EHLERS-DANLOS SYNDROME IN FOUR GENERATIONS

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Summary

Thirteen cases of Ehlers-Danlos syndrome are being reported from a twentyfive member family. All had type II (mitis) variety of Ehlers-Danlos syndrome with autosomal dominant transmission.

KEY WORDS: Ehlors-Danlos syndrome.

Introduction

Ehlers-Danlos syndrome is a generalised hereditary disorder of loose connective tissue, manifesting clinically with fragility and hyperstrechability of skin and loose-jointedness. The clinical manifestations of the disease have been aptly classified into several clinical variants[1].

Hippocrates in the fourth century B.C. described lax joints and numerous burn-like scars in several scythians[2]. Van Meekeren in 1682 described unilateral hyperelasticity of skin[2]. Koop in 1888 reported hypermobile joints with strechable skin[2]. Ehlers first noted easy bruisability of skin. Danlos laid down four diagnostic criteria of the syndrome consisting of hypermobility of joints, hyperelasticity of skin, fragility of skin and subcutaneous molluscum pseudotumour formation. Only a few cases of this syndrome have been reported from India[3,4,5]. Occurrence of this syndrome in four generations of a kindred has not been reported so far from our country. This prompted us to report the present series.

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Case Reports

Case 1

A 22 years old Hindu female attended the medical out-patient department of Associated Group of Hospitals attached to S. P. Medical College, Bikaner with the complaints of gradually increasing looseness of joints and skin for 3 years. She gave history of easy bruising of the skin with even very trivial trauma but no episode of major haemorrhagic accident had ever occurred in the past. She was born full term after a normal delivery and had no neonatal or perinatal morbidity.

Physical examination revealed averagely nourished and normally built lady with velvety skin all over the body. There was no evidence of cyanosis, jaundice, digital clubbing or lymphadenopathy. Systemic examination did not reveal any abnormality.

Besides being velvety and smooth, the skin was hyperelastic, this being best demonstrable over the elbows and

knees. A cigarette-paper thin scar was present on the skin over tibia. The joints were hypermobile showing hyperextensibility of wrists, elbows, knees and interphalangeal joints. No dislocation of joints or scoliosis was present. There was no evidence of flat foot.

Routine investigations of blood and urine did not reveal any abnormality. Coagulogram was normal. Blood urea, sugar and electrolytes were normal. Skiagram of joints did not reveal any abnormality. Barium meal and enema examination did not show any evidence of diverticulosis. Electrocardiogram was within normal limits.

Case 2

A 50 years old lady, mother of the above case, was otherwise asymptomatic but on examination was found to have laxity of skin, hyperextensibility of joints, easy bruisability, flat feet and genurecurvatum. Systemic examination revealed no abnormality. Routine investigations of urine and blood were normal. Skiagrams of joints and barium studies of G.I.T. were normal.

Additional eleven cases of Ehlers-Danlos syndrome which subsequently proved to represent four generations of the kindred were found on interrogation of Case No. 1. All the family members were examined.

Microscopic pathology

Histopathological examination of 6 out of 13 patients were carried out. This showed increased length and number of elastic fibres but lack of uniformity. Collagen fibres appeared coarse, irregular and fragmented. Upper portion of dermis appeared matted together. Blood vessels and lymph spaces were dilated.

Out of 25 members of the kindred 13 were found to be having evidence of Ehlers-Danlos syndrome (Fig. 1.) Nine out of these 13 were adults. The clinical features of the adults affected are listed in Table 1. The fourth generation (Case No. 10, 11, 12 and 13) were mostly children of preschool age. The minimal criteria for involvement of these patients included hyperelasticity of skin and hypermobility of joints.

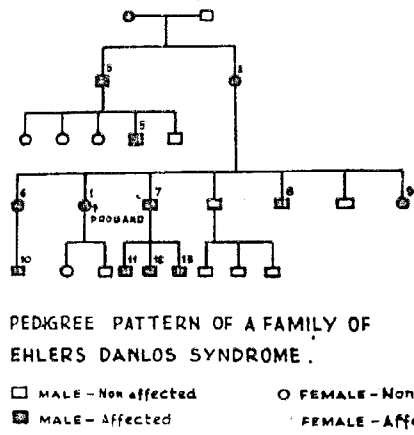

Fig. 1 Pedigree pattero of a family of Ehlers-Danlos Syndrome.

TABLE 1
Clinical manifestations of the Ehlers-Danlos Syndrome in 9 adult members of the kindred

Clinical Manifestations	Case Numbers								
	1	2	3	4	5	6	7	8	9
Hyperelasticity of skin	+	+	+	+	+	+	+	+	+
Cigarette paper scars	+	−	−	−	−	−	+	−	−
Skin fragility	+	+	−	−	−	−	−	−	−
Hyperextensibility of joints	+	+	+	+	+	+	+	+	+
Genu-recurvatum	+	+	−	−	−	+	+	−	−
Flat foot	−	+	−	+	+	−	+	−	+

None of the cases showed pseudotumour molluscum or subcutaneous spherules Cardio-respiratory systems were normal. Nothing abnormal was observed on ocular examination.

Discussion

Various clinical and biochemical features have assisted in classifying

Ehlers-Danlos syndrome into 7 clinical variants[1]. The cases under review had pattern of autosomal dominant transmission with features of primarily joints and skin involvement suggesting that these belong to type II variant of the disease.

The familial occurrence of the disease was described by Koop in 1888[2]. Four cases of this disease in one generation in a Negro family were reported for the first time. Two of them were found to have haemoglobin S[6]. Papp et al[2] described 32 affected cases from a kindred of 3 generations consisting of 50 members. He suggested transmission through an autosomal dominant gene with low penetrance in his cases with a male-female ratio of 2 : 1. An affected set of twins was also reported. In the kindred described here 8 males were affected as compared to 5 females, with an autosomal dominant gene with low penetrance.

The aetiology of this syndrome is still unknown. However, the deficiency of certain enzymes has been detected, of which procollagen lyslhydroxylase and procollagen protease are important[2]. This results into defective cross linking of various hydroxyproline and hydroxylysine units. The collagen meshwork thus formed is loose and is largely responsible for the clinical manifestations of the disease.

It is possible that many cases of Ehlers-Danlos Syndrome are not diagnosed clinically when they may present as forme-fruste because of very low penetrance of the gene. An awareness of the disease entity will be necessary for proper genetic counselling.

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