plastic surgery can also lead to problems as previously noted.

CONCLUSION

EDS, the classic type is inherited disorder of autosomal-dominant type . It is estimated that approximately 50% of the affected individuals have inherited mutant gene from an affected parent, and about 50% of the affected individuals may have a de novo disease-causing mutation.

Although about 50% of the individuals diagnosed with classic EDS have an affected parent, the family history may seem to be negative because of failure to recognize the disorder in family members. Requests for prenatal testing for conditions such as classic EDS that do not affect intellect of the individual or life span are not common. Differences in perspective may exist among various medical professionals and within families regarding the use of prenatal testing [2] .

From an oral physicians perspective its important to be aware of the risks of bruising, bleeding and joint hyper extensibility during various dental procedures being carried out in the patient. Also it is important to make the patient and related aware of the importance of need for optimum maintenance of oral hygiene to avoid the oral disorders patient is more susceptible to.