

Case Report: Ehlers-Danlos Syndrome in an adolescent presenting with Chronic Daily Headache

Suzy Mascaro Walter

West Virginia University School of Nursing, PO Box 9640, 6400 Health Sciences South, Morgantown, WV 26506-9640, USA

E-mail: *Suzy Mascaro Walter - swalters@hsc.wvu.edu

*Corresponding author

Received: 07 July 14 Accepted: 10 July 14 Published: 13 November 14

This article may be cited as:

Walter SM. Case Report: Ehlers-Danlos syndrome in an adolescent presenting with Chronic Daily Headache. *Surg Neurol Int* 2014;5:S475-8.

Available FREE in open access from: <http://www.surgicalneurologyint.com/text.asp?2014/5/14/475/144629>

Copyright: © 2014 Walter SM. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Classic Ehlers-Danlos syndrome (EDS) is a connective tissue disorder characterized by skin hyperextensibility, skin fragility as well as joint hypermobility. EDS has been associated with psychiatric disorders, fatigue, dizziness, musculoskeletal pain, and stomach pain that are common complaints associated with adolescent chronic daily headache (CDH). This case report discusses an adolescent who presents with CDH and is subsequently diagnosed with EDS based upon the presenting symptoms for headache including syncope and chronic musculoskeletal pain as well as a history of hypermobility.

Case Description: A 15-year-old female presented to an outpatient headache clinic with a 10-year history of headache, which had become daily over the past 3 months and awakened her in the middle of the night. Past history also revealed chronic musculoskeletal pain, syncope, fatigue, and hypermobility of joints. Subsequent referral to a geneticist confirmed mild classic EDS.

Conclusion: Along with the major manifestation of EDS, other signs and symptoms that characterize this disorder include musculoskeletal pain, fatigue, dizziness/vertigo, depression, and anxiety, which are often associated with CDH in adolescents. Clinicians treating CDH need to be aware of the major clinical manifestations of EDS as well as the other signs and symptoms that characterize both of these chronic pain disorders. An understanding of this syndrome will lead not only to a diagnosis of EDS but also initiation of a treatment plan specific for an adolescent with CDH and EDS.

Key Words: Adolescent, chronic daily headache, Ehlers-Danlos Syndrome, hypermobility

Access this article online

Website:

www.surgicalneurologyint.com

DOI:

10.4103/2152-7806.144629

Quick Response Code:



INTRODUCTION

Classic Ehlers-Danlos syndrome (EDS) is an autosomal dominant inherited connective tissue disorder, which is typically characterized by skin hyperelasticity, tissue fragility (manifested by atrophic scarring), and joint hypermobility.^[7,11,13] Collagen supports the connective

tissue (skin, ligaments, tendons, internal organ walls, cartilage, blood vessels) and defects in the collagen subsequently result in weakness leading to the above characteristics. Mutations in COL5A1 and COL5A2 are associated with classic EDS. Classic EDS typically occurs due to a nonfunctional COL5A1 allele contributing to haploinsufficiency of type V collagen or, less commonly,

structural mutations in COL5A1 or COL5A2 resulting in the formation of a functionally defective type V collagen protein.^[13]

It is estimated that the prevalence of classic EDS is 1 in 20,000.^[3] Diagnosis can be challenging since EDS cases can be “ambiguous and do not fit in any of the well-described subtypes”.^[9] The classic EDS signs of joint hypermobility, hyperelastic skin, and atrophic scarring are well published. Joint hypermobility can be assessed using the Beighton scale in which a score of 5/9 or greater defines hypermobility. The total score is obtained by the following:^[2]

Characteristic	Score
Passive dorsiflexion of the little fingers beyond 90°	1 point for each hand
Passive apposition of the thumbs to the flexor aspect of the forearm	1 point for each hand
Hyperextension of the elbows beyond 10°	1 point for each elbow
Hyperextension of the knees beyond 10°	1 point for each knee
Forward flexion of the trunk with knees fully extended so that the palms of the hand rest flat on the floor	1 point

Headache is a common chronic pain syndrome in pediatric and adolescent patients.^[18] A systematic review of population-based studies revealed a prevalence of pediatric headache of 58%.^[1] Chronic daily headache (CDH) refers to at least 15 headache days per month and includes tension type and migraine headaches. CDH has been reported by school age children and approximately 54% of children have reported a headache for 4 consecutive weeks, 30% for 8 consecutive weeks and 22% for 12 consecutive weeks.^[14] The association of EDS with adolescent headache is sparse, however, studies in the adult population have described headache as a characteristic finding in EDS.^[6,8] Reports of EDS also demonstrate correlations with psychiatric disorders, fatigue, dizziness, musculoskeletal pain, and stomach pain.^[5,13,15] This is important to understand since children with CDH also report musculoskeletal pain, stomachache, fatigue, dizziness/vertigo, and many have clinically significant mental health issues including depression and anxiety.^[10,16,18,20]

Medication intervention, maintaining good daily habits as well as biopsychological interventions are often a part of treatment plans for children with CDH. However, despite these interventions, some children continue to complain of CDH. Clinicians should not only be aware of the major manifestations but should also recognize the other characteristics for EDS in order to appropriately diagnose and treat children with both EDS and CDH.

CASE REPORT

Patient history and initial examination

A 15-year-old female presented to an outpatient headache clinic with a 10-year history of intractable headache, which had become daily over the past 3 months and also awakened her in the middle of the night. She noted the pain was frontal and radiated to her neck. She had migrainous characteristics including photophobia, phonophobia, nausea, vomiting but denied visual changes, numbness, tingling weakness, or focal deficits. She complained of three migraine headaches a week while the other days she described a tension type headache, which consisted of pain only. She did complain of dizziness, which typically occurred upon standing.

Her daily habits included at least 8-9 h of sleep during the school week but she reported nighttime awakenings, daytime sleepiness, and sleeping more hours on the weekends. She drank occasional caffeine and ate three regular meals a day.

She had a history of syncope, joint, and back pain over the past 2-3 years and had evaluations in cardiology and rheumatology. Rheumatology diagnosed her with hypermobility of her joints. Cardiology diagnosed her with vasovagal syncope and she was placed on a hyperhydration protocol. She had a history of a minute patent foramen ovale, which had undergone spontaneous closure per a recent echocardiogram. She had plain films of her cervical, thoracic, and lumbar spine, which were unremarkable. She also reported easy bruising and occasional bleeding of her gums with oral hygiene. Recent labwork, including a complete blood count (CBC/diff), was unremarkable.

There was a strong family history of mental health disorders. The patient had previously been referred to a psychiatrist and was subsequently diagnosed with depression and anxiety but medication intervention had not yet been initiated.

The patient had a history of developmental delay and she did not walk independently until 2 years of age. She is now developmentally appropriate and is an A/B/C student in the 8th grade.

On general exam, she showed elasticity of her skin, joint laxity of her extremities but no atrophic scarring. Her neurological examination was unremarkable.

Treatment plan

Due to a recent history of increased headache frequency and awakening in the middle of the night with headache, she underwent an magnetic resonance imaging (MRI) brain that was unremarkable. She also revealed a history of snoring, nighttime awakenings, and daytime sleepiness.

A polysomnography was ordered and demonstrated mild obstructive sleep apnea.

She had an appointment to see psychiatry and discuss medication intervention for her depression and anxiety. Often, treatment of underlying depression and anxiety can help alleviate headache, thus, it was agreed that medication intervention for headache be deferred and a trial of Mg was started.

Given the above history, she was referred to Genetics and, based on history and examination, the diagnosis of mild classic EDS was confirmed. Recommendations included hydrotherapy to strengthen muscles, Vitamin C and maintenance of good hydration. Genetics also noted and discussed with parents that if surgical intervention were to be considered for her apnea, she would need to be closely monitored due to an increased risk for postoperative bleeding.

DISCUSSION

The general clinical manifestations of EDS include hyperextensibility of the skin, skin fragility (atrophic scars), and joint hypermobility.^[12] Once the general clinical manifestations of EDS have been confirmed, other forms of EDS should be considered (e.g. hypermobility, vascular, and kyphoscoliotic types).^[13] Specific treatment plans should then be tailored to the patient. In this report, a patient presenting with headache reported symptoms that met the criteria for mild classic EDS (hyperextensibility of the skin, joint hypermobility, easy bruising, tendency to bleeding, and motor delay).

Headache type in adults with EDS have been reported as migraine with aura, migraine without aura, tension type or a combination of migraine and tension type headache.^[8] In one study, approximately half of patients with EDS reported headache.^[17] The actual pathophysiology of headache in EDS is poorly understood. However, cervical spine instability, temporomandibular joint dysfunction, and intracranial hypotension have been noted as possible causes of headache in patients with EDS.^[5] Headache may also be a manifestation of fatigue (due to poor sleep from chronic pain), poorly controlled or undiagnosed depression/anxiety or from analgesic overuse (used to treat chronic joint pain).

In the absence of acute treatable causes for headache, clinicians treating headache patients with EDS need to develop a treatment plan that addresses sleep issues and fatigue, depression/anxiety, and pain management. Pain in EDS has been described as both nociceptive and neuropathic, thus, treatment plans in EDS patients with chronic headache may be tailored to use of antiepileptics or antidepressants as opposed to nonsteroidal antiinflammatory drugs (NSAIDs; to avoid analgesic overuse headache).^[4]

These patients require referral for genetic counseling. A comprehensive clinical evaluation by a geneticist is important since diagnosis is typically based on clinical features.^[19] Initial management should include a baseline echocardiogram (aortic diameter measurement for patients <10 years of age) and evaluation of clotting factors in the presence of easy bruising.^[13] Medication interventions that affect platelet function and prolong bleeding should be avoided including aspirin, dipyridamole, clopidogrel and NSAIDs such as ibuprofen and diclofenac; however, acetaminophen and celecoxib are considered safe since they do not affect hemostasis.^[12] Exercise regimens with little strain on the joint (hydrotherapy) should be initiated to promote muscle development but should exclude contact sports that involve heavy strain on the joints.^[12]

CONCLUSION

The above case study underscores the importance of recognizing characteristics for EDS when evaluating adolescents with CDH (tension type headache and migraine). Along with the major manifestation of EDS, other signs and symptoms that characterize this disorder include musculoskeletal pain, fatigue, dizziness/vertigo, depression, and anxiety, which are often associated with CDH in adolescents. This case study reported on a 15-year-old with a 2-3-year history of chronic pain in terms of neck, back, and headache. She had a confirmed diagnosis for vasovagal syncope, depression, anxiety, and hypermobility when she presented for evaluation of headache. Once seen in an outpatient headache clinic, she was subsequently referred to genetics and the diagnosis for mild classic EDS was confirmed. A treatment plan was then developed that included therapies for classic EDS including hydrotherapy, initiation of Vitamin C, encouragement of good hydration and initiation of medication intervention for her depression and anxiety.

REFERENCES

1. Abu-Arafeh I, Razak S, Sivaraman B, Graham C. Prevalence of headache and migraine in children and adolescents: A systematic review of population-based studies. *Dev Med Child Neurol* 2010;52:1088-97.
2. Beighton P, De Paepe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: Revised nosology, Villefranche, 1997. Ehlers-Danlos National Foundation (USA) and Ehlers-Danlos Support Group (UK). *Am J Med Genet* 1998;77:31-7.
3. Byers P. Disorders of collagen biosynthesis and structure. In: Scriver CR., Beaudet AR, Sly WS, Valle D, editors. *The metabolic and molecular bases of inherited disease*. 2nd ed. Edinburgh: Churchill Livingstone; 2001. p. 1065-81.
4. Camerota F, Celletti C, Castori M, Grammatico P, Padua L. Neuropathic pain is a common feature in Ehlers-Danlos Syndrome. *J Pain Symptom Manage* 2010;41: e2-e4 [Epub ahead of print].
5. Castori M, Morlino S, Celletti C, Celli M, Morrone A, Colombi M, et al. Management of pain and fatigue in the joint hypermobility syndrome (a.k.a. Ehlers-Danlos syndrome, hypermobility type): Principles

- and proposal for a multidisciplinary approach. *Am J Med Genet A* 2012;158A:2055-70.
6. Di Palma PF, Cronin AH. Ehlers-Danlos syndrome: Correlation with headache disorders in a young woman. *J Headache Pain* 2005;6:474-5.
 7. Giunta C, Nuytinck L, Raghunath M, Hausser I, De Paepe A, Steinmann B. Homozygous Gly530Ser substitution in COL5A1 causes mild classical Ehlers-Danlos syndrome. *Am J Med Genet* 2002;109:284-90.
 8. Jacome DE. Headache in Ehlers-Danlos syndrome. *Cephalalgia* 1999;19:791-6.
 9. Karaa A, Stoler JM. Ehlers Danlos Syndrome: An unusual presentation you need to know about. *Case Rep Pediatr* 2013;2013:764659.
 10. Mack KJ, Johnson JN, Rowe PC. Orthostatic intolerance and the headache patient. *Semin Pediatr Neurol* 2010;17:109-16.
 11. Malfait F, Coucke P, Symoens S, Loeys B, Nuytinck L, De Paepe A. The molecular basis of classic Ehlers-Danlos syndrome: A comprehensive study of biochemical and molecular findings in 48 unrelated patients. *Hum Mutat* 2005;25:28-37.
 12. Malfait F, De Paepe A. The Ehlers-Danlos syndrome. *Adv Exp Med Biol* 2014;802:129-43.
 13. Malfait F, Wenstrup RJ, De Paepe A. Clinical and genetic aspects of Ehlers-Danlos syndrome, classic type. *Genet Med* 2010;12:597-605.
 14. Nyame YA, Ambrosy AP, Saps M, Adams PN, Dhroove GN, Suresh S. Recurrent headaches in children: An epidemiological survey of two middle schools in inner city Chicago. *Pain Pract* 2010;10:214-21.
 15. Pasquini M, Celletti C, Berardelli I, Roselli V, Mastroeni S, Castori M, et al. Unexpected association between joint hypermobility syndrome/ Ehlers-Danlos syndrome hypermobility type and obsessive-compulsive personality disorder. *Rheumatol Int* 2014;34:631-6.
 16. Rhee H, Miles MS, Halpern CT, Holditch-Davis D. Prevalence of recurrent physical symptoms in U.S. adolescents. *Pediatr Nurs* 2005;31:314-9, 350.
 17. Sacheti A, Szemere J, Bernstein B, Tafas T, Schechter N, Tsipouras P. Chronic pain is a manifestation of the Ehlers-Danlos syndrome. *J Pain Symptom Manage* 1997;14:88-93.
 18. Strine TW, Okoro CA, McGuire LC, Balluz LS. The associations among childhood headaches, emotional and behavioral difficulties, and health care use. *Pediatrics* 2006;117:1728-35.
 19. Whitelaw SE. Ehlers-Danlos Syndrome, classical type: Case management. *Pediatr Nurs* 2003;29:423-6.
 20. Zernikow B, Wager J, Hechler T, Hasan C, Rohr U, Dobe M, et al. Characteristics of highly impaired children with severe chronic pain: A 5-year retrospective study on 2249 pediatric pain patients. *BMC Pediatr* 2012;12:54.