Hypermobile Ehlers Danlos Syndrome and Postural Orthostatic Tachycardia can be mistaken for Fibromyalgia and Chronic Fatigue.

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Fibromyalgia is a diagnosis that is commonplace in outpatient physical therapy settings. The condition is defined by the presence of pain in multiple areas of the body that cannot be otherwise explained. Associated symptoms generally include chronic pain, sleep disturbances, and fatigue[1]. Fibromyalgia is considered, at least in part, to be a diagnosis of exclusion meaning that alternative explanations should first be ruled out[2]. Once potential systemic and autoimmune conditions are excluded, however, providers may confirm the clinical diagnosis of fibromyalgia using the the American College of Rheumatology Criteria and the Manual Tender Point Survey[3].

Similar to fibromyalgia, Ehlers Danlos Syndrome (EDS) can also cause chronic pain symptoms. This is particularly true of the subtype hypermobile Ehlers Danlos Syndrome (hEDS). Individuals with this condition also commonly experience symptoms of postural orthostatic tachycardia syndrome (POTS), which is often mistaken for chronic fatigue syndrome. To an untrained eye, hEDS/POTS can be easily overlooked and presumed to be fibromyalgia/chronic fatigue syndrome. Because treatment recommendations and expectations can vary greatly, it is important for clinicians to be able to differentiate between these conditions so that interventions and outcomes are optimized.

EDS is a genetic anomaly of the connective tissue which can affect multiple body systems including skin, blood vessels, and internal organs[4]. hEDS is a form of EDS which has only been officially recognized since 2017[5]. People living with hEDS are much more prone to pain and injury because the condition affects the connective tissue around their joints and manifests itself as joint hypermobility[6].

An EDS diagnosis is made through clinical interpretation of signs and symptoms, exclusion of other causes, and a thorough medical history including familial history of the genetic disorder. EDS encompasses a group of heritable connective tissue disorders and can be detected with genetic testing. Though hEDS is thought to be the most common subtype of EDS[7], genetic testing is not currently able to identify this subtype specifically.

When a patient presents to primary care with complaints of pain and fatigue in the absence of other obvious systemic conditions that would show up with blood testing, the patient may come away with a diagnosis of fibromyalgia and chronic fatigue syndrome. Key clinical red flags to look for are joint hypermobility indicators and subjective reports consistent with pre-syncope versus fatigue. Primary care doctors do not routinely

screen for joint hypermobility and this condition may be easier identified by the physical therapist.

A general medical practitioner might not initially recognize hEDS as a possible explanation for patient symptoms, partially because it is not extremely common (however, it is estimated that as much as 3.4% of the population is affected by symptomatic joint hypermobility[8]) and also it is not always easy to detect just by visual inspection alone. Physical therapists can help in screening for this disorder. Physical therapists spend more time evaluating the musculoskeletal system and may be better suited to identify subtle impairments. Hallmark clinical signs include a long, lanky, marfanoid morphology with hypermobile joints. Hyperextension at the elbows and knees is common, as is the ability to forward bend and place palms flat on the floor. Long fingers and thumbs capable of extending far beyond neutral are also frequently observed. The Beighton Score can be a useful tool to help identify and document pathologic joint hypermobility. It should be noted that joint hypermobility in older adults may be harder to identify as joints tend to stiffen with age, injury or surgery. If hEDS is suspected in an older patient, asking questions to explore a potential history of hypermobility symptoms may be indicated[9]. Other visual markers are unexplained stretch marks, skin hyperextensibility, and atrophic scarring - all of which are signs consistent with connective tissue problems[10]. When placing hands on the patient, the clinician might notice the skin having a velvety texture with an elastic quality (one can literally pinch the skin and pull it several centimeters away from the body)[11]. When assessing joint mobility, the clinician may notice difficulty in finding any sort of firm end feel. The “Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome” is a comprehensive checklist that can help clinicians in their efforts to identify the classic clinical signs of hEDS. This tool, and other helpful resources for patient and medical providers, can be found on the Ehlers Danlos Society webpage.(www.ehlers-danlos.com).

Because hEDS is a connective tissue disorder, associated health concerns can extend well beyond joint hypermobility. Many people with hEDS also have cardiac and digestive issues, abnormal scar tissue formation, and generally poor surgical outcomes[11]. A common health problem associated with hEDS is postural orthostatic tachycardia syndrome (POTS). POTS is thought to occur when blood pools in the lower extremities during standing, and the body is unable to accommodate. This in turn causes a rapid increase in heart rate leading to symptoms of presyncope or actual syncope (the person passes out). POTS can also be associated with periods of prolonged bed rest or some autonomic nervous system disorders. Individuals with hEDS are more prone to POTS because the connective tissue matrix supporting circulatory vessels is inherently incompetent. The result is compromised structural

integrity which allows too much stretching within the vessel walls and subsequent blood pooling in the lower extremities[11]. Symptoms of POTS are similar to that of orthostatic hypotension, however, in POTS, the heart rate is elevated but the blood pressure does not drop.

People living with POTS tend to report poor standing activity tolerance, which may be mistakenly interpreted by medical providers as chronic fatigue or deconditioning[12]. If these symptoms are reported, clinical screening using the Stand Test[10] can offer valuable insight. The Stand Test is initiated by establishing a baseline heart rate which is taken after 5 minutes of resting in supine. The baseline is then compared to the heart rate recorded after quickly standing and then at 2, 5, and 10 minute intervals thereafter. A 40+ beat per minute increase in heart rate, in the absence of orthostatic hypotension, is suggestive of POTS. A more conclusive medical diagnosis of POTS would typically require evaluation by a cardiologist. In addition to ruling out other cardiac conditions, a Tilt Table Test would likely also be completed as it is considered to be the gold standard procedure for identifying POTS[12,13].

From assisting with diagnostic efforts to providing education, Physical Therapists are in an excellent position to offer impactful support to persons with hEDS and POTS[11]. Manual techniques, modalities, strengthening and stabilization exercises, proprioceptive training, and postural correction can all be utilized to help reduce limiting pain symptoms. Physical therapists should recognize that treating hEDS is not without limits. Many people with hEDS are unable to tolerate high levels of resistance training due to the fragility of connective tissues. These tissues may be less capable of generating high force and can therefore be more susceptible to pain and injury. It is then imperative for exercise efforts to be appropriately titrated with this population. When beginning an exercise routine, it is common for people with POTS to only tolerate supine or seated exercise. Use of supportive compression garments or aquatic exercise may help to mitigate limiting symptoms, allowing for a gradual progression toward more functional standing exercise. The Dallas Protocol can be a useful resource by providing a structured progression of exercise for those difficult cases[12]. With these cautions in mind, it is important to reinforce to patients that exercise can in fact be of great benefit by facilitating improved compression and pump action to support venous return to the heart [10].

It is important for the health care provider to be able to recognize hEDS and so that treatment can accommodate physical challenges. Education of the patient helps to increase understanding of the condition and may reduce frustration, help the patient advocate for themselves, and improve their interactions with the health care system.

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