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Case Report

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Ehlers Danlos, POTS, and Occult Cerebrospinal Fluid Leak: A Case Report

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Abstract

Ehlers Danlos syndromes (EDS) are associated with spontaneous intracranial hypotension (SIH) and postural orthostatic tachycardia syndrome (POTS). We hypothesized that some POTS patients might in fact have occult SIH due to unappreciated EDS. We describe a 26-year-old female with a history of POTS and headache who presented to us with negative imaging for cerebrospinal fluid leak (CSF). Upon examination with clinical evidence of EDS and supportive history, we performed an epidural blood patch despite repeat imaging evidence negative for CSF leak resulting in resolution of the patient's POTS, headache, and cognitive symptoms. Patients with POTS and connective tissue disorders associated with dural weakness may be suffering from occult chronic CSF leaks. MRI imaging may be falsely reassuring and dissuade clinicians from performing epidural blood patching among patients who can be cured.

Introduction

Spontaneous intracranial hypotension (SIH) was first recognized by George Schaltenbrand in the 1930s, and since then, the International Classification of Headache Disorders has defined SIH has a headache attributed to spontaneous or idiopathic low cerebrospinal fluid (CSF) pressure with some degree of relative intracranial hypotension even though CSF pressure may be within normal limits. In the past several years, there has been growing appreciation and interest in causes of SIH, including connective tissue disorders [1, 2]. Postural Orthostatic Tachycardia Syndrome (POTS) is a syndrome in which patients feel worse when upright and has been reported to be accompanied by orthostatic headache in as many as 60% of patients, thus raising the possibility of confusion with SIH [3]. Furthermore, POTS and Ehlers Danlos Syndrome (EDS) are also associated with each other [4]. Therefore, we hypothesized that some EDS patients diagnosed with POTS might have occult SIH. We asked the Autonomic Disorders Program at our institution for patients with POTS and EDS for evaluation of possible CSF leak. Here we present the first such patient, a 26-year-old female with POTS who was evaluated for occult CSF leak and her subsequent treatment.

Case Presentation

A 26-year-old female presented with history of dizziness and headaches since age 7 with diagnosis of POTS at age 17 after autonomic testing with waxing and waning symptoms. At her time of presentation to us, the patient presented having been given diagnosis of both POTS and chronic migraine. Recently, her symptoms of headache and dizziness had worsened. The patient was bedbound most of the day, unable to stand secondary to both pain and dizziness.

The patient had visited the ED at our institution multiple times and had trialed multiple therapies including dihydroergotamine infusions, anti-convulsants, botulinum toxin injections, nonsteroidal anti-inflammatory therapy and physical therapy without significant or sustained improvement. All previous neuroimaging had been reported negative, including MRI, magnetic resonance (MR) angiogram, and MR venography.

Upon careful review of systems, a constellation of physical exam findings and history were consistent with joint hypermobility syndrome (JHS) and EDS, hypermobility type (EDS-HT). Notable findings included mitral regurgitation with mitral valve prolapse, Beighton Score five out of nine points for joint hypermobility, hyperelastic skin, scoliosis confirmed by X-ray, frequent joint dislocation, and a positive family history including a brother with pectus excavatum, and mother and grandmother with symptoms consistent with POTS.

We ordered a heavily T2 weighted MR myelogram of the brain and full spine with and without contrast that showed no signs of SIH. A CT myelogram was obtained showing a 5mm outpouching in the left lateral recess at the L5-S1 level favored to represent a perineural cyst as well as perineural nerve root spread of contrast at C7-T1; both were felt to be normal variants by our neuroradiologists. We performed an epidural blood patch at L2-3 (20 cc), the site of her CT myelogram lumbar puncture and C7-T1 (8 cc), the site of perineural nerve root contrast spread. She felt 80% recovered from all her symptoms within 2 days. Two months post patch she described the complete cessation of POTS, headache symptoms, and cognitive dysfunction. She stopped disability and returned to full time work and was enjoying cycling and camping for exercise. She later had partial recurrence of symptoms and two more patches

before experiencing durable relief following a cervicothoracic epidural blood patch.

Discussion

Ehlers Danlos syndromes are associated with both SIH and POTS, and both conditions are marked by orthostatic conditions. Our first patient with evidence of EDS and a diagnosis of POTS demonstrated negative MRI imaging but had almost complete resolution of symptoms with epidural blood patching. JHS and EDS-HT are two clinically overlapping connective tissue disorders thought to have a frequency of 1/5000 and widely undiagnosed with subtle clinical signs [1]. In one case review of 58 patients with CSF leak, 9 exhibited connective tissue disorder, reinforcing that dural weakness may predispose patients to spontaneous CSF leak [5]. In a second prospective study, out of 50 patients referred for CSF leak, 9 had connective tissue disorders, and in 7 patients, CSF leak was the first noted manifestation [2].

Studies have demonstrated varying sensitivities of MRI imaging for SIH, with one study showing 83% sensitivity with brain MRI and 94% with spine MRI with the most common finding on spine MRI being epidural fluid collections and dural sac collapse [6]. Studies have found varying sensitivity of CT myelography ranging from 64%-89% [7]. However, since patients without imaging evidence for a CSF leak are rarely explored surgically for a dural tear, this is no other gold standard for knowing if patient has a CSF leak and it is unclear how many people with normal imaging may in fact have a CSF leak. In other words, the true sensitivity of current imaging techniques may be much lower than estimated.

Patients with POTS and connective tissue disorders associated with dural weakness may be suffering from occult chronic CSF leaks. MRI imaging may be falsely reassuring as was the case for our patient and dissuade clinicians from performing epidural blood patching among patients who can be cured. High clinical suspicion with careful physical examination and history may reveal previously overlooked JHS/EDS-HT disorders in patients with orthostatic symptoms and headache who may benefit from directed epidural blood patching despite negative imaging.

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