Musculoskeletal Conditions in a Pediatric Population with Ehlers-Danlos Syndrome

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Objective To describe musculoskeletal conditions in children with Ehlers-Danlos syndrome (EDS).

Study design A retrospective medical record review was performed, which evaluated 205 patients with EDS (ages 6-19 years) seen in sports medicine or orthopedic clinic at a large pediatric hospital over a 5-year period.

Results Female (n = 147) and male (n = 57) patients were identified (mean age 12.7 years). The most common EDS subtype (55.6%) was hypermobility type. Patients had between 1 and 69 visits (median 4), and 764 diagnoses were recorded, most commonly laxity/instability, pain, subluxation, and scoliosis/spinal asymmetry. Nearly one-half of patients (46.8%) received a general diagnosis of pain because no more specific cause was identified, in addition to 8.3% who were diagnosed with chronic pain syndrome. The most common sites of presenting issue were knee (43.4%), back (32.2%), and shoulder (31.2%). Over three-fourths (77.1%) of patients had imaging. Most (88.1%) were prescribed physical therapy and/or other conservative measures, such as rest (40.5%), orthotics (35.6%), and medication (32.2%). Surgery was recommended to 28.8% of the study population.

Conclusions Many pediatric and adolescent patients with EDS experience joint pain, instability, and scoliosis, along with other musculoskeletal issues. Despite extensive workup, the etiology of pain may not be identified. Large numbers of office visits, imaging studies, treatment prescriptions, and specialist referrals indicate considerable use of medical resources and highlight a great need for injury prevention and additional study. *(J Pediatr 2017;181:261-6).*

Characteristics of Ehlers-Danlos syndrome (EDS), a group of connective tissue disorders, include joint hypermobility, skin hyperextensibility, and tissue fragility.[1,2] Multiple gene mutations are associated with EDS.[2-4] Six subtypes are currently recognized.[2] Genetic testing is currently available for the classical, arthrochalasia, kyphoscoliosis, dermatosparaxis, and vascular types. The molecular basis for the hypermobility form (Ehlers-Danlos syndrome hypermobility type [EDS-HT]) is poorly understood, and diagnosis is based on family history and clinical examination.[1] The classical and hypermobility types of EDS are believed to account for greater than 90% of cases,[5] and a preponderance of female patients has been reported, particularly in the hypermobility type.[6,7]

EDS-HT is the most prevalent form[5,6,8] and is diagnosed by clinical criteria.[1,2,4] Pain and joint complications are more commonly seen in female patients with EDS-HT than in male patients.[1] In addition to joint pain, women with EDS-HT have impaired muscle and physical function,[6] and significantly lower quality of life compared with age- and sex-matched healthy controls.[9] One study found that women with EDS-HT had worse physical, psychosocial, and overall function than women with rheumatoid arthritis, and similar physical and overall function to women with fibromyalgia.[10] Scheper et al[11] described the negative effects of general connective tissue laxity in children on motor development, proprioception, psychological function, and quality of life.

Much of the existing research on the musculoskeletal manifestations of EDS focuses on adults. This study was designed to describe and analyze the musculoskeletal issues that impact children with EDS, and to review the patterns of visits to sports medicine and orthopedics clinics over a 5-year period. We hypothesized that pediatric and adolescent patients with EDS would frequently experience instability and pain of multiple joints and that most patients would be treated with a combination of physical therapy and bracing, and surgical intervention would be less common.

Methods

The study was approved by the hospital's institutional review board. A computerized chart search was performed on all sports medicine and orthopedic clinics of a large academic pediatric medical center initially over a 10-year period (January

EDS	Ehlers-Danlos syndrome
EDS-HT	Ehlers-Danlos syndrome hypermobility type
MRI	Magnetic resonance imaging

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1, 2004, through December 31, 2013), using the key words "Ehlers," "Danlos," and "EDS." This search returned 3130 charts. Given the large number of charts, the timeframe was reduced to the most recent 5-year period (January 1, 2009-December 31, 2013), and the medical records were subsequently reviewed to identify those patients with EDS, between the ages of 6 and 19 years, who were seen in sports medicine or orthopedics clinic. Inclusion criteria included all patients who had a clear diagnosis of EDS noted in the medical record, either as part of the sports medicine or orthopedic notes or documented through the genetics department records. Exclusion criteria included patients with significant relevant comorbidities.

Two hundred nine unique patients were identified from the 5-year study period. Three patients were excluded from the study because of comorbid disease states that had a high likelihood of affecting presenting issues (Charcot-Marie-Tooth disease, Osteogenesis imperfecta, and Marfan syndrome). In addition, 1 patient originally diagnosed with EDS was later believed not to have the condition and was subsequently diagnosed with arterial tortuosity syndrome. For the remaining 205 patients, all visits to sports medicine or orthopedic clinics within the 5-year study period were evaluated. Data were extracted from the medical record and analyzed for descriptive statistics and risk factors, including age, sex, EDS subtype, sports participation, number of clinic visits per patient, body part(s) involved, imaging studies, diagnoses, additional consultations, and treatments prescribed.

For the purpose of this study, pain was used as a diagnosis only when it was explicitly listed in the medical record as a diagnosis without a more specific diagnosis or cause of the pain. Similarly, other general diagnoses, such as "soft tissue injury," were only used if they were the only diagnosis listed in the chart without more specific reference to a diagnosed injury or underlying cause of pain.

Each individual diagnosis, involved body part, specific type of imaging, particular referral, or prescribed treatment was only recorded once per patient, even if it applied multiple times. Therefore, the data represent the number of patients with each diagnosis, referral, or treatment. All statistical analyses were performed with SPSS v 23 (SPSS Inc, Chicago, Illinois).

Results

Two hundred five patients (148 female, 57 male) with a diagnosis of EDS seen in sports medicine or orthopedic clinic within the study time period (January 1, 2009-December 31, 2013) were included. The mean age at presentation was 12.7 ± 3.6 years (range 6-19 years). Over one-half of the patients had EDS-HT, and 30% did not have an EDS subtype specified in the clinical notes (Table I).

The knee was the most common site of the presenting problem, followed by back and shoulder. Female patients were more likely to be seen with back (37% vs 21%; $P = .034$) and hip (35% vs 9%; $P < .001$) issues than were male patients. No other significant relationship was noted between sex of the patient and location of presenting problem. Many patients were noted to have had injury or pain in multiple areas of the body (Table II). A total of 764 diagnoses were recorded. The average number of diagnoses per patient was 3.7 ± 3.1. On average, female patients had more diagnoses recorded than did male patients (4.2 vs 2.5; $P < .001$). The most frequent diagnoses were laxity/instability, pain, subluxation, and scoliosis/spinal asymmetry (Table III).

Thirty patients were diagnosed with dislocations, primarily involving the patella (17 patients) and shoulder (13 patients). In terms of fractures, a total of 30 patients were diagnosed with 56 traumatic fractures, stress fractures, or stress injuries. The majority of these fractures were treated conservatively without reduction or surgery. Five wrist fractures required closed reduction, and 1 wrist and 1 foot fracture required surgery. Seven spinal stress fractures were diagnosed.

For 96 patients, the general diagnosis of pain was recorded because no more specific diagnosis or explanation for symptoms was given in the medical record. Seventeen patients were given the specific diagnosis of a pain syndrome, such as chronic regional pain syndrome. Female patients were more likely to have tendinopathy (14% vs 2%; $P = .010$), impingement (13% vs 2%; $P = .017$), muscular weakness/deconditioning (9% vs 0%; $P = .021$), and contusion (8% vs 0%; $P = .022$) compared with male patients. Female patients were less likely to have pes planus (4% vs 12%; $P = .049$). There was a statistically significant association between EDS-HT and the diagnosis "sprain" ($P = .038$). No other diagnoses were significantly associated with an EDS subtype.

Table I. EDS type

Variables	Total		Male	Female
EDS type, N = 205	n	%	n	n
Hypermobile	114	55.6	30	84
Classical	20	9.8	4	16
Vascular	6	2.9	2	4
Kyphoscoliosis	2	1.0	1	1
Not specified	63	30.7	20	43
Total	205	100.0	57	148

Table II. Body sites involved by number and percentage of patients

Body sites	n	%
Knee	89	43.4
Back	66	32.2
Shoulder	64	31.2
Ankle	58	28.3
Hip	57	27.8
Foot/toe	50	24.4
Wrist	38	18.5
Hand/finger	33	16.1
Leg	14	6.8
Elbow	14	6.8
Neck	11	5.4
Clavicle	6	2.9
Head	5	2.4
Arm	2	1.0
Rib	2	1.0