

Case Report

Ehlers-Danlos syndrome- a not so rare entity

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Abstract The patient was a young girl who presented with 5 years history of excessive joint mobility, difficulty in wound healing and formation of thin scars over the extensor aspects of the limbs. There was no history of any bleeding tendency, joint subluxation or eye complaints. On examination, the skin was soft and hyperextensible and the joints exhibited a great range of mobility. There were multiple paper-thin scars over the extensor aspects of elbows, knees and shins. There was a 'molluscoid pseudotumour' over her right elbow. The patient was diagnosed as a case of EDS type I on the basis of history and clinical examination. The tumour was excised and the histopathology report was consistent with the diagnosis of molluscoid pseudotumour. She was prescribed Tab Vitamin C 500mg daily. The patient and the parents were explained about the disease, its prognosis and complications.

Key words

Ehlers-Danlos syndrome

Introduction

Ehlers-Danlos syndrome (EDS) is a group of generalized disorders of connective tissue. It is characterized by fragility of the skin and blood vessels, hyperextensibility of the skin and joint hypermobility.¹ At least 10 clinical types have been defined, although some patients fail to fit neatly into one category.

This is the first case report of EDS appearing in Pakistani literature. The purpose of this case report is to present the key features of this syndrome and to briefly discuss the features of other types of the syndrome. It is a rare syndrome and a clear knowledge of the disease and its complications is must for all the practicing dermatologists.

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Case report

A 10-year-old girl reported in Skin OPD of Combined Military Hospital Peshawar with five years history of hypermobility of all the joints of her body and difficulty and delay in wound healing. The wounds healed by leaving large scars. There was also a history of a soft, nodular and painless mass over her right elbow since last one month. There was no history of any bruising or bleeding tendency, periodontal disease, varicose veins, hernias or any ocular complaint. The patient was 2nd among the two brothers and two sisters. Rest of the family members were all healthy.

On general physical examination, the girl was of thin and lean build. She was well oriented in time and space. Her vital signs were all stable. Her systemic examination revealed no abnormality, however all of



Figure 1 Skin is hyper extensible but springs back to its position when released.



Figure 2 Multiple paper-thin scars over her right knee and front of her leg.

her joints showed hypermobility. The skin examination revealed hyperextensible skin, which was not lax (**Figure 1**). There were multiple paper-thin scars over her both forearms and legs, especially over the knees and shins (**Figure 2**). There was a 2x2 cm soft, nodular, skin-coloured growth over her right elbow, which was not tender (**Figure 3**).

Discussion

Based upon the history and clinical appearance the diagnosis of EDS type-I



Figure 3 A soft, nodular, skin-coloured growth over the right elbow. Note the extensive pronation of the right forearm.

was made. Excision biopsy of the soft nodular growth was made and the histopathology revealed a mixture of fat cells and mucoid material in a fibrous stroma. The parents were explained at length about the disease, its mode of inheritance, possible complications and the prognosis. The patient was placed on Tab Vitamin C 500mg/day and instructed to pay regular visits to the Skin OPD.

The Ehlers-Danlos syndrome is a heterogeneous group of generalized connective tissue disorders, the major manifestations of which are skin fragility, skin hyperextensibility, and joint hypermobility. The clinical and molecular definition of more than ten types of EDS has, more than ever, emphasized the importance of correct diagnosis because the natural history and mode of inheritance differ among the types.²

This disorder affects approximately 1 in 5,000 live births, including males and females of all racial and ethnic groups.³ Specific biochemical abnormalities involving the collagen fibers are identified in several types, although type IX also affects elastin metabolism⁴ and type X has a defect in fibronectin.⁵ **Table 1** provides

Table 1 Current classification of Ehlers-Danlos syndrome

<i>Types</i>	<i>Clinical features</i>	<i>Inheritance</i>	<i>Biochemical Defect</i>
I Gravis*	Soft, hyper extensible skin; easy bruising; thin, atrophic scars; hypermobile joints; varicose veins; prematurity of affected newborns	AD	Mutation in pro α 1(V) or pro α 2(V) chains of type V collagen (COL5A1, COL5A2) in some families
II Mitis*	Similar to EDS type I but less severe	AD	Same as EDS I
III Familial hypermobile	Soft skin; large and small joints are hyper mobile	AD	Not known
IV Arterial	Thin, translucent skin with visible veins; easy bruising; absence of skin and joint extensibility; arterial, bowel and uterine rupture	AD	Mutations in COL3A1; abnormal type III collagen synthesis, secretion or structure
V X-linked [^]	Similar to EDS type II	XLR	Not known
VI	Soft skin, muscle hypotonia; scoliosis; joint laxity; hyperextensible skin	AR	Lysyl hydroxylase deficiency; mutations in PLOD gene
VII Arthrochalasia multiplex Type VIIA, B	Congenital hip dislocation, severe joint hyper mobility; soft skin with normal scarring	AD (type VIIA, B)	Deletion of exons from type I collagen gene that encodes amino-terminal propeptide cleavage site of COL1A1 (type VIIA) or COL1A2 (type VIIB)
VII Type VIIC	Severe skin fragility; sagging, redundant skin	AR (type VIIC)	Recessive mutations in type I collagen N-peptidase (type VIIC)
VIII Periodontal #	Generalized periodontitis; soft hyperextensible skin; chronic purple-hued scarring over shins	AD	Not known
IX X-linked cutis laxa \pm	Soft lax and hyper extensible skin; short arms; limited pronation/ supination, occipital horns, broad clavicles; bladder diverticula; inguinal hernia	XLR	Defect in lysyl oxidase
X [^]	Similar to EDS type II, with abnormal clotting studies	AR	Proposed defect in fibronectin

* In proposed new classification, merged as a single entity, [^] Found only in a single family, # May be a variant of EDS type I/II rather than a distinct entity, \pm Probably not a separate entity. Related to Menkes syndrome, Note: AD - autosomal dominant, AR - autosomal recessive, XLR - X linked recessive

the currently acceptable classification, known biochemical defects; brief clinical features and modes of inheritance in different types of EDS.

EDS type-I is the commonest variety of this syndrome. It is inherited as an autosomal dominant trait. In both the types I and II syndromes, it is suspected that

there are some genetic abnormalities that result in abnormal type I collagen fibril structure because electron micrographs have detected abnormally thick type I collagen fibrils.⁶ In the skin of some patients with EDS I and II, the fiber bundles are abnormally small. Linkage studies have excluded type I collagen genes themselves as the genetic defect in

some families with EDS types I and II.⁷ Interest in type V collagen as a candidate molecule in EDS came about because type V collagen and type I collagen molecules form heterotypic collagen fibrils.⁸ There are now several published reports of linkage to COL5A1 and/or mutations in the coding regions of pro α 1(V) chains in EDS families.^{9,10} There is also an evidence of locus heterogeneity, because mutations in the triple-helical domain of pro α 2(V) chains of type V collagen can also cause the classic EDS type I/II phenotype.¹¹

Skin in EDS type I is soft, velvety and can be stretched easily, and when released springs back immediately to its original position. The skin is not otherwise lax, until later in life, when redundant folds form at the elbow. The dermis is fragile and is easily bruised. Striae do not develop. Scars after trauma or surgical procedures are thinned and atrophic and may stretch considerably after healing, having a characteristic "cigarette paper" appearance. Sutures may tear out repeatedly. Blue-grey spongy tumours, "molluscoid pseudotumours" are formed on extensor surfaces of joints, in the foot or on shins. Joints are hyper mobile, which may cause pain while walking. Furthermore, joint hyper mobility may lead to subluxation of large joints, scoliosis, pes planus (flat foot) and osteoarthritis in 3^d or 4^h decade. Muscle tone is often poor leading to diaphragmatic eventration and gastric torsion.¹² Other complications include varicose veins, prematurity due to rupture of fetal membranes, mitral valve prolapse, dilatation and rupture of ascending aorta or proximal pulmonary artery. As physical

and mental developments are normal, life expectancy is not reduced.

The diagnosis is made primarily on the basis of a detailed history and clinical examination. The laboratory diagnosis can be done only in specialized laboratories working on molecular biology of collagen.

The treatment is highly unsatisfactory. Some benefit may be achieved by giving oral ascorbic acid in a dose of 500-3000 mg daily. It is found that 4 grams of vitamin C daily produce a significant improvement in the quality of newly synthesized collagen but do not alter the pre-formed collagen.¹³ Suture should be buttressed and tension avoided. However re-excision of ugly scars gives a good cosmetic result.¹⁴

Conclusion

Ehlers-Danlos syndrome is not a commonly encountered disease. A clear understanding of the key feature of this syndrome is vital for the diagnosis and knowledge of its complications and prognosis is important to satisfy the patients and their relatives.

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