ARCHIVES OF Health Sciences

RELATO DE CASO
ISSN 2318-3691

DOI: 10.17696/2318-3691.28.1.2021.1969

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Contribuição dos autores: NML: delineamento do estudo, elaboração do manuscrito, redação do manuscrito, discussão dos achados e etapas de execução. CBV: etapas de execução e discussão dos achados.
GMAF: discussão dos achados e etapas de execução.
MML: delineamento do estudo, elaboração do manuscrito, discussão dos achados e etapas de execução. MPM: delineamento do estudo, elaboração do manuscrito, redação do manuscrito, discussão dos achados e etapas de execução.

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Conflito de interesses: Não

Financiamento: Recursos próprios

Recebido: 23/07/2020
Aprovado: 03/08/2021

Transtorno do espectro do autismo e síndrome de Ehlers-Danlos - tipo hipermobilidade: um relato de caso

Autism spectrum disorder and Ehlers-Danlos syndrome - hypermobility type: a case report

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RESUMO

Introdução: O Transtorno do Espectro do Autismo (TEA) e a Síndrome de Ehlers-Danlos - Tipo Hipermobilidade (SED-TH), podem ocorrer concomitantemente, com sobreposição das características das duas condições. O diagnóstico precoce contribui na prevenção do sofrimento e de lesões em pacientes com ambas as condições. **Objetivo:** Relatar o caso de um adolescente com autismo grave e SED-TH, com manifestações musculoesqueléticas e extra-esqueléticas, e como isso pode interferir na vida do paciente e de sua família. **Relato de caso:** Este relato mostra a história clínica dos sinais e sintomas da SED-TH, evidenciados principalmente por dor generalizada, fadiga, luxações e incapacidade motora, devido à Hipermobilidade Articular (HA). Essas manifestações podem não ser percebidas por familiares e profissionais de saúde, devido à incapacidade comunicativa que faz parte das manifestações relacionadas ao TEA. **Conclusão:** A identificação precoce de sinais e sintomas de SED-TH na infância poderia possibilitar uma melhor compreensão de suas manifestações em pacientes com TEA. Possibilitaria também a prevenção de luxações articulares e proposição de um design ergonômico adequado do ambiente doméstico para minimizar o sofrimento do paciente e sua família.

Palavras-Chave: Transtorno do Espectro Autista; SÍndrome de Ehlers-Danlos; Instabilidade Articular; Dor.

ABSTRACT

Introduction: *Autism Spectrum Disorder (ASD) and Ehlers-Danlos Syndrome – Hypermobility type (EDS-HT) can occur concomitantly, with the overlap of the characteristics of both conditions. Early diagnosis helps prevent suffering and injuries in patients with these conditions.* ***Objective:*** *To report the case of an adolescent with severe autism and EDS-HT, with musculoskeletal and extra-skeletal manifestations, and how it may affect the patient´s life of and his family.* ***Case Report:*** *This report shows the clinical history of the signs and symptoms of EDS-HT, mainly evidenced by generalized pain, fatigue, dislocations and motor disability, due to Joint Hypermobility (JH). These manifestations may not be noticed by the family members and health professionals, due to the communicative impairment that is part of the manifestations related to ASD.* ***Conclusion:*** *The early identification of signs and symptoms of EDS-HT in childhood could enable a better understanding of its manifestations in patients with ASD. It also enables the prevention of joint dislocations and the proposition of a proper ergonomic design for the home environment to minimize suffering of the patient and his family.*

Keywords: *Autism Spectrum Disorder; Ehlers-Danlos Syndrome; Joint Instability; Pain.*

INTRODUCTION

Autism Spectrum Disorder (ASD) is a group of disorders characterized by a variety of signs and symptoms, such as difficulties related to social interaction and communication skills, as well as uncommon repetitive behavior[1]. Sensory atypicality are evident throughout the entire spectrum from childhood to adulthood, although evidence suggests that such atypicality may diminish with age. There is a consensus that autistic individuals are susceptible to experiencing an impact on the development of a gamut of skills, including social and cognitive skills, due to the greater evasion of social stimuli[2].

The Ehlers-Danlos Syndromes (EDS) is a group of genetic connective tissue disorders that results from the synthesis of defective proteins. There are several subtypes, but common characteristics are generalized tissue frailty, an inherent tendency toward mechanical tissue failure and joint hypermobility (JH). The latter aspect is an abnormally large range of motion of the joints, which is evaluated using the Beighton score[3]. The most common subtype is the hypermobility type (EDS-HT) and has systemic manifestations. Pain and fatigue are the most common complaints in the daily clinical practice[4]. According to Baeza-Velasco et al. (2016)[5], this subtype is reported in a range of 45% cases of EDS-HT in England[6] and 39% in Chile[7], and the characteristic of JH alone is identified between 10% to 30% of the population worldwide[8]. In

Brazil, in a study with 1749 children aged 7 to 12 years, 41% were identified with JH, suggestive of progressing to disorders associated with the JH[9]. However, EDS-HT is an under-recognized condition, which causes considerable delay in the diagnosis, even though cases of concomitant EDS-HT and ASD are found in the literature. In a population-based study, Cederlöf et al. (2016)[10] reported records of associations between EDS and psychiatric disorders, including ASD.

The ASD and EDS-HT are two conditions with a clinical spectrum that undergo similar phenotypic characteristics. However, there is a lack of awareness on this subject, as demonstrated by the scarcity of references in the literature addressing ASD and EDS. A study presented by Shetreat-Klein et al.[11] reports greater joint mobility in children with ASD than healthy controls as well as greater frequencies of hypermobile joints and symptoms of autonomic dysfunction in ASD adults in comparison to individuals with other psychiatric conditions and healthy controls. Moreover, studies involving a genetic evaluation of children with delayed global development suggest connections among ASD, JH and Synaptic Ras GTPase-activating protein 1 (SYNGAP1)[12]. The SYNGAP1 is a downstream component that downregulates the activation of enzymes and receptors in transit to the post-synaptic excitatory membrane; which constitute a comorbidity in children with ASD[13].

In this context, an adolescent diagnosed with ASD and EDS-HT was reported to show how the characteristic of JH can aggravate the clinical condition of a patient with ASD, through its manifestations of musculoskeletal and extra-skeletal signs and symptoms, and how it can interfere with the individual's life and the family members.

METHODS

The analysis of the case described herein comprises a detailed clinical history, passive physical examination and observation, parental reports, complementary exams, an analysis of generalized hypermobile joints using the Beighton score and analysis of the diagnostic criteria[14]for the identification of EDS-HT, since new classification had not been provided at the time. However, a new international classification was published for EDS[15] , with new diagnostic criteria subsequent to this study, in 2017.

This paper reports a case of concomitant ASD and EDS-HT and discusses diagnostic methods and prevalence. A bibliographic survey of international journals was carried out in Medline, PubMed, SciELO and Cochrane Library databases using the keywords: Autism spectrum disorder, Ehlers-Danlos syndromes, Joint hypermobility, SYNGAP 1 and pain.

From the scientific literature, 17 articles were used; 16 in English and one in Spanish; 70% of the articles were published in the last five years.

CASE REPORT

White male, 18 years of age, born through cesarean birth with normal gestation, but interrupted at eight months due to considerable reduction in amniotic fluid. With 49 cm in length at birth; currently, height: 1.75 m; body weight: 47 kg; arm span: 174 cm; large hands and feet, with arachnoid appearance. Diagnosis was carried out by a multidisciplinary team and called Severe Autism, at the age of three, after excluding differential diagnoses and identifying pronounced signs of absence of social interaction, repetitive patterns with the hands (hands in flaping), interests restricted by movement of water and moving equipment.

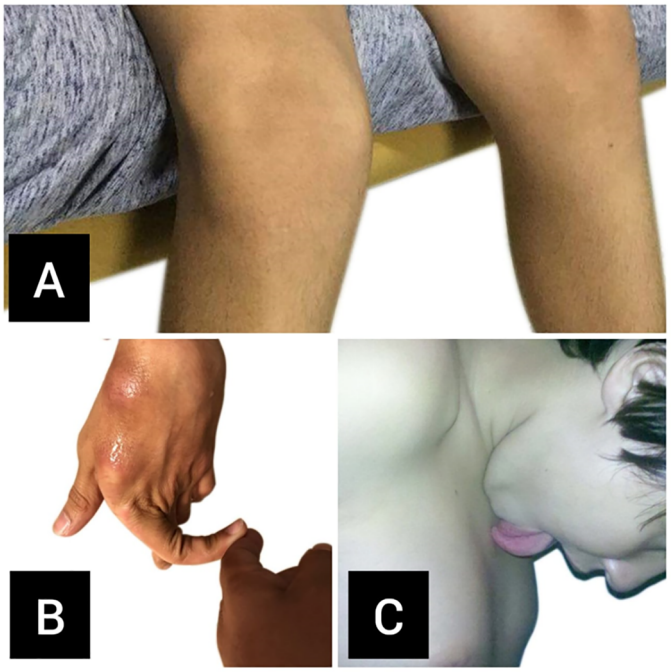

Figure 1. Joint dislocation in the knees (A). Joint hypermobility in the fingers of the hand (B). Hyperflexion of the head due to the cervical joint hypermobility (C).

Diagnosis of EDS-HT in 2014, with whole exome sequencing in 2015, in which SYNGAP1 was identified. Manifestations of pain with the identification of the location began at 14 years of age and the characteristic of JH was identified in 2014. The patient currently walks (monitored by parents) with forward lean of the head and pelvic retroversion. During gait, the lower limbs are in internal rotation, feet in inversion, elbows flexed and wrists in hyperextension at 90º, associated with frequent episodes of joint dislocations of the knees (Fig. 1A), hips and wrists, followed by manifestations of pain and crying, with hands placed on the painful region and an antalgic posture. He sits in "W" position; has plano-valgus foot, frequent, generalized joint crepitus, with visible hypermobile joints in hands.

Neuropsychomotor development was normal until seven months of age, sat in "W" position and crawled in sitting position. The patient smiled socially, ate regularly and adequately for age, had normal grip strength, lifted food to mouth, handled and played with toys. At seven months of age, he exhibited generalized muscle hypotonia after a fever of unknown etiology. Achieved independent gait at four years of age, staggering and "dragging" one leg. At eight years of age, he climbed stairs without assistance.

At 12 months of age, the patient demonstrated behavior indicating pain in the lower limbs, accompanied by crying and indication of the location of the site by placing pressure with the hands, predominantly on the knees and in the gluteus region. Pain currently occurs in lumbosacral region and temporomandibular joints (TMJ). Debilitating manifestations of pain along spinal column occurred weekly. Debilitating dislocations of knees and hips occurred seven or more times a day. Spontaneous bruising emerged at 12 months of age, increased in frequency and in different regions of the body, predominantly the lower limbs and left hip (specifically in the gluteus region and calves). Dislocations began at 13 years of age, accompanied by crying and screaming, occurring exclusively in knees and ankles up to 2016 and subsequently in hip, TMJs and, also, in fingers of the hands (Fig. 1B), accompanied by pain, frequent audible joint crepitus with functional disability; currently, the dislocations occur predominantly in hip and TMJs more sporadically, but remain

debilitating. Frequency of dislocations increased during period of growth spurt, along with debilitating manifestations of pain while walking, with negative impact on activities of daily living. Patient demonstrates characteristic behavior of fatigue when sits down abruptly, but without the manifestation of characteristics suggestive of pain. He exhibits highly frequent signs of synovitis in knees and has diagnosis of bilateral femoropatellar chondromalacia, which is greater on right side. Sleep disorder, agitated sleep with screaming that is difficult to control. The patient exhibits signs of allergy on skin, predominantly in flexor region of elbows and hands. After acute disability at 14 years of age, he was unable to walk for six months due to temporary loss of motricity in lower limbs, supposedly due to spondylolisthesis, during hyperflexion of the head by JH in the cervical region (Fig. 1C); regained locomotion in this year with no other sequalae. At 15 years of age, lost consciousness after complete flexion of head and placing tongue on thorax. Beginning with growth spurt at 13 years of age, manifestations of pain, bruising and joint dislocations increased in frequency in different regions of the body; apparent manifestation of severe bruxism.

Currently, the patient has independent gait under the supervision and protective support of parents (permanently monitored). He exhibits rectification of physiological curves of the spine, with postural and functional deformities of the hands and feet (plano-valgus, inverted feet), valgus knees and pelvic retroversion. Hands and feet have hypermobile joints with extreme ranges of motion; deformities and characteristics of arachnodactyly in feet and hands. Crepitus in several joints, but predominantly in knees and wrists. Muscle strength is apparently normal and suggestive of grades 3 to 5, with lower degrees of strength in elbows, hands and feet. Muscle tone appears impaired, with significant hypotrophy, motricity and joint ranges maintained at or beyond extremes. Musculoskeletal palpation exam hindered due to characteristics related to ASD. Hand posture with hyperflexion of wrist, passive apposition of thumb is complete upon touching the flexor region of the forearm, bilaterally; hyperextension of fifth finger is 120º, totalizing Beighton score of four points. Hypermobile hip, knees, angles and toes due to numerous episodes of dislocation presumed to cause sequelae.

DISCUSSION

Concomitant ASD symptoms and EDS-HT were described by Baeza-Velasco et al. (2016)[5], which are in agreement with the present study. Since pain may be overlooked in ASD, especially in patients without functional language, to be awareness of the association between ASD and EDS-HT may be useful to identify who among the ASD patients may suffer from chronic pain[16]. Preventive measures should be taken through constant manifestations of pain, fatigue, joint dislocations, anxiety and sleep disorders in children and adolescents with JH Fig. 1A.

Such care did not occur in the present case due to unawareness with regard to joint instability stemming from hypermobile joints. There are records of debilitating pain manifested by antalgic posture and crying.

In the present case, the parental reports and results of the analyses demonstrated a loss of functional health of the locomotion system and delayed motor development[11]. In this context, the identification of children and adolescents with hypermobile joints and other characteristics is extremely important for the establishment of early intervention Fig. 1A.

CONCLUSION

The analysis based on the clinical history obtained from the parents, observations, physical examination and the application of the diagnostic criteria revealed the characteristics of hypermobile joints, generalized pain, signs of fatigue and joint dislocations in different regions of the body. Thus, in addition to diagnosis of ASD, the patient has EDS-HT, which suggests suffering due to pain and the acquisition of physical disability, which increases the suffering and anguish of the family. The early identification of signs and symptoms of EDS-HT in childhood could enable a better understanding of the manifestations associated with ASD, the prevention of joint dislocations and a proper ergonomic design of the home environment to minimize suffering on the part of the patient and family. Finally, there is a need for population-based and longitudinal studies involving patients with a diagnosis of ASD to enable the earliest possible identification of the hypermobility type of EDS as well as a better understanding of the possible association between these conditions.

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