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CLINICAL CASE REPORT

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Ehlers–Danlos syndrome in a young woman with anorexia nervosa and complex somatic symptoms

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Abstract

The Ehler–Danlos syndromes (EDS) are a group of clinically heterogeneous connective tissue disorders characterized by joint hypermobility, hyperextensibility of the skin, and a general connective tissue fragility that can induce symptoms from multiple organ systems. We present a case of comorbid anorexia nervosa and EDS in a 23-year old woman with a multitude of somatic symptoms that were initially attributed to the eating disorder but that were likely caused by the underlying EDS. Various EDS symptoms, such as gastrointestinal complaints, smell and taste abnormalities, and altered somatosensory awareness may resemble or mask an underlying eating disorder, and vice versa. Because of the large clinical heterogeneity, correctly identifying symptoms of EDS presents a challenge for clinicians, who should be aware of this group of underdiagnosed and potentially serious syndromes. The Beighton Hypermobility Score is an easily applicable screening instrument in assessing potential EDS in patients with joint hypermobility.

KEYWORDS

anorexia nervosa, connective tissue diseases, comorbidity, eating disorders, Ehlers–Danlos syndrome, joint hypermobility

1 | INTRODUCTION

The Ehlers–Danlos syndromes (EDS) are a group of genetically heterogeneous connective tissue disorders with joint hypermobility, hyperextensibility of the skin, and general connective tissue fragility as clinical hallmarks. Thirteen EDS subtypes are recognized (Malfait et al., 2017), each with various additional symptoms, such as atrophic scarring, easy bruising, muscle hypotonia, early onset kyphoscoliosis, osteopenia, blue sclerae, progressive cardiac-valvular problems, etc. The spectrum of joint hypermobility ranges from asymptomatic conditions to severe disabling symptoms. To be classified as a case of the hypermobile EDS subtype (hEDS), further symptom prerequisites must be fulfilled, such as the presence of musculoskeletal pain, recurrent joint dislocations, rectal or uterine prolapse, and mitral valve prolapse (Castori et al., 2017). There is no cure for EDS; treatment focuses on symptom management and prevention of complications through physiotherapy and pain medication.

We report a case of EDS in a young woman with anorexia nervosa (AN) presenting with various EDS-related somatic symptoms that had previously been attributed primarily to her eating disorder. To the best of our knowledge, ours is the first case report that examines the diagnostically challenging overlap of symptomatology in comorbid AN and EDS. There are a few published reports of severe weight loss due to disordered eating in EDS (Baeza-Velasco, den Bossche, Grossin, & Hamonet, 2016; Zarate et al., 2010); however, they have mainly focused on the risk of wrongfully attributing such weight loss to AN. A case of pneumomediastinum after screaming intensively during a rock music performance in a patient with AN and EDS has been described (Miles, Robinson, & Miles, 2007); however, the focus in that report was solely on the possible causes of pneumatosis and the implications of potential symptom overlap were not discussed. Finally, eating disorders have occasionally been described in other connective tissue disorders, such as osteogenesis imperfecta or CREST syndrome (Kaplan & Katz, 1992).

2 | CASE REPORT

A 23-year-old woman, born in a South-East Asian country, with a 12-year history of AN (restrictive subtype) had undergone specialist treatment in various settings for the past 8 years. She had recently been an inpatient at a specialist hospital ward for eating disorders treatment for 3 months, during which time her body mass index (BMI) had increased

TABLE 1 The beighton hypermobility score

Maneuver	Score
Passive dorsiflexion of the little fingers beyond 90°	
Right	1
Left	1
Passive apposition of the thumbs to the flexor aspects of the forearms	
Right	1
Left	1
Hyperextension of the elbows beyond 10°	
Right	1
Left	1
Hyperextension of the knees beyond 10°	
Right	1
Left	1
Forward flexion of the trunk, with knees straight, so that the palms of the hands rest easily on the floor	1
Maximum score	9

from just below 17 to 19.7. Upon discharge, she entered intensive day treatment at our clinic. The clinical picture was marked by a strong fear of fat-containing foods, so severe that she also reported washing herself meticulously with dish soap to remove fat from her skin, afraid that it would otherwise induce weight gain. Besides intensive physical exercise, there were no compensatory behaviors.

Various somatic conditions contributed to a complex clinical picture. The disordered eating was complicated by numerous food allergies (peanuts, eggs, shellfish, grains, etc.). She had also suffered from various recurrent gastrointestinal complaints, such as diffuse pains, bloating, and nausea, for about 10 years. An appendectomy had been performed the year before. She reported general joint hypermobility, a tendency to bruise easily, joint pain, recurrent patellar and acromioclavicular dislocation, and lumbar lordosis. Additionally, she had a history of severe bilateral leg pain, which had been diagnosed as chronic compartment syndrome. There was also a history of intermittent tachycardia and syncope. A 48 h electrocardiogram had been normal while a tilt table test showed postural hypotension but no arrhythmia. Notably, most of these symptoms had been the focus of various clinical examinations, but since no definitive pathology was found the gastrointestinal and cardiac symptoms as well as a persistent fatigue, muscle cramps, and joint pain had for several years been attributed primarily to AN.

The patient underwent 3 months of intensive day treatment based on an enhanced cognitive behavioral therapy model and an additional 6 months of outpatient follow-up. Notably, treatment was complicated by the fact that she had to be hospitalized briefly on two occasions, because of an anaphylactic reaction and because her appendectomy scar suddenly fissured. In spite of this, she was able to engage in treatment and achieved overall healthy eating patterns, maintained a normal weight, displayed enhanced body esteem, and resumed social functioning. However, the AN going into remission did not ameliorate the musculoskeletal, gastrointestinal, and cardiac symptoms.

Towards the end of the follow-up period, the patient finally sought a rheumatologist. Here, in addition to the aforementioned symptoms, she reported a history of sprained ankles and wrists and always being very agile and performing yoga end poses with ease. Her skin was thin, atopic and bruised easily; furthermore, her gingiva often bled when she brushed her teeth. In addition to the appendectomy scar fissure described above, an earlier tendency of breaking skin sutures was noted and several atrophic scars were seen upon examination. She had previously used braces because of an overbite and had four teeth removed; notably, dental crowding and a high and narrow palate are diagnostic criteria of hEDS. She also reported poor previous effect of local anesthetics. She scored 6 out of 9 on the Beighton Hypermobility Score (see Table 1), a diagnostic rating scale measuring joint hypermobility where values $\geq$5 are usually considered as potentially pathological. Based on overall history and findings, she was diagnosed with hEDS. Echocardiography revealed no valvular manifestations of EDS and an ultrasound of the kidneys showed no signs of renal engagement.

The patient received a knee orthosis and was offered specialized physiotherapy. Her general practitioner continued the efforts to optimize pain medication. However, because of onset of nausea, involuntary vomiting, dysphagia, and weight loss the patient underwent gastroscopy whereupon a relatively large hiatal hernia and mild esophagitis were found. She contacted our clinic again 6 months after completing outpatient follow-up, worried that these new symptoms were going to cause a relapse into AN. At this point, however, there was no reoccurrence of cognitive restraint or weight phobia. Over the next couple of months, the nausea and gastrointestinal discomfort escalated further to the point where the patient found it almost impossible to eat. Her BMI dropped to 17.4, but she continued to deny the presence of any AN-related cognitions. Meclizine and high doses of ondansetron were prescribed with limited effect. A consultant gastroenterologist concluded that the escalating gastrointestinal symptoms were primarily due to EDS, possibly aggravated by opioid medication against EDS-related pain. For lack of other options it was decided that continuous nasogastric feeding would be initiated in order to reduce symptoms and prevent further weight loss; however, this did not lead to symptom remission and instead a percutaneous endoscopic gastrostomy was performed and a jejunal extension tube was administered. Despite these serious gastrointestinal symptoms, the patient still displayed no cognitive restraint at a follow-up appointment at our clinic 16 months after completing day treatment.

3 | DISCUSSION

Because of the large clinical heterogeneity, correctly identifying symptoms of EDS presents a challenge for clinicians. Patients have described a delay between first symptoms and a correct EDS diagnosis of 14 years on average; for patients with psychiatric comorbidity, this delay was 22 years (Kole & Faurisson, 2009). In the case reported here, numerous symptoms commonly seen in EDS had for several years been attributed primarily to AN. It may also not be obvious that such

phenomena as easy bruising, dental crowding, or poor effect of local anesthetics (Hakim, Grahame, Norris, & Hopper, 2005) could point to a systemic connective tissue syndrome.

Gastrointestinal symptoms are very common in patients with EDS, who frequently meet diagnostic criteria for functional gastrointestinal disorders (Castori, Morlino, Pascolini, Blundo, & Grammatico, 2015; Fikree, Chelimsky, Collins, Kovacic, & Aziz, 2017; Zarate et al., 2010). Additionally, there is some evidence that hiatal hernia and esophagitis are more common in patients with EDS, and nausea and vomiting are often reported (Nelson et al., 2015). The clinical picture in EDS is often also complicated by dysphagia, fragility of the oral mucosa, and smell and taste abnormalities, which can lead to food selectivity and patterns of disordered eating (Bulbena et al., 2017). Although the pathogenesis is largely unknown, dysautonomy and capillary fragility have been suggested as important factors behind functional gastrointestinal manifestations and peritoneal ligamentous laxity and increased compliance of the hollow viscera may contribute to structural manifestations (Castori, Morlino, Pascolini, Blundo, & Grammatico, 2015). Interestingly, a study on gastrointestinal symptoms in EDS highlights the fact that while several components of the gut wall, such as the microbiota, mucosa, and interactions between neural and immune system, have been investigated, there has been little focus on the complex connective tissue matrix in which these structures are embedded (Zarate et al., 2010). This could prove to be an area of interest in eating disorder research as well. In eating disorders, functional gastrointestinal symptoms are frequently reported by patients (Norris et al., 2016) and may be temporarily exacerbated during treatment. Other gastrointestinal complications to AN, such as delayed gastric emptying or superior mesenteric artery syndrome, also typically cause symptoms that may be difficult to distinguish from gastrointestinal manifestations of EDS in comorbid cases.

Postural hypotension is common in patients with AN and the occurrence of postural orthostatic tachycardia syndrome (POTS) in patients with AN has been described in the literature (Sachs, Harnke, Mehler, & Krantz, 2016). Importantly, cardiovascular autonomic dysfunction, including POTS, is also commonly seen in hEDS, although the causal mechanisms are unclear (Hakim et al., 2017).

A connection between joint hypermobility/hEDS and anxiety disorders has been recognized for decades. Studies have shown an increased prevalence of anxiety disorders in clinical and nonclinical samples with hypermobile joints, as well as an unusually high presence of joint hypermobility in patients with panic disorder (Bulbena et al., 2017; Bulbena, Pailhez, Bulbena-Cabre, Mallorqui-Bague, & Baeza-Velasco, 2015). Preliminary data show that joint hypermobility may also be overrepresented in patients with AN (Goh, Olver, Huang, Millard, & O'Callaghan, 2013); whether this reflects an increased prevalence of actual EDS is unknown.

Interestingly, enhanced somatosensory awareness has been observed in patients with hEDS, amplifying pain and increasing attention to potentially anxiety-provoking stimuli (Baeza-Velasco, Gely-Nargeot, Vilarrasa, Fenetrier, & Bravo, 2011; Bulbena et al., 2017). An increased olfactory sensitivity and distorted proprioception in EDS have also been suggested (Bulbena et al., 2017, 2015), which could contribute to food selectivity, distorted body schemata and disordered eating behaviors. Furthermore, low levels of body esteem, which may also in turn increase the risk of disordered eating, are often seen in persons with disabilities (Taleporos & McCabe, 2005). Visible EDS symptoms such as easy bruising, atrophic scars, spine abnormalities, dental crowding, etc. could potentially contribute to such body dissatisfaction.

As described above, there has been concern that EDS-associated weight loss could wrongfully be interpreted as an eating disorder. In the present case, however, the patient could vividly describe the presence of intentional restrictive eating and weight phobia at the time of the AN debut and could not recall any prior food selectivity or abnormalities of smell or taste; thus, there was nothing to suggest that AN had developed secondary to EDS-associated disordered eating. Instead, this case illustrates a converse risk of AN symptoms masking and delaying proper diagnosis of co-morbid EDS. Furthermore, the case points to the potentially severe gastrointestinal symptoms of EDS as a risk factor for reoccurring weight loss and AN relapse; however, this particular patient was followed for 16 months after completing day treatment without reoccurrence of cognitive restraint despite continuous gastrointestinal complaints.

We suggest that the Beighton Hypermobility Score (see Table 1; originally described in Beighton, Solomon, & Soskolne, 1973) should be used in eating disorders services whenever a patient displays joint hypermobility. This rating scale can easily be applied in a few minutes and when values $\geq$5 are discovered, patients should be referred to a rheumatologist for further assessment. It should be noted that joint mobility varies with age, sex, and ethnicity, and that EDS-related pain may in fact decrease mobility; still, even though the Beighton Hypermobility Score cannot be used as a definitive diagnostic instrument, it is very useful as a screening tool.

In conclusion, EDS presents a challenge to clinicians due to the heterogeneous presentation. Various EDS symptoms may resemble or mask an underlying eating disorder, and vice versa. Gastrointestinal manifestations of EDS could also potentially be a risk factor for developing disordered eating. Clinicians should be aware of this group of underdiagnosed and potentially serious syndromes.

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