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Insomnia due to a dislocation storm in hypermobile Ehlers-Danlos syndrome with small fibre neuropathy and recurrent syncope

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Abstract

The aim of this work was to report on a patient with hypermobile Ehlers-Danlos Syndrome (EDS) with SFN in whom frequent dislocations during sleep led to sleep deprivation. The patient is a 19-year-old female with hypermobile EDS manifested by frequent dislocations of large joints and Small Fiber Neuropathy (SFN) presenting as recurrent syncope. The dislocations occurred spontaneously or triggered by voluntary or involuntary movements with such frequency, even during the night, that sleep was disturbed. The maximum sleep duration was between 4 and 5 hours. Bedding, analgesics, muscle relaxants and physiotherapy only marginally improved the pain and discomfort caused by the dislocations. This case demonstrates that hypermobile EDS can manifest phenotypically with insomnia due to pain and discomfort from frequent dislocations during the night. Patients with hypermobile EDS should undergo polysomnography to determine the cause of the sleep disturbance and initiate the most appropriate treatment for insomnia in a timely manner.

Key Words: Ehlers-Danlos syndrome, hypermotility, luxations, syncopes, small fibre neuropathy.

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Ehlers-Danlos Syndrome (EDS) is an inherited multisystem disorder caused by mutations in >20 genes, most commonly in COL5A1 or COL5A2.[1] Phenotypically, EDS manifests as musculocontractual EDS or EDS with hypermobile, weak joints prone to subluxation or dislocation, causing discomfort, pain and damage to joints and surrounding structures.[2] Other systems potentially affected in EDS include the skin (hyperlaxity, impaired scarring), heart (valve abnormalities), arteries (aortic aneurysm) and peripheral nerves (polyneuropathy, small fiber neuropathy, SFN).[3] SFN occurs particularly in the hypermobile type of EDS.[4,5] Hypermobile EDS with SFN and frequent dislocations leading to sleep disturbances have not been reported to date.

Case Report

The patient is a 19-year-old woman, 170.5 cm tall, weighing 62 kg, who was already conspicuous as a child for dizziness, repeated falls, joint hypermotility and a first hip dislocation. In addition, she had had repeated falls and syncope since the age of 10. Nevertheless, she regularly practiced kickboxing. The hypermotility of her joints allowed her to assume unusual positions, like rubber people. From the age of 11 to 12, these symptoms worsened and she developed recurrent dislocations and subluxations several times a day, especially of the large joints (e.g. shoulder, hip, kneecap, elbow, temporomandibular joint), as well as syncope 1-2 times a week. Even minimal passive or active movements could lead to dislocation of the joints, so that the voluntary or involuntary turning of her body before or during sleep led to dislocations several times during the night. As these dislocations were associated with pain and discomfort, sleep disturbance occurred in the sense of phase sleep with a maximum sleep duration of 4-5 hours per night. As the family history was positive for hypermobility in the mother, brother, maternal grandmother, all aunts and uncles, paternal cousins, paternal grandmother and one paternal uncle, EDS was suspected. However, genetic testing for the most common variants associated with EDS was negative.

In addition, her medical history was positive for attention deficit hyperactivity disorder (ADHD), an intra-articular ganglion in the left ankle, and allergic asthma since the age of 13. At the age of 16, she underwent surgery for a torn labrum using SLAP and Bankert and a pushlock anchor on her right shoulder. As the follow-up MRI of the right shoulder at the age of 17 showed a recurrent lesion of the ventro-caudal labrum, bone marrow edema of the humeral head and a Hill-Sachs dent (Figure 1), a second arthroscopic Bankert and remplissage repair with pelvic chip and arthrex

fibretape-cerclages was performed at the age of 18. Postoperatively, she complained of permanent right-sided hypoesthesia in the buttocks, lower abdominal quadrant, groin, and anterior and medial thigh, prompting referral to the neurologist.

The clinical neurological examination revealed myopia (3.5 diopters), a high arched palate, reduced tendon reflexes in the upper limbs, hypoesthesia in the right groin and medial thigh area, reduced patellar tendon reflexes, hypoesthesia in the left instep area, dizziness after standing up and unsteadiness with a tendency to fall on the Unterberger test, Romberg test and line and blind gait. The sensory disturbances were attributed to previous operations. The Holter ECG was normal. Echocardiography showed a hypermobile atrial septum and an open foramen ovale of 5 mm. The X-ray of the cervical spine showed only an extensor deformity. The visual evoked potentials showed normal latencies and amplitudes on both sides. Electroencephalography (EEG) was inconclusive. Nerve conduction studies were non-informative. Doppler sonography of the lower limbs and oscillography as well as duplex sonography of the aorta were normal. Postural Tachycardia Syndrome (POTS) was diagnosed by tilt table examination. She was taking only the pill regularly. She was registered for a polysomnography.

Discussion

The case presented is of interest due to hypermobile EDS and SFN, which was frequently complicated by syncope and spontaneous and induced recurrent dislocations/subluxations of large joints even during sleep, leading to chronic sleep deprivation due to concomitant pain and discomfort. Sleep in EDS may also be disturbed by Ob-

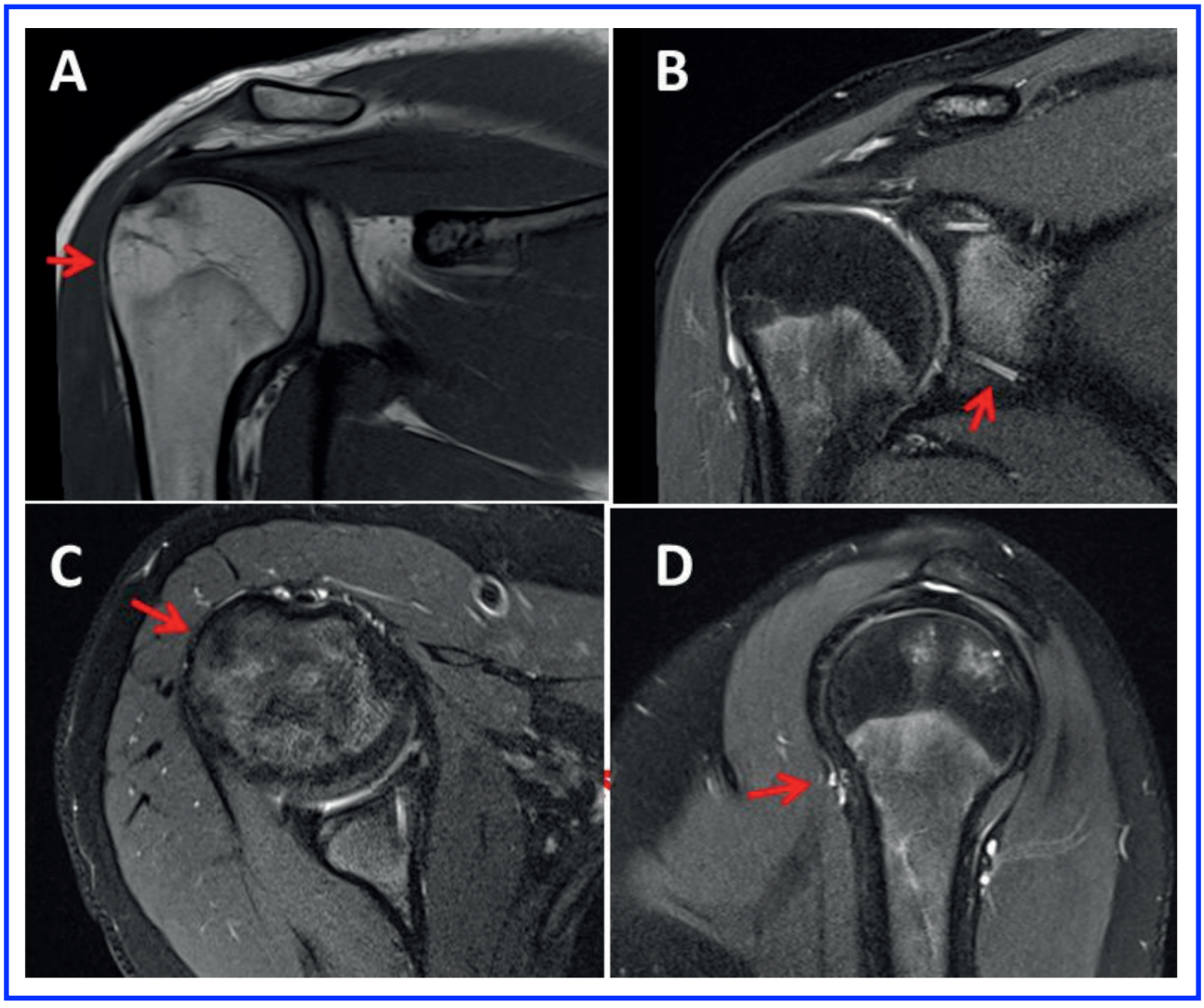

Figure 1. *Postoperative condition with multiple drill canals in the caudal, ventral and superior glenoid (panel B), striated signal alteration of the ventro-caudal labrum (panel C), patchy bone marrow edema centrally in the humeral head (panels C and D), and small Hill-Sachs dents (panel A)*

structive Sleep Apnea Syndrome (OSAS), which did not occur in the index patient but has been repeatedly reported in EDS.[6] Narcolepsy was even reported in a single patient with EDS.[7] In a meta-analysis of the prevalence of OSAS in patients with EDS or Marfan Syndrome (MAS), the prevalence of SAS was almost 50% in 13 included studies.[8] The prevalence of OSAS was higher in MFS patients than in EDS patients. OSAS was also found in 42% in a study of 24 pediatric patients with EDS.[9] EDS patients had lower scores on most of the Child Health Questionnaire (CHQ) scales and higher scores on Sleep-Related Breathing Disorders (SRBD) and the Epworth Sleepiness Scale (ESS) than control subjects.[9] It was concluded that OSAS is a previously underestimated EDS-related complication that increases the burden of disease.[9] However, in a study of 56 patients with hypermobile EDS, insomnia was found in only 22%, OSAS in 26%, periodic limb movement disorders in 17% and hypersomnia in 15% of patients.[10] Sixty-five percent of these patients required pharmacologic treatment for the sleep disorder and 29% were referred to behavioral sleep medicine.[10] Two patients with OSAS required continuous positive airway pressure.[10] PSQ, ESS and PedsQl scores improved significantly under these treatments.[10] In a prospective parallel study of 100 EDS patients, the prevalence of OSAS was 32%, daytime sleepiness was frequent, and quality of life was impaired.[11] It was found that the prevalence of OSAS is increased in EDS patients and that OSAS is associated with fatigue and excessive daytime sleepiness.[11]

Although the index patient did not have OSAS, she also reported chronic fatigue and daytime sleepiness. Whether SFN contributed to the sleep disturbance in the index patient remains speculative, but it is conceivable that the wake-night rhythm is strongly dependent on the ballance between the sympathetic and parasympathetic nervous system.[12] The extent to which ADHD contributed to sleep deprivation in the index patient also remains speculative, but since the patient never required pharmacologic treatment for ADHD, it is unlikely to have caused the sleep disorder alone.

In summary, this case shows that hypermobile EDS can manifest phenotypically with insomnia due to "stormy" dislocations and that SFN is responsible for the habitual syncope. Patients with hypermobile EDS should undergo polysomnography to assess the cause of the sleep disorder and initiate the most appropriate treatment for insomnia.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interst

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Availability of supporting data

Data supporting the results are available from the corresponding author.

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