

Kyphoscoliosis type of Ehlers-Danlos Syndrome in a Family

Md. Azizul Haque¹, Md. Aminul Islam², ARMS Ekram³,
Laila Shamima Sharmin⁴, Muhatarima Tabassum⁵, Syed Mahbub Alam⁶

ABSTRACT

Ehlers-Danlos syndrome (EDS) is a generalized disorder of connective tissue characterized by hyperextensibility of skin, hypermobility of joints, and fragility of skin and blood vessels. According to new nomenclature EDS is classified in six major types. We are reporting kyphoscoliosis type of Ehlers-Danlos syndrome in two siblings.

KEY WORDS: Ehlers-Danlos Syndrome, Kyphoscoliosis.

Pak J Med Sci October - December 2010 Vol. 26 No. 4 978-981

How to cite this article:

Haque Md.A, Islam Md.A, Ekram ARMS, Sharmin LS, Tabassum M, Alam SM. Kyphoscoliosis type of Ehlers- Danlos Syndrome in a Family. Pak J Med Sci 2010;26(4):978-981

INTRODUCTION

Ehlers-Danlos syndrome (EDS) is a generalized disorder of connective tissue characterized by hyperextensibility of skin, hypermobility of joints, and fragility of skin and blood vessels.¹ The first comprehensive description of a syndrome comprising laxity and fragility of the skin associated with hypermobility of the large joints was published in 1892 by Tschernogobow in Moscow.² With remarkable insight, he interpreted the cause of the phenotype as a systemic defect in connective tissue.

However, this syndrome bears the names of Ehlers, a Danish dermatologist and Danlos, a French dermatologist, who published their observations independently in the first decade of the 20th century. Ehlers first noticed the easy bruisability of the skin. Danlos drew attention to the peculiar cigarette paper scars and pseudotumor formation of the skin and also laid down four diagnostic criteria, namely, hyperelasticity of skin, fragility of skin, hypermobility of joints and subcutaneous molluscus pseudotumor formation.^{3,4} It is a hereditary disorder, the inheritance being usually autosomal dominant with low penetrance. Autosomal recessive and X-linked recessive varieties are also known.⁵ In 1988 an international nosology of connective tissue that defined nine subcategories of EDS was proposed. With recent developments and increased medical expertise, a simplified classification of EDS has been revised into six major types namely Classical, Hypermobility, Vascular, Kyphoscoliosis, Arthroclasia, and Dermatosparaxis.⁶ Kyphoscoliosis type of EDS (Type VI in previous classification) is attributed to a deficiency in lysyl hydroxylase (LH), the enzyme that hydroxylates specific lysine residues in the collagen molecule to form hydroxylysines with 2 important functions. More than 20 mutations are identified in the *LH1* gene that contributes to LH deficiency and clinical kyphoscoliosis type of Ehlers-Danlos syndrome.⁷ We are reporting kyphoscoliosis type of Ehlers-Danlos syndrome in two siblings.

1. Md. Azizul Haque, MBBS, FCPS, MRCP.
Assistant Professor, Department of Medicine.
2. Md. Aminul Islam, MBBS.
Postgraduate Student, Department of Medicine.
3. ARMS Ekram, MBBS, FCPS, PhD, FACP, FRCP.
Professor, Department of Medicine.
4. Laila Shamima Sharmin, MBBS, FCPS.
Registrar, Department of Neonatology.
5. Muhatarima Tabassum, MBBS,
Postgraduate Student, Department of Medicine.
6. Syed Mahbub Alam, MBBS,
Postgraduate Student, Department of Medicine.
- 1-6: Rajshahi Medical College,
GPO-6000, Bangladesh.

Correspondence:

Dr. Md. Azizul Haque,
Assistant Professor,
Department of Medicine,
Rajshahi Medical College, GPO-6000,
BANGLADESH.
E-mail: drazadbd@gmail.com

- * Received for Publication: April 24, 2010
- * Accepted: June 26, 2010



Figure-1: Kyphoscoliosis and atrophic "cigarette paper" scar.

CASE REPORT

A 23 year old lady, one of 10 children out of a consanguineous marriage, was admitted in Department of Medicine of Rajshahi Medical College with the complaints of deformity of her back, laxity of skin and hypermobility of joints since infancy. According to patient's mother, she was very floppy after being born and had deformity of her back at birth. Over the years, the deformity became more pronounced. She did not give any history of bruising of the skin. During childhood her mother also noted that her skin and joints were more lax than her peers. She had 9 siblings, 4 of them male and 5 were female. Out of them two of her sisters and three brothers had similar presentation like her. One sister and one brother died few days after birth. Both of them had deformity of their spine and were so floppy that they could not even suck breast milk. One of her affected brother had died suddenly at the age of 18 after developing chest pain. One affected sister committed suicide at the age of 21 because of social stigma about her disease. One brother aged 31 was still alive and had similar clinical features like her. The father had remarried and all four of the children out of that marriage are healthy.

During examination of anemia, it was noted that her facial skin was too lax and stretches more easily



Figure-2: Hypermobility of thumb.

than normal. Subsequently it was found that skin all over her body is hyper-extensible to the extent of about 3" to 4". The stretching was painless. Atrophic "cigarette paper" scars were present on her lower back and both knees. Skeletal examination revealed kyphoscoliosis, and hypermobile joints (Beighton scale score 9/9). Examination of the eye revealed microcornea, and blue sclera affecting the upper outer



Figure-3: Hypermobility of the spine.



Figure-4: Hypermobility of knee

quadrants of both sclera. Her visual acuity was 6/6. Examination of the fundus did not reveal retinal detachment, angioid streaks or other abnormalities. There was no subluxation or dislocation of lens. Her elder brother had similar physical findings except the Beighton scale score, which was 7/9 in his case. Both of her mother and father are apparently healthy and do not have such manifestations.



Figure-5: Hyperextensibility of skin.

X-Ray of the dorsal spine revealed gross kyphoscoliosis; complete blood count, liver function, renal function, CXR, ECG, echocardiogram and USG of whole abdomen were reported normal.

Both of the siblings had three major criteria - generalized joint laxity (Fig. 2, 3, 4); severe muscle hypotonia at birth; scoliosis at birth which is progressive (Fig. 1, 6) and three minor criteria - tissue fragility, including atrophic scars (Fig. 1, 7), microcornea; and family history, i.e., affected sib for kyphoscoliosis type of Ehlers-Danlos syndrome. Though measurement of total urinary hydroxylsyl pyridinoline ("Pyridinoline") and lysyl pyridinoline ("Deoxypyridinoline") crosslinks after hydrolysis by HPLC could not be done because of lack of facility in Bangladesh, fulfillment of clinical criteria in both siblings are strongly in favor of our diagnosis.



Figure-6: Kyphoscoliosis of patient's brother.



Figure-7: Atrophic "Cigarette paper" scar on brother's knee

DISCUSSION

Although well defined, the kyphoscoliosis, arthrochalasia, and dermatosparaxis types are considerably less common than the classical, hypermobility, and arterial types of EDS. Classical, hypermobility, arterial and arthrochalasia types are inherited as autosomal dominant, kyphoscoliosis, and dermatosparaxis types are inherited as autosomal recessive manner.^{8,9}

Beighton P et al proposed diagnostic criteria for each major type of EDS.⁶ The major diagnostic criteria for kyphoscoliosis type of EDS included: generalized joint laxity characterized by Beighton scale score 5/9 or more; severe muscle hypotonia at birth; scoliosis at birth which is progressive; scleral fragility and rupture of the ocular globe. The minor criteria's are tissue fragility, including atrophic scars, easy bruising; arterial rupture; marfanoid habitus; microcornea; radiologically considerable osteopenia; and family history, i.e., affected sibs. The presence of three major criteria is suggestive of the diagnosis, and laboratory testing is warranted.⁶ The recommended laboratory test to diagnose kyphoscoliosis type of Ehlers-Danlos syndrome is the measurement of total urinary hydroxyllysyl pyridinoline ("Pyridinoline") and lysyl pyridinoline ("Deoxypyridinoline") crosslinks after hydrolysis by HPLC, a test with very high degree of sensitivity and specificity. Determination of lysyl hydroxylase activity in fibroblasts and/ or mutational analysis of the PLOD gene can be performed on a research basis only.¹⁰ There is no cure and treatment is supportive, including close monitoring of cardiovascular system, especially in vascular and kyphoscoliosis type of EDS.

CONCLUSION

The clinical variability and genetic heterogeneity of Ehlers-Danlos syndrome have long been

recognized. Though incurable by current management strategies; early diagnosis, supportive treatment and genetic counseling are quite helpful in managing patients with Ehlers-Danlos syndrome.

Permission: Permission has been taken from the patients and their family for publication.

Author's contribution: First author has written and revised the article. Last five authors had substantial contributions to preparation, conception and design. There is no potential conflict of interest.

REFERENCES

1. Burton JL, Lovell CR. Disorders of connective tissue. In: Textbook of Dermatology, Champion RH, Burton JL, Ebling FJG editors, 6th ed. Oxford, London: Blackwell Science; 1998. p 2003-71.
2. Tschernogobow A. Cutis laxa. *Mhft Prakt Dermatol* 1892;14:76.
3. Dänische dermatologische Gesellschaft. 15. Sitzung vom 15. Dezember 1900. *Dermatol Z* 1901;8:173-175.
4. Danlos M. Un cas de cutis laxa avec tumeurs par contusion chronique des coudes et des genoux. *Bull Soc Fr Dermatol Syphiligr* 1908;19:70-72.
5. Bruno, Narasimhan, P. The Ehlers Danlos syndrome-A report of 4 cases in 2 generations of a Negro family. *New Eng J Med* 1961;264:274-277.
6. Beighton P, De Paepe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: Revised nosology. *Am J Med Genet* 1998;77:31-37.
7. Yeowell HN, Walker LC. Mutations in the lysyl hydroxylase 1 gene that result in enzyme deficiency and the clinical phenotype of Ehlers-Danlos syndrome type VI. *Mol Genet Metab* 2000;71(1-2):212-224.
8. Beighton P. The Ehlers-Danlos syndromes. In: Beighton P (ed) "Heritable Disorders of Connective Tissue," 5th ed. St. Louis: Mosby, 1993: 189-251.
9. Pope FM, Martin GR, Lichtenstein JR, Penttinen R, Gerson B, Rowe DW, McKusick VA: Patients with Ehlers-Danlos syndrome type IV lack type III col-lagen. *Proc Natl Acad Sci USA* 1975;72:1314-1316.
10. Steinmann B, Royce PM, Superti-Furga A. The Ehlers-Danlos syndrome. In: Royce PM, Steinmann B (eds) *Connective tissue and its heritable disorders*. Wiley-Liss, New York, 1993;351-407.