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Case Report

A Case of Idiopathic Intracranial Hypertension and Concomitant Postural Orthostatic Tachycardia Syndrome

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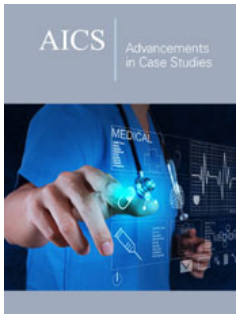

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Abstract

This study explores a case of idiopathic intracranial hypertension and concomitant postural orthostatic tachycardia syndrome. Here we examine how two cooccurring complex ailments can affect early diagnosis, and we analyze several potential treatments. A 26-year-old, previously healthy, female with a BMI of 33 and polycystic ovary syndrome (PCOS) presented to a Florida emergency department five times over the course of six days with complaints of evolving headaches, nausea, vomiting, and blurred peripheral vision. She was admitted to the hospital after presenting to the ED for the fifth time. An ophthalmologic exam to assess for papilledema was not performed until eight days after her initial presentation, due to confounding psychologic and autonomic symptoms. After MRI proved nondiagnostic and symptoms worsened to include pulsatile tinnitus, a fundoscopic exam was performed by ophthalmology which revealed bilateral papilledema. The diagnosis of idiopathic intracranial hypertension was presumed and the patient was initially started on a taper of topiramate. However, due to persistent patient anxiety related to lack of symptom resolution, topiramate was discontinued after three days of treatment and acetazolamide was initiated instead. The patient reported symptom improvement four days after beginning treatment with acetazolamide and 19 days after discontinuing isotretinoin use.

Keywords: Idiopathic intracranial hypertension; Postural tachycardia syndrome; Pseudotumor cerebri; Ehlers-Danlos syndrome; Optic nerve sheath fenestration; Lumbar-peritoneal shunt; Ventriculoperitoneal shunt; Venous sinus stent; Quality improvement

Introduction

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, was previously known as benign intracranial hypertension [1]. Due to potential vision threatening complications, the name of the condition was changed to no longer include the term "benign". IIH is defined as laboratory values and symptoms of elevated intracranial pressure (ICP) without evidence of a cause such as a mass obstruction, which is a common cause of secondary intracranial hypertension [2]. Papilledema occurs when raised ICP mechanically disrupts the axoplasmic flow within the optic nerve [3]. Any entity that increases ICP may lead to papilledema. Therefore, fundoscopic exams to confirm presence of papilledema are a crucial component of the physical exam when increased ICP is suspected.

IIH primarily affects females of childbearing age who are overweight or obese [4,5]. Although the mechanism connecting IIH and obesity is not clear, obesity is associated with an approximate 20-fold increase in incidence of IIH in women 20 to 45 years old, and both the incidence and prevalence of IIH within the population are rising in parallel with obesity rates [6]. Other known risk factors of developing IIH include endocrine diseases, such as PCOS, and use of drugs such as oral retinoids and tetracyclines [4]. Symptoms of drug associated IIH have been found to typically resolve within 2-4 weeks of stopping the offending medication [7-9].

Here we present a patient in which there was difficulty diagnosing IIH, despite several known risk factors, due to confounding symptomatology. Among her symptoms were syncope and orthostatic tachycardia in the absence of hypotension, and anxiety. These seemingly disparate set of symptoms, with no unifying syndrome, led to early assumptions of somatic symptom disorder and may have prolonged the time to diagnosis.

Case

A 26-year-old female veteran presented to the emergency department (ED) for a right sided headache. Her past medical history was limited to generalized anxiety disorder (GAD), PCOS, and obesity. Her headaches were accompanied by a "little spot" in her right field of vision, photophobia, phonophobia, and nausea. She was discharged from the ED after receiving a migraine cocktail and prophylactic migraine medications. She returned to the ED four more times with unrelenting symptoms and was sent home with diagnoses of migraines and anxiety. In the ED, the psychiatry service evaluated our patient and concluded that she had symptoms of somatic symptom disorder and unspecified mood disorder. On her next visit to the ED, the patient reported a recent episode of witnessed syncope, for which she was ultimately admitted.

Orthostatic vitals in the ED showed tachycardic changes without changes in blood pressure. Upon admission, her vital signs were stable with heart rate 98 bpm, blood pressure 136/76 mmHg, and pulse oximetry 100%. CBC, CMP, and UA were all within normal limits except for a blood glucose of 120. The patient described her syncope in further detail, reporting 3 episodes in which symptoms were precipitated by a change in position from sitting to standing. She denied all prodromal symptoms. During these episodes, her wristwatch alerted her to elevated heart rates that ranged from 160 to 180 bpm. Additionally, she endorsed constant nausea for one week with inadequate intake of nutrition and fluids. When prompted about any changes in medication, she disclosed that she had discontinued taking Metformin 2 days prior due to nausea and recent isotretinoin use, which she was instructed to discontinue by her dermatologist due to headache side effects 2 weeks prior to admission. Orthostatic vitals continued to show significant tachycardia on minimal exertion, additionally the patient also complained of light headedness and dizziness with the associated episodes of tachycardia. Neurology was consulted and recommended obtaining an MRI for nonspecific headaches to rule out IIH, migraine cocktail as needed, and Depakote for acute abortive therapy. The recommendations specified that Depakote use is contraindicated in PCOS patients due to its association with weight gain, as such, topiramate was also recommended as prophylaxis for both headache and weight gain and its potential to improve symptomology associated with IIH as a carbonic anhydrase inhibitor. Although MRI findings (seen in Figure 1) were severely limited due to extensive artifact from the patient's braces and patient motion, a fundoscopic exam performed by ophthalmology revealed bilateral papilledema, further supporting the diagnosis of IIH. After lumbar puncture was offered by neurology and declined by the patient, she was started on Topiramate 25mg nightly for 7 days. After discharge, the patient presented several more times to the ED for worsening anxiety due to lack of symptom resolution. As a result, her outpatient neurology clinic discontinued her topiramate and started acetazolamide 500mg PO BID in place. Additionally, she was started on trazadone for sleep and venlafaxine for mood. The patient continued to present to the ED for right sided headaches and worsening right eye blurred vision. A second fundoscopic exam revealed worsening papilledema, with the retinal nerve fiber layer (RNFL) demonstrating an enlarged blind spot in the right eye and more thickening of the nerve. The patient eventually consented to a lumbar puncture which was performed 2 days later, the opening pressure was unremarkable, 12cm H2O. Within the same day as the LP, she reported improvement in both blurred vision and headaches.

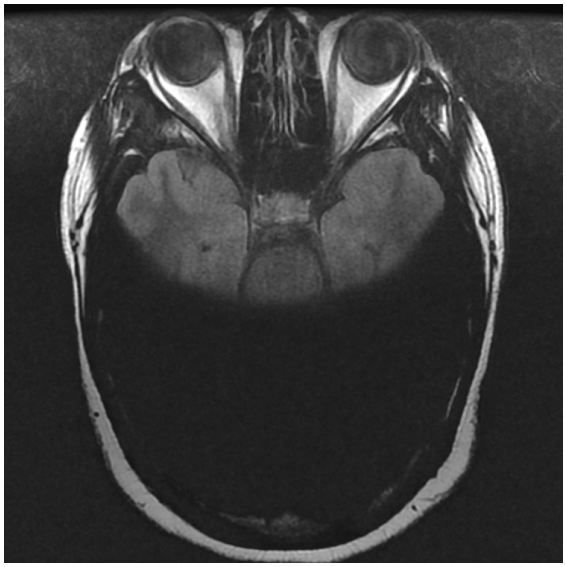

Figure 1: Brain MRI with IV contrast severely limited due to extensive artifact from dental hardware and patient motion. Findings of multiple small nonspecific white matter FLAIR hyperintensities which do not demonstrate a morphology or distribution typical for Multiple Sclerosis. Pictured: view of optic nerves.

Discussion

The goal of this paper is to explore a unique case of IIH in which the presentation was complicated by symptoms meeting the criteria for concomitant postural orthostatic tachycardia syndrome (POTS) and crucial diagnostic steps were delayed due to anxiety being confounded for possible somatic symptom disorder. Exploring this topic may allow for a more expedient diagnosis in future patients with similar presentations and may incite further research into a possible connection between the two ailments.

Postural tachycardia syndrome (POTS)

Postural tachycardia syndrome (POTS) is defined as an elevation of at least 30 beats or more within 10 minutes of standing or head-up tilt with associated symptoms of cerebral hypoperfusion but no orthostatic hypotension [10,11]. Common symptoms include headache, syncope, palpations, and dyspnea which are often relieved by supine rest [11,12]. Similar to IIH, approximately 80% of patients with POTS are female, and the majority are 15-25 years old at presentation [13-15]. There are several known pathways for the pathogenesis of POTS. Neuropathic POTS is believed to be caused by the degradation of autonomic nerves in the lower extremities which results in inadequate compensatory vasoconstriction upon orthostasis, consequent vascular pooling, and tachycardia [12,15]. Hyperadrenergic POTS is another subtype of POTS with hallmark features of abnormally elevated norepinephrine and resultant increased blood pressure upon orthostasis [15,16]. Another common form of POTS is hypovolemic POTS which is characterized by chronic hypovolemia and paradoxically reduced plasma renin and aldosterone levels [16,17].

Idiopathic intracranial hypertension (IIH)

IIH is defined by the modified Dandy criteria as elevated ICP of over 25cm H2O, symptoms of elevated ICP (e.g. headache, papilledema, and vision impairment), no focal neurological findings (except a possible deficit in cranial nerve 6), and no other explanation for elevated ICP including abnormal MRI/CT findings [18,19]. While the exact pathogenesis of IIH remains unclear, a number of risk factors have been identified. Of particular note, IIH occurs at much higher rates in females between the age of 15-44, obese patients, and patients with a recent weight gain of 5-15% regardless of BMI [4,5,20-23]. In a 2017 population-based cohort study, Kilgore et al. found that the incidence of IIH has more than doubled since 1990, mirroring the coincident increase in obesity in the US [23]. Similarly, a nationwide study of all medical records from 2005-2007 in Israel found that 83.4% of patients with IIH were obese [5]. In addition, for IIH patients over the age of 17, the patients were 6 times more likely to be female, but for IIH patients ages 11-17, the female-to-male ratio fell significantly to approximately 2:1 [5]. This suggests that sex difference plays a more significant role in the pathophysiology of IIH in patients over the age of 17. Common presenting symptoms include headache, transient visual obscuration, pulsatile tinnitus, back pain, and retrobulbar pain (Figure 2) [21,24].

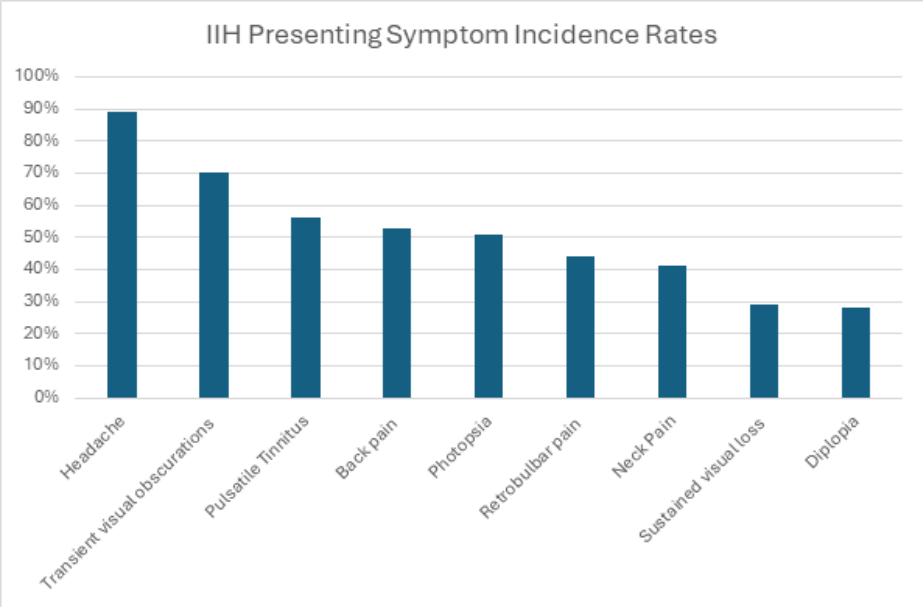

Figure 2: IIH Presenting Symptom Incidence Rates [21,24].

The symptoms detailed in Figure 2 presented either individually or in combination are not specific for IIH. In 1991, researchers used an 83-item questionnaire given at the time of diagnosis to 50 IIH patients and 100 age-matched control patients recruited from hospital waiting areas [22]. Although prevalence, severity, and frequency of symptoms were lower, they were commonly found in age and gender-matched control patients. Daily occurrence of these symptoms was much more common in IIH patients than in the control group. Additionally, the most useful distinguishing feature appeared to be the presence of pulsatile tinnitus. Therefore, researchers concluded that young obese women with daily symptoms of headaches and either transient visual obscuration's or intracranial noises should alert clinicians to the diagnosis of IIH.

Given that 5% of patients with IIH have reported a family history, many studies have endeavoured to elucidate a genetic cause [25]. However, to date, no clear genetic component has been found [26-28]. Several medications have also been shown to increase the incidence of IIH, including the use of growth hormone in children, tetracycline antibiotics and all-trans retinoic acid [29-34]. A number of theories have been proposed for the pathogenesis of IIH including cerebral spinal fluid (CSF) outflow impairment at the level of the arachnoid granulation tissue and glymphatic system (brain lymphatic system) or elevated intracranial venous pressure [19,35]. Regarding the theory of elevated intracranial venous pressure, recent studies have reported significant rates of stenosis in the transverse venous sinus which could account for increased ICP through CSF backflow. In fact, a recent retrospective chart review by Cappuzzo et al. [36] found that of 18 patients with IIH who underwent stent intervention of the transverse sinus, 88.9% reported improvement of symptoms, including complete resolution of papilledema [36].

Proposed relationship between IIH and POTS

In recent years, research has highlighted a strong positive association between hypermobile Ehlers-Danlos syndrome (hEDS) and POTS. For instance, a recent study by Miller et al. found that 32% of recruited patients with POTS met criteria for hEDS and another 28% exhibited sub-hEDS hypermobility [37]. Similarly, several studies have reported a possible association between IIH and hEDS [38-40]. Consequently, hEDS may represent a common pathway between POTS and IIH. However, to our knowledge, no formal study has examined the incidence rates of hEDS in patients with IIH, and this may represent a route for future research.

Another possible relationship between POTS and IIH may be through a shared pathogenesis of reduced cerebral perfusion. Reduced cerebral perfusion pressure (CPP) is a hallmark feature of POTS [41]. In IIH, CPP may be reduced by increased ICP according to the cerebral perfusion pressure formula CPP = MAP – ICP [42,43].

Anxiety, POTS and somatic symptom disorder

There are an extensive number of nonspecific symptoms associated with POTS that are unrelated to postural changes. Of those symptoms, commonly seen is anxiety phenomenologically distinct from generalized anxiety disorder and panic disorder [44,45]. In POTS patients, anxiety appears to be driven by heightened awareness of internal somatic sensations likely due to autonomic overexcitation. In this case of POTS with concomitant undiagnosed IIH, the patient's anxiety was suspected and eventually diagnosed as somatic symptom disorder whereas somatic hypervigilance may have been more appropriate.

Somatic symptom disorder can occur with or without a known underlying medical illness that explains the somatic symptoms [46]. According to the DSM-5, while the specific somatic symptoms may change, the disorder must be persistent for six months with specific somatic symptoms that cause distress or psychological impairment from excessive thoughts associated with the somatic symptoms [47]. In the setting of patients with a significant medical disorder, the key to establish if they also have somatic symptoms disorder is determining whether the patient's psychologic responses to the medical disease are excessive compared to other most patients [48]. In this case, the patient was experiencing symptoms of both POTS and IIH – IIH causing somatic symptoms of migraine-like headaches and POTS causing somatic hypervigilance.

Initial workup of suspected IIH

The initial workup for suspected IIH is a complete history including questions regarding use of growth hormone, tetracycline and all-trans retinoic acid and recent weight gain. A comprehensive neurological physical exam should also be included with a fundoscopic exam for signs of papilledema. Next, an MRI may be performed to rule out secondary causes of increased ICP. MRI findings associated with IIH include empty sella turcica, optic nerve protrusion, distension of the optic nerve sheath, optic nerve tortuosity, posterior globe flattening, and venous sinus stenosis [49]. Lastly, a lumbar puncture may be performed to establish opening pressure and ensure a normal CSF sample [50]. This diagnostic pathway has been detailed in Figure 3.

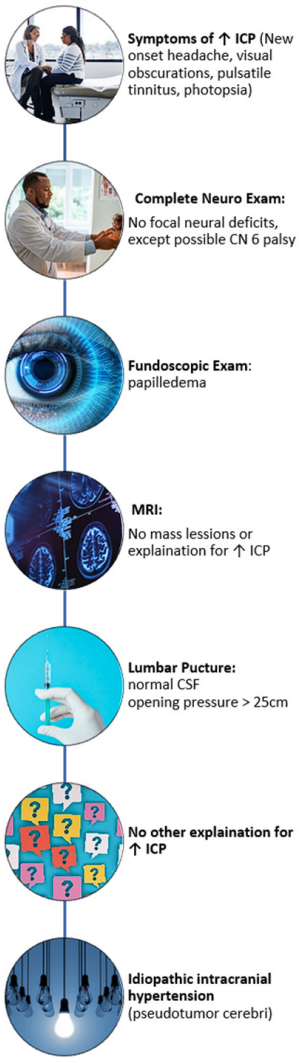

Figure 3: Diagnostic Pathway of IIH [50].

Surgical management of IIH

There are several avenues for surgical management of elevated ICP in the setting of IIH to alleviate the progression of vision loss, including optic nerve sheath fenestration, lumbar-peritoneal shunt (LPS), a ventriculoperitoneal shunt (VPS), or a venous sinus stent placement [51,52].

Optic nerve sheath fenestration is a procedure in which the optic nerve sheath is surgically decompressed to advert vision loss from elevated pressure [53]. While this procedure is associated with a high success rate and a low rate of relapse or need of revision, it remains a second line option for surgical management due to a historically high association with post operative complications including diplopia and traumatic optic neuropathy and vision loss with some literature reporting complication rates as high as 45% [51,54,55]. However, more recent research suggests that major complication rates may be lower than 5%, perhaps due to more recent advances in surgical technique or training [54,56-58].

LP shunt surgery involves placing a tube between the elevated pressure of the spinal subarachnoid space and the comparatively lower pressure environment of the peritoneal abdominal space [52]. This allows for the drainage of excess CSF from the subarachnoid space and a potential resolution or stabilization of symptoms associated with IIH. LPS was previously the mainstay for surgical treatment of IIH [59]. However, a number of studies demonstrated an apparent advantage of VPS over LPS with regards to failure and revision rates [52]. This has resulted in VPS advancement as the most prevalent surgical management for IIH.

Similar to LPS, VPS involves placing a catheter between the CSF containing ventricles of the brain and the peritoneal space of the abdomen [60]. While VPS represent the mainstay of neurosurgical treatment of IIH, VPS face a number of challenges and avenues for failure including obstruction and infection [61]. Venous sinus stenting, a procedure in which stents are endovascularly deployed in cerebral sinuses to increase flow and reduce ICP, represents a promising neurosurgical treatment for IIH [62]. A recent meta-analysis by Nicholson et al. [63] showed a headache reduction of 79.6%, a relapse rate of 9.8% and a major complications rate of 1.9% [63]. While these results are promising, more research is needed to identify the ideal patient population. The OPEN-UP trial which will compare the effectiveness of venous sinus stenting to surgical management is currently being conducted with an estimated completion date of 2024 [NCT02513914].

Diagnostic pitfalls of this case and steps for quality improvement

An obese 26-year-old female presented to the ED for four days complaining of a daily throbbing headache with associated phonophobia, photophobia, and blurred vision. She was subsequently misdiagnosed with migraine at every visit and discharged with minimal workup. In the setting of a young adult with new onset headaches and changes in vision, fundoscopic exam and MRI were warranted. Lack of further workup was likely the result of somatic hypervigilance due to concomitant POTS in this patient, which led to an assumption of somatic symptom disorder.

Despite daily headaches and transient visual obscurations, increased ICP was only suspected in the setting of IIH after the patient was admitted to the hospital and disclosed isotretinoin use that had been discontinued ten days prior. Upon learning of the patient's recent isotretinoin use, IIH was suspected but it was not until the patient developed worsening blurred vision peripherally and pulsatile tinnitus that a funduscopic exam was performed by ophthalmology in which papilledema was found. In part, this delay in fundoscopy was due to a lack of understanding in the relationship between isotretinoin use and IIH. The half-life of Accutane is relatively short, 21 +/- 8.2 hours for the parent drug and 24 +/- 5.3 hours for the metabolite, and undetectable after 4-5 days [64]. Since our patient had discontinued isotretinoin use 10 days prior, there was a misconception that drug induced IIH was a less likely diagnosis. However, despite the half-life, there is strong evidence that in terms of drug induced IIH, discontinuing the offending drug leads to a resolution of IIH only after 2-4 weeks [7].

Eight days after the patient initially sought medical treatment for symptoms, IIH was the presumed diagnosis with consideration to patient demographics, symptomatology, and risk factors. The appropriate treatment was started. Symptom improvement occurred 19 days after discontinuing isotretinoin with minimal pharmacologic therapy. It is difficult to assess if the pharmacotherapy contributed to symptom resolution or if improvement was due to the tincture of time. Despite a short course of topiramate and acetazolamide the patient complained of worsening headaches and blurred vision and repeat fundoscopy found worsening papilledema. However, two days after worsening papilledema was found, the lumbar puncture demonstrated normal opening pressures and the patient reported improvement in vision and headache following the procedure.

Conclusion

The aim of this case study was to examine a complex case involving a delayed diagnosis of IIH with concomitant POTS. Our analysis revealed that the presence of confounding symptomatology from POTS, and clinicians' failure to advance diagnostic workup resulted in multiple lapses in patient management.

We suspect that the anxiety symptoms displayed by the patient were secondary to POTS-associated somatic hypervigilance to increasing intracranial pressures from IIH. The misdiagnoses of somatic symptom disorder in the ED led providers to attribute the patient's worsening headache symptoms to an excessive psychological response to a migraine, instead of recognizing them as a clinical indication for escalating workup and expanding the differential to include secondary causes of headache.

This case underscores the importance of clinical decision-making in terms of patient outcomes. It highlights the need for clinicians to recognize when advancing the patient's workup is necessary, especially when patients present with the same chief complaint and minimal response to prior therapies. By considering a wide range of differential diagnoses, clinicians are

more likely to conduct thorough patient interviews and review past medical history adequately. By conducting a more comprehensive patient interview and workup, clinicians can potentially reduce unnecessary testing, improve diagnosis accuracy, and promote better patient outcomes with early intervention.

Author Contributions

Virginia Flores: Conception, Drafting, Critical revision; Jonathan Willman: Conception, Drafting, Critical revision, Submission and correspondence; Matthew Willman: Drafting, Critical revision; Roshni Prakash, MD: Conception, Critical revision; Brandon Lucke-Wold, MD: Senior Author, Conception, Critical revision; All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Digre KB, Bruce BB, McDermott MP, Galetta KM, Balcer LJ, et al. (2015) Quality of life in idiopathic intracranial hypertension at diagnosis: IIH Treatment Trial results. Neurology 84(24): 2449-2456.
2. Wakerley B, Tan M, Ting E (2015) Idiopathic intracranial hypertension. Cephalalgia 35(3): 248-261.
3. Tso MO, Hayreh SS (1977) Optic disc edema in raised intracranial pressure. IV. Axoplasmic transport in experimental papilledema. Arch Ophthalmol 95(8): 1458-1462.
4. Radhakrishnan K, Ahlskog JE, Cross SA, Kurland LT, O'Fallon WM (1993) Idiopathic intracranial hypertension (pseudotumor cerebri). Descriptive epidemiology in Rochester, Minn, 1976 to 1990. Arch Neurol 50(1): 78-80.
5. Kesler A, Gadoth N(2001) Epidemiology of idiopathic intracranial hypertension in Israel. J Neuroophthalmol 21(1): 12-14.
6. Curry WT, Butler WE, Barker FG (2005) Rapidly rising incidence of cerebrospinal fluid shunting procedures for idiopathic intracranial hypertension in the United States, 1988-2002. Neurosurgery 57(1): 97-108.
7. Lochhead J, Elston JS (2003) Doxycycline induced intracranial hypertension. BMJ 326(7390): 641-642.
8. Jay WM, Jay S (1978) Benign intracranial hypertension with tetracycline therapy. The Journal of Pediatrics 93: 901.
9. Stuart BH, Litt IF (1978) Tetracycline-associated intracranial hypertension in an adolescent: A complication of systemic acne therapy. The Journal of Pediatrics 92(4): 679-680.
10. Mathias CJ, Low DA, Iodice V, Owens AP, Kirbis M, et al. (2012) Postural tachycardia syndrome-current experience and concepts. Nat Rev Neurol 8(1): 22-34.
11. Freeman R, Wieling W, Axelrod FB, Benditt DG, Benarroch E, et al. (2011) Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. Clin Auton Res 21(2): 69-72.
12. Zadourian A, Doherty TA, Swiatkiewicz I, Taub PR (2018) Postural orthostatic tachycardia syndrome: Prevalence, pathophysiology and management. Drugs 78(10): 983-994.
13. Sheldon RS, Grubb BP, Olshansky B, Shen WK, Calkins H, et al. (2015) 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia and vasovagal syncope. Heart Rhythm 12(6): e41-e63.
14. Grubb BP (2008) Postural tachycardia syndrome. Circulation 117(21): 2814-2817.
15. Naeini PS, Razavi M (2020) Postural orthostatic tachycardia syndrome. Texas Heart Institute Journal 47(1): 57-59.
16. Mar PL, Raj SR (2020) Postural orthostatic tachycardia syndrome: Mechanisms and new therapies. Annu Rev Med 71: 235-248.
17. Vernino S, Bourne KM, Stiles LE, Grubb BP, Fedorowski A, et al. (2021) Postural Orthostatic Tachycardia Syndrome (POTS): State of the science and clinical care from a 2019 national institutes of health expert consensus meeting-part 1. Autonomic Neuroscience 235: 102828.
18. Kosmorsky GS (2014) Idiopathic intracranial hypertension: Pseudotumor cerebri. Headache: The Journal of Head and Face Pain 54(2): 389-393.
19. Burkett JG, Ailani J (2018) An up-to-date review of pseudotumor cerebri syndrome. Curr Neurol Neurosci Rep 18(6): 33.
20. Ireland B, Corbett JJ, Wallace RB (1990) The search for causes of idiopathic intracranial hypertension. A preliminary case-control study. Arch Neurol 47(3): 315-320.
21. Wall M, George D (1991) Idiopathic intracranial hypertension: A prospective study of 50 patients. Brain 114 (Pt 1A): 155-180.
22. Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991) Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): A case-control study. Neurology 41(2(Pt 1)): 239-244.
23. Kilgore KP, Lee MS, Leavitt JA, Mokri B, Hodge DO, et al. (2017) Re-evaluating the Incidence of Idiopathic Intracranial hypertension in an era of increasing obesity. Ophthalmology 124(5): 697-700.
24. Wall M, Kupersmith MJ, Kieburtz KD, Corbett JJ, Feldon SE, et al. (2014) The idiopathic intracranial hypertension treatment trial. JAMA Neurol 71: 693(6)-701.
25. Keltner JL, Johnson CA, Cello KE, Wall M (2014) Baseline visual field findings in the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT). Invest Ophthalmol Vis Sci 55(5): 3200-3207.
26. Madriz Peralta G, Cestari DM (2018) An update of idiopathic intracranial hypertension. Current Opinion in Ophthalmology 29(6): 495-502.
27. McGeeney BE, Friedman DI (2014) Pseudotumor cerebri pathophysiology. Headache 54(3): 445-458.
28. Behbehani R, Ali A, Al-Mousa AJ, Albuloushi SN (2022) Familial non-obese idiopathic intracranial hypertension. American Journal of Ophthalmology Case Reports 27: 101619.
29. Reeves GD, Doyle DA (2002) Growth hormone treatment and pseudotumor cerebri: Coincidence or close relationship? Journal of Paediatric Endocrinology and Metabolism 15(2): 723-730.
30. Rogers AH, Rogers GL, Bremer DL, McGregor ML (1999) Pseudotumor cerebri in children receiving recombinant human growth hormone. Ophthalmology 106(6): 1186-1189.
31. Martín Begué N, Mogas E, Dod CW, Alarcón S, Clemente M, et al. (2021) Growth hormone treatment and papilledema: A prospective pilot study. J Clin Res Pediatr Endocrinol 13(2): 146-151.
32. Orme DR, Vegunta S, Miller MA, Warner JEA, Bair C, et al. (2020) A comparison between the clinical features of pseudotumor cerebri secondary to tetracyclines and idiopathic intracranial hypertension. American Journal of Ophthalmology 220: 177-182.
33. Paley GL, Sheldon CA, Burrows EK, Chilutti MR, Liu GT, et al. (2015) Overweight and obesity in paediatric secondary pseudotumor cerebri syndrome. American Journal of Ophthalmology 159(2): 344-352.e1.
34. Holmes D, Vishnu P, Dorer RK, Aboulafia DM (2012) All-trans retinoic

acid-induced pseudotumor cerebri during induction therapy for acute promyelocytic leukaemia: A case report and literature review. Case Reports in Oncological Medicine 2012: e313057.

35. Mondejar V, Patsalides A (2020) The role of arachnoid granulations and the glymphatic system in the pathophysiology of idiopathic intracranial hypertension. Curr Neurol Neurosci Rep 20(7): 20.

36. Cappuzzo JM, Hess RM, Morrison JF, Davies JM, Snyder KV, et al. (2018) Transverse venous stenting for the treatment of idiopathic intracranial hypertension, or pseudotumor cerebri. Neurosurgical Focus 45(1): E11.

37. Miller AJ, Stiles LE, Sheehan T, Bascom R, Levy HP, et al. (2020) Prevalence of hypermobile Ehlers-Danlos syndrome in postural orthostatic tachycardia syndrome. Autonomic Neuroscience 224: 102637.

38. Herdes RE, El Haija MA, Johnson K, Shepard WE, Zak Y, et al. (2021) Experience with vertical sleeve gastrectomy in adolescent and young adult Ehlers Danlos syndrome patients: A case series and review of the literature. Obes Surg 31(9): 4168-4173.

39. Henderson FC, Austin C, Benzel E, Bolognese P, Ellenbogen R, et al. (2017) Neurological and spinal manifestations of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 175(1): 195-211.

40. Kurian M, Solomon GD (2013) Can elevated IGF-1 levels among patients with Ehlers Danlos syndrome cause idiopathic intracranial hypertension? Headache 53(10): 1666-1669.

41. Blitshteyn S (2022) Is Postural Orthostatic Tachycardia Syndrome (POTS) a central nervous system disorder? J Neurol 269(2): 725-732.

42. Randolph SM, Stephen AM (2007) On call neurology. (3rd edn), Saunders, USA, pp. 155-165.

43. Pinto VL, Tadi P, Adeyinka A (2022) Increased intracranial pressure. StatPearls Publishing, StatPearls, Treasure Island (FL).

44. Owens AP, Low DA, Iodice V, Critchley HD, Mathias CJ (2017) The genesis and presentation of anxiety in disorders of autonomic overexcitation. Auton Neurosci 203: 81-87.

45. Khurana RK (2006) Experimental induction of panic-like symptoms in patients with postural tachycardia syndrome. Clin Auton Res 16(6): 371-377.

46. Löwe B, Levenson J, Depping M, Hüsing P, Kohlmann S, et al. (2022) Somatic symptom disorder: A scoping review on the empirical evidence of a new diagnosis. Psychol Med 52(4): 632-648.

47. Dimsdale JE, Creed F, Escobar J, Sharpe M, Wulsin L, et al. (2013) Somatic symptom disorder: An important change in DSM. J Psychosom Res 75(3): 223-228.

48. Dimsdale JE, Levenson J (2013) What's next for somatic symptom disorder? AJP 170(12): 1393-1395.

49. Barkatullah AF, Leishangthem L, Moss HE (2021) MRI findings as markers of idiopathic intracranial hypertension. Curr Opin Neurol 34(1): 75-83.

50. Mollan SP, Davies B, Silver NC, Shaw S, Mallucci CL, et al. (2018) Idiopathic intracranial hypertension: consensus guidelines on management. J Neurol Neurosurg Psychiatry 89(10): 1088-1100.

51. Uretsky S (2009) Surgical interventions for idiopathic intracranial hypertension. Current Opinion in Ophthalmology 20(6): 451-455.

52. Mukherjee N, Bhatti MT (2014) Update on the surgical management of idiopathic intracranial hypertension. Curr Neurol Neurosci Rep 14(3): 438.

53. Mudumbai RC (2014) Optic nerve sheath fenestration: indications, techniques, mechanisms and results. International Ophthalmology Clinics 54(1): 43-49.

54. Dai YL, Ramsey DJ, Athappilly GK, Tucker SM (2023) Visual recovery after unilateral optic nerve sheath fenestration for pseudotumor cerebri syndrome. Orbit 42(4): 397-403.

55. Plotnik JL, Kosmorsky GS (1993) Operative complications of optic nerve sheath decompression. Ophthalmology 100(5): 683-90.

56. Gilbert AL, Chwalisz B, Mallery R (2018) Complications of optic nerve sheath fenestration as a treatment for idiopathic intracranial hypertension. Seminars in Ophthalmology 33(1): 36-41.

57. Jefferis JM, Littlewood RA, Pepper IM, Hickman SJ, Salvi SM (2021) Optic nerve sheath fenestration via a supero-medial eyelid skin crease approach for the treatment of idiopathic intracranial hypertension in a UK population. Eye 35(5): 1418-1426.

58. Obi EE, Lakhani BK, Burns J, Sampath R (2015) Optic nerve sheath fenestration for idiopathic intracranial hypertension: A seven-year review of visual outcomes in a tertiary centre. Clinical Neurology and Neurosurgery 137: 94-101.

59. Friedman DI, Jacobson DM (2004) Idiopathic intracranial hypertension. Journal of Neuro-Ophthalmology 24(2): 138-145.

60. Abou-Al-Shaar H, Mallela AN, Algattas HN, Rogers R, Friedlander RM (2022) Ventriculoperitoneal shunt failure due to distal peritoneal catheter kinking. Am J Case Rep 23: e935077.

61. Paff M, Abrams DA, Muhonen M, Loudon W (2018) Ventriculoperitoneal shunt complications: A review. Interdisciplinary Neurosurgery 13: 66-70.

62. Puffer RC, Mustafa W, Lanzino G (2013) Venous sinus stenting for idiopathic intracranial hypertension: A review of the literature. Journal of NeuroInterventional Surgery 5(5): 483-486.

63. Nicholson SE, Watts LT, Burmeister DM, Merrill D, Scroggins S, et al. (2019) Moderate traumatic brain injury alters the gastrointestinal microbiome in a time-dependent manner. Shock 52(2): 240-248.

64. (2023) Isotretinoin-an overview | ScienceDirect Topics n.d.

