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RESEARCH ARTICLE

A CASE OF EHLER DANLOS SYNDROME REVEALED BY POLYARTHRALGIA: CASE REPORT AND LITERATURE REVIEW

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Abstract

Ehlers-Danlos Syndrome (EDS), a disorder affecting connective tissue, can be incapacitating in certain instances. This disorder is marked by varying levels of skin hyperextensibility, joint hypermobility, and vascular fragility. These symptoms of EDS stem from abnormal collagen, particularly involving types I, III, and V collagen. Complications include musculoskeletal pain, dislocations, atrophic scars, easy bleeding, vessel or viscera rupture, obstetric complications, and severe scoliosis. Accurate identification of EDS patients is crucial to initiate proper treatment. Herein we report a 5-year-old male with polyarthralgia, skin desquamation, hyperhidrosis, recurrent oral aphthosis, and diffuse abdominal pain. Physical exam showed joint hypermobility (Beighton score 6/9), skin hyperelasticity, and blue sclera, leading to a diagnosis of Ehlers-Danlos syndrome. He is undergoing analgesic treatment and functional rehabilitation.

Introduction:-

Ehlers-Danlos syndrome (EDS) is a connective tissue disorder marked by joint hypermobility, skin hyperextensibility, atrophic scars, fragile skin, and easy bruising [1-3]. Named in 1949 after Danish dermatologist Edvard Ehlers [4] and French dermatologist Henri-Alexandre Danlos [5], EDS inheritance can be autosomal dominant, autosomal recessive, or X-linked [6]. The most prevalent types are I, II, and III. Types I and II are noted for joint and skin hypermobility, fragile skin, and atrophic scars, while type III is characterized by joint hypermobility, pain, and dislocations [7]. Classic EDS accounts for 50% to 90% of all cases 5,6, with a prevalence estimated at 1 in 20,000 [8]. The syndrome is likely underdiagnosed, making incidence estimates challenging [9].

Herein we report a 5-year-old male presenting with polyarthralgia, skin desquamation, hyperhidrosis, recurrent oral aphthosis, and diffuse abdominal pain. Physical examination revealed joint hypermobility (Beighton score 6/9), skin hyperelasticity, and blue sclera. Polyarthralgia can sometimes be a sign of Ehlers- Danlos syndrome, as seen in this case, leading to its diagnosis. The patient is receiving analgesic treatment and functional rehabilitation.

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Case Presentation

We report a 5-year-old child, the only child of non-consanguineous parents, who was admitted for polyarthralgia, with a history of a popliteal synovial cyst. The arthralgia is mechanical in nature, associated with mucocutaneous involvement: skin desquamation, hyperhidrosis with recurrent oral aphthosis, and diffuse abdominal pain. The condition evolves in flare-ups and remissions.

Physical examination revealed joint hypermobility with a Beighton score of 6/9 (dorsiflexion of the fingers over 90°, exaggerated thumb apposition to the forearm, and hyperextension of both elbows), skin hyperelasticity, and blue sclera (Figures 1, 2, 3 and 4).

Figure 1:- Physical examination revealing joint hypermobility of finger joints.

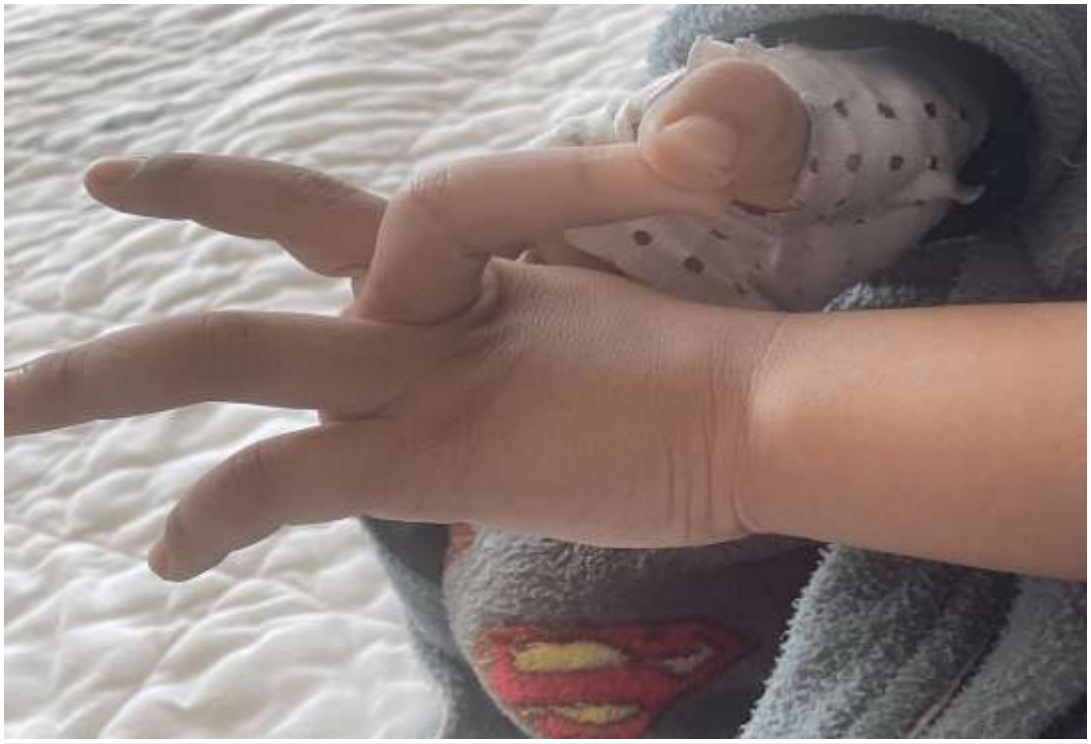

Figure 2:- Joint hypermobility in form of dorsiflexion of the fingers over90°.

Figure 3:- Physical examination revealing skin hyperelasticity.

Figure 4:- Blue sclera revealed by physical examination.

Examination of the parents revealed hypermobility of the tongue in the mother (Figure 5).

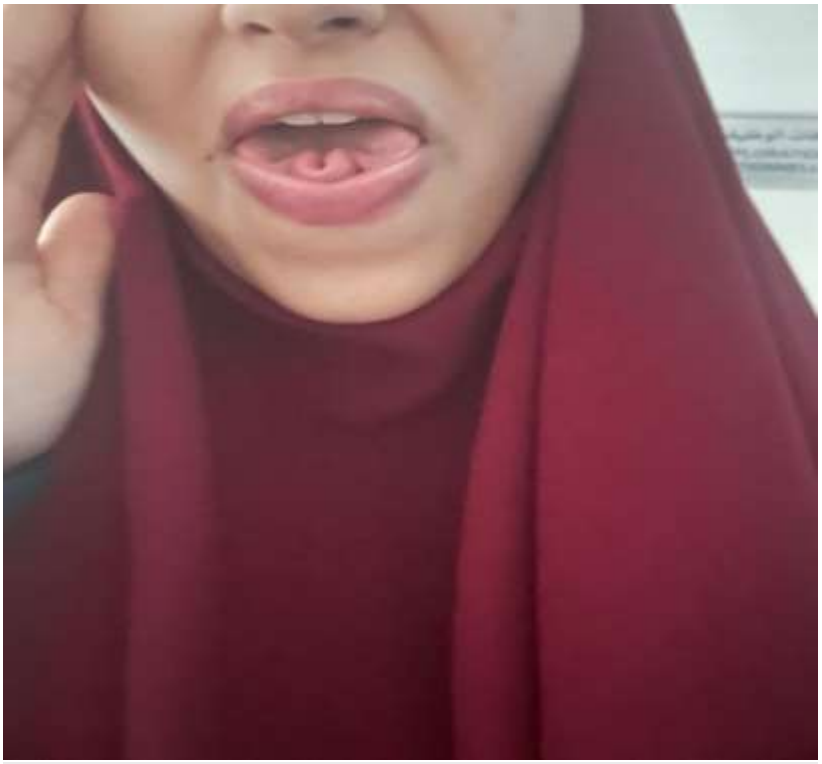

Figure 5:- Examination revealed hypermobility of the tongue in the mother.

Ehlers-Danlos syndrome was suspected based on the combination of clinical criteria: joint hypermobility with a Beighton score of 6/9, skin hyperelasticity, blue sclera, and similar findings in the mother, along with polyarthralgia, skin desquamation, recurrent oral aphthosis, chronic abdominal pain, and a history of synovial cysts. Ophthalmological examination was normal.

An echocardiogram showed an ascending aorta diameter of 19 mm, at the upper limit of normal, requiring cardiological follow-up (Figure 6).

Figure 6:- Echocardiogram showed an ascending aorta diameter of 19mm.

The patient is being treated with analgesics and functional rehabilitation.

Discussion:-

EDS is often attributed to mutations causing abnormal collagen, affecting collagen-rich tissues like skin, ligaments, joints, and vessels. Mutations in types I, III, and V collagen are common, each type associated with specific mutations [10].

In 1997, a revised classification was developed in Villefranche to refine the previous Berlin nosology for EDS, defining six basic types: classical, hypermobile, vascular, kyphoscoliosis, arthrochalasia, and dermatosparaxis. The classical and hypermobile types collectively account for over 90% of cases [11], but the most common type remains uncertain [12]. The vascular type is the third most common, affecting approximately 1 in 250,000 individuals [13]. Kyphoscoliosis, arthrochalasia, and dermatosparaxis types are rare, with approximately 30, 60, and 12 reported cases worldwide, respectively [13]. Other types of EDS are even rarer, often occurring in one to a few families. Classification into a specific type is based on major and minor criteria. Major criteria, such as skin involvement and generalized joint hypermobility, are more diagnostically specific as they are uncommon in other conditions and the general population. Minor criteria, such as recurrent dislocations, chronic pain, and positive family history, are less specific [9].

Pain is a frequent symptom linked to various forms of Ehlers-Danlos syndrome (EDS) [14], especially in classical and hypermobile types of EDS [9].

In 1994, Lumley et al. [15]. were pioneers in suggesting that chronic pain might significantly impact the quality of life for EDS patients. In addition, their study examined the psychosocial status of 48 individuals with different types of EDS. Voermans et al. [16]. conducted a study involving 273 patients with various forms of Ehlers-Danlos syndrome (EDS), including the classic, hypermobility, and vascular types. They found that severe pain, often linked to functional impairment, was a common result. The intensity of pain was associated with hypermobility, dislocations, and prior surgeries [15].

Clinically, recurrent joint pain is the most prevalent symptom of hypermobility EDS, as reflected in the application of the Brighton diagnostic criteria [17]. Diagnosis of hypermobility EDS can be made with either two major criteria or one major and two minor criteria, or with the presence of four minor criteria. Joint pain was reported in 88% of patients by Stanitski et al [18], with 61% experiencing limited walking. Voermans et al found pain in 90% of patients and functional impairment in 87%. This pain can result from hypermobility, dislocations, or past surgeries. For some, the pain is nociceptive, caused by ongoing stimulation of nociceptors and related to joint damage. However, for others, it is neuropathic, stemming from a primary lesion or dysfunction in the nervous system [20]. Patients with classical or hypermobility- type EDS have also been reported to develop complex regional pain syndrome [21].

Some other symptoms associated with EDS and its subtypes include muscle cramps [22,23], fibromyalgia [15], and neuropathic pain [16]. Our case shows that polyarthralgia can sometimes be a sign of Ehlers-Danlos syndrome, as seen in this case, leading to its diagnosis.

Chronic fatigue, dizziness, and depression have been key in confirming the diagnosis. Berglund et al. [24] reported high levels of anxiety and depression in a study of 365 adult EDS patients from the National Sweden Association.

Common issues in clinical practice include the lack of standardization for major symptoms like pain and connective tissue laxity, as well as the exclusion of other clinical signs [25]. Many patients with EDS are either undiagnosed or experience significant delays in diagnosis. It is crucial for clinicians to identify individuals with generalized ligamentous laxity who may need further evaluation. An accurate diagnosis of EDS facilitates proper screening for vascular complications, improves musculoskeletal management, and can help reduce risks such as wound dehiscence, aortic rupture, or organ rupture. The diagnosis of EDS typically begins with a thorough history and physical examination, focusing on symptoms such as joint issues, pain, easy bruising, and poor wound healing. Evaluating cardiovascular and family histories is important. The physical exam includes assessing skin condition, joint mobility, and cardiac health. Skin hyperextensibility and joint hypermobility are tested, and genetic consultation is recommended for certain cases. Confirmatory genetic testing is available for specific types, and ophthalmology and cardiology consultations may be needed based on symptoms [26]

Hypermobility in patients can stem from various conditions, leading to a broad range of differential diagnoses. These include benign joint hypermobility syndrome, Loeys-Dietz syndrome, and Marfan syndrome. Additionally, there are other disorders characterized by ligamentous laxity, such as osteogenesis imperfecta, skeletal dysplasias, developmental syndromes, pseudoxanthoma elasticum, and cutis laxa syndrome, which often exhibit more prominent symptoms than just joint hypermobility [27].

According to the natural history of EDS, pain is a variable symptom, with its impact influenced by individual adaptation strategies to manage it [13]. The absence of consensus on treatment or general treatment guidelines poses a problem [25].

Managing EDS can be challenging and significantly impact patients' lives. A multidisciplinary approach is essential, including mental health support to address declining psychological well-being. Patients value providers who engage them as partners in their care, listen to their findings, and connect them with support groups. Support resources such as the Ehlers-Danlos National Foundation and local

groups, as well as online sources like the National Library of Medicine, the Ehlers-Danlos Syndrome Network, and the Ehlers-Danlos National Foundation, can be invaluable [9].

Effective pain management is crucial, with anti-inflammatory treatments often effective for nociceptive pain, and antidepressants, antiepileptics, and opioids more suited for neuropathic pain [9]. Additionally, conventional therapies like phonophoresis and electric stimulation may be beneficial, and assistive devices could be necessary [18].

Conclusion:-

EDS is a connective tissue disorder characterized by skin hyperextensibility, ligamentous laxity, and vascular fragility. Several types are genetically linked, with mutations impacting collagen types I, II, and III, as well as tenascin X. Accurate diagnosis is the primary challenge in managing Ehlers-Danlos syndrome, a complex and multisystemic condition. Addressing clinical heterogeneity, disease classification, and ensuring adequate pain diagnosis and treatment are crucial aspects that require interdisciplinary cooperation. Our reported case shows that polyarthralgia can sometimes be a sign of Ehlers-Danlos syndrome, as seen in this case, leading to its diagnosis. The patient is receiving analgesic treatment and functional rehabilitation.

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