



# Orthostatic Headaches Associated With Spontaneous Intracranial Hypotension and Autonomic Dysfunction—A Case Series in Young Patients

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## Abstract

**Background:** Orthostatic headaches can be noted in spontaneous intracranial hypotension and orthostatic intolerance. We present a case series of young patients diagnosed with spontaneous intracranial hypotension and were treated for the same but subsequently developed orthostatic intolerance. **Methods:** We retrospectively reviewed charts for seven young patients with orthostatic headaches related to spontaneous intracranial hypotension and orthostatic intolerance. **Results:** Patients were diagnosed with spontaneous intracranial hypotension. Diagnosis was confirmed by identifying epidural contrast leakage and three of seven patients were noted to have early renal contrast excretion on computerized tomography myelography. Patients were treated with epidural blood patches. All patients showed persistent symptoms of autonomic dysfunction after treatment of spontaneous intracranial hypotension and orthostatic intolerance was confirmed with head-up tilt table test. **Conclusions:** Patients with spontaneous intracranial hypotension failing to improve following epidural blood patching should be evaluated for orthostatic intolerance.

## Keywords

Spontaneous intracranial hypotension, postural headache, orthostatic intolerance, dysautonomia, POTS, head up tilt table test

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## Introduction

Spontaneous intracranial hypotension (SIH) due to spinal cerebrospinal fluid (CSF) leaking is an increasingly recognized cause of orthostatic headaches. Although well recognized in adults, SIH is considered rare in pediatric patients.<sup>1</sup> Furthermore, orthostatic headaches also occur in patients with orthostatic intolerance.<sup>2</sup>

The spectrum of orthostatic intolerance includes orthostatic hypotension, postural tachycardia syndrome (POTS), and syncope.<sup>3,4</sup> Clinical differentiation of SIH and orthostatic intolerance may be difficult due to overlapping symptoms.<sup>5</sup> International Classification of Headache Disorders (ICHD) third edition recommends treating patients with typical orthostatic headaches with no apparent cause and after exclusion of POTS with autologous lumbar epidural blood patch (EBP).<sup>6</sup> SIH and orthostatic intolerance may co-exist in adults<sup>5,7</sup> but

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**Table 1.** Demographics and Summary of Diagnostic Tests Performed in Each Patient.

Patient	Gender/ Age	BMI (kg/ m <sup>2</sup> )	Headache location	Headache duration (months)	Pain characteristics	Prior history	CSF OP (cm H2O)	HUTT
1	F/12	21	Bifrontal	1	Throbbing	Migraine	5	++
2	M/11	30	Holocephalic	1	Throbbing	Migraine	12	++
3	F/18	18	Occipital and neck pain	1	Throbbing	Migraine	19	++
4	F/17	27	Holocephalic	2	Throbbing	Migraine	14	++
5	F/20	26	Holocephalic and neck pain	1	Throbbing	Migraine	10	++
6	F/15	18	Occipital	3	Throbbing	none	10	++
7	F/17	24	Holocephalic	3	Throbbing	Migraine	8	+++

Abbreviations: BMI, Body mass index; OP, opening pressure; HUTT, Head up tilt table test; moderate:++, severe:+++.

have not been described in young patients. We report a series of seven young patients presenting with orthostatic headaches with an initial diagnosis of SIH and subsequently shown to have orthostatic intolerance on evaluating persistence of symptoms.

## Methods

Retrospective case series of young patients with orthostatic headaches diagnosed with SIH and orthostatic intolerance. All patients were evaluated at our Child Neurology Clinic from 2009 to 2014. A diagnosis of CSF dural leak was based on computed tomographic (CT) myelography and a diagnosis of orthostatic intolerance was based on head up tilt table test (HUTT). All patients had HUTT conducted per our standard protocol approved by our institutional review board (IRB).<sup>8,9</sup> Patients, who were supine for a minimum of 10 min were then tilted to 70 degrees upright for 30 min and repositioned to supine for 7 min. Continuous heart rate (HR), beat-to-beat blood pressure (BP), cardiac stroke volume (SV), cerebral perfusion depicted by near infra-red spectroscopy (NIRS) and sympathetic/parasympathetic tone were monitored. A HUTT was considered normal if the patient completed 30 min upright and was asymptomatic. Patients with moderate orthostatic intolerance were able to finish the 30 min HUTT, however patients with severe orthostatic intolerance were not able to finish the test as they developed symptoms such as nausea, severe headaches, and shortness of breath or fatigue. Patients with both moderate and severe orthostatic intolerance had significant physiological changes such as HR>30 bpm, SV decrease  $\geq 30\%$  and two-fold increase above the baseline of sympathetic/parasympathetic tone.

## Results

A total of seven young patients were diagnosed with SIH and orthostatic intolerance over a period of five years. (Table 1). There were six females and one male. Average age at time of onset of orthostatic headaches was 15 years (age range of 11-20 years). Headache location varied but with characteristic severe pulsating pain in the morning in all patients. Six of seven patients (85%) had prior migraine headaches without aura and were treated prophylactically. One patient was obese, and two patients were noted to be underweight (BMI  $\leq 18$ ). Neurological examination, including fundoscopy, was normal in all patients. All patients had magnetic resonance imaging (MRI) of brain and entire spine, with and without contrast. Two patients had abnormal neuroimaging including syringomyelia and cerebellar tonsillar ectopia (Table 2). Six of seven patients were noted to have normal CSF opening pressure (OP) and one patient had a low OP (normal range: 6-20 cm H<sub>2</sub>O).<sup>10</sup> All patients had CT myelography which confirmed dural leak and three of seven patients showed early excretion of renal contrast (Table 2). All patients were treated with EBP. Patients were noted to have persistent symptoms of syncope and orthostatic headaches after multiple EBPs. Subsequent HUTT confirmed orthostatic intolerance and patients were treated accordingly.

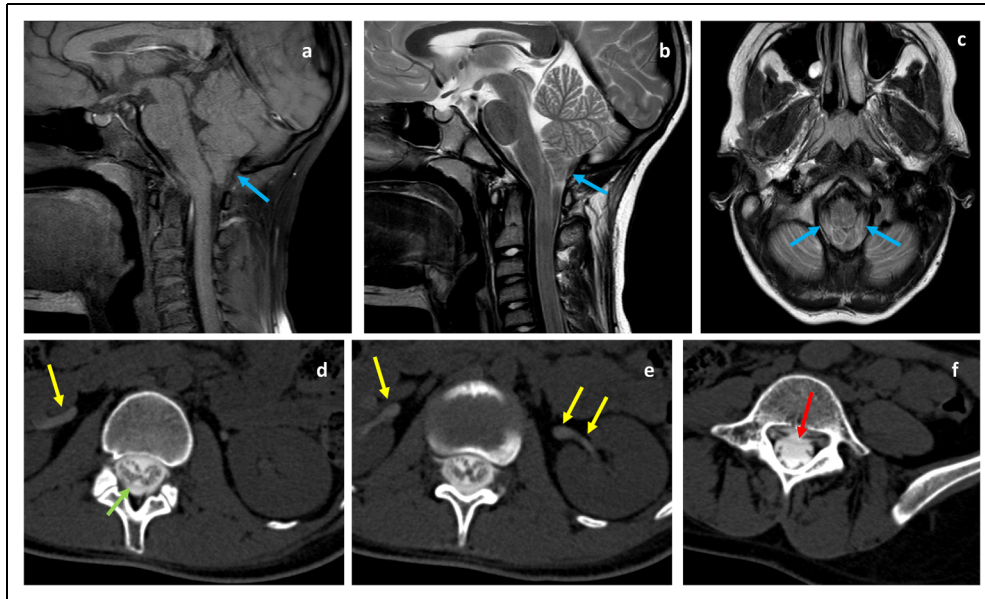
## Representative Case

A 12 year old female (patient 1) presented with increasing headaches for one month. Headaches were bifrontal, throbbing in

**Table 2.** Neuroimaging Findings of Patients with SIH and OI.

Patient	MRI Brain	MRI Spine	Dural leak on CT myelography	Early renal contrast excretion
1	cerebellar ectopia (2 mm)	normal	L1-L4	+
2	normal	normal	L2-L3	-
3	normal	normal	T10-S1	+
4	normal	normal	T12-L3	-
5	normal	normal	L2-L3	-
6	normal	normal	C8-L2	+
7	cerebellar ectopia (4 mm)	syringomyelia (3.5 mm)	L2-L3	-

Early renal contrast excretion: + : present; -: absent.



**Figure 1.** Shows findings of MRI Brain and CT Myelography of patient 1. Figure a, b, and c shows Sagittal T1, Sagittal and Axial T2 weighted images demonstrating mild low-lying cerebellar tonsils (blue arrows) causing mild crowding of sub-arachnoid fluid spaces across the foramen magnum. Figure d- f shows Axial CT myelogram images demonstrating dorsal (green arrows) and ventral (red arrows) epidural contrast leakage extending from T12 to L5. Note is also made of early contrast excretion through the kidneys (yellow arrows).

nature and were associated with photophobia and nausea. Headaches worsened with bending forwards and walking and relieved by lying supine. She had been treated with medications to prevent or to acutely treat migraine headaches (metoprolol, topiramate, rizatriptan). Her neurological examination was normal. LP showed CSF opening pressure of 5 cmH<sub>2</sub>O. MRI brain and spine with and without contrast showed minimal cerebellar tonsillar ectopia (2 mm descent). CT myelography showed dural leak at L1-L4 on the left side. Additionally, early excretion of renal contrast was noted on CT myelography (Figure 1). EBP was performed twice, however she continued to have orthostatic headaches and episodes of syncope. Repeat brain and spine neuroimaging was normal. HUTT showed orthostatic intolerance with baseline HR of 61 bpm and increased to 115 bpm at 7 min of tilting. Cardiac SV decreased by 40% with increased sympathetic activity. Cerebral perfusion (near infrared spectroscopy) decreased by 6 points. Her systolic BP was 112 mm Hg at baseline and increased to 122 mm Hg at 7 min of tilting. She was prescribed fludrocortisone with improvement of symptoms of orthostatic intolerance.

## Discussion

Our case series demonstrates that SIH and orthostatic intolerance together can cause orthostatic headaches in an individual patient. Most spontaneous CSF dural leaks occur at the thoracic spine level,<sup>11</sup> as opposed to most of our patients who had either cervical or lumbar CSF leaks.

Contrast enhanced MRI of brain and spine is usually the first modality of investigation however, it can be normal 20 to 25% of time.<sup>11,12</sup> Mokri proposed that CSF hypovolemia results in

sagging of the brain and stretching of pain sensitive structures giving rise to postural symptoms in SIH. Based on the Monro-Kellie doctrine, CSF hypovolemia results in intracranial volume decompensation, leading to spontaneous subdural hematomas, engorgement of epidural venous plexus and venous hyperemia with abnormal MRI findings of diffuse pachymeningeal enhancement.<sup>13,14</sup> In our series, only two of seven patients had abnormal neuroimaging showing cerebellar tonsillar ectopia and syringomyelia.

LP is helpful in making a diagnosis of SIH if the CSF OP is low<sup>11,12</sup> (<6 cm H<sub>2</sub>O). In our case series only one out of seven patients had low CSF OP. Schievink et al.<sup>11</sup> described in a study of 106 patients with SIH, only 34% of patients had low CSF OP. Diagnosis of SIH for all our patients was confirmed with CT myelography. Three of seven patients were noted to have early visualization of contrast in the renal collecting system suggesting a possibility of underlying CSF-venous fistula.<sup>15</sup>

In the upright position, patients with orthostatic intolerance have an abnormal autonomic nervous system response with impaired venous return to the heart and decreased perfusion of the brain,<sup>8</sup> which leads to syncope. Clinical symptoms of SIH and orthostatic intolerance overlap.<sup>5</sup> Previous authors suggest that dysautonomia should be suspected in patients with orthostatic headaches when no evidence of CSF leak is found.<sup>2</sup> Graf et al. described a retrospective study of 57 adult patients (48 patients with orthostatic intolerance and 9 patients with SIH) having overlapping clinical symptoms such as nausea (78%), dizziness (67%) and light headedness (22%).<sup>5</sup> In this study, all 9 patients with SIH had an increase in HR during HUTT and showed features of orthostatic intolerance. Kato Y et al.<sup>7</sup> described an adult female having SIH associated with

orthostatic intolerance. Orthostatic headaches in orthostatic intolerance is postulated to be due to relative CSF hypovolemia.<sup>2</sup> It is unclear why patients with SIH could have features of autonomic dysfunction. Franzini and colleagues proposed that SIH could be caused by decreased venous flow to the inferior vena cava leading to epidural venous hypotension.<sup>16</sup> In orthostatic intolerance there is decreased venous return in the inferior vena cava resulting in decreased blood flow to the heart with compensatory increase in HR. This hypothesis could be a possible unifying mechanism for development of autonomic dysfunction and SIH. Limitation of this study relates to its retrospective analysis in a small group of patients.

In conclusion, our case series shows that young patients with SIH can have overlapping symptoms with orthostatic intolerance, however treatment of both the conditions is quite different. We recommend that young patients with SIH who do not obtain significant headache relief after multiple blood patches be evaluated for autonomic dysfunction with physiological studies such as HUTT. All our patients improved with treatment for both SIH and orthostatic intolerance.

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### Author Contributions

AG is the first author who reviewed the charts, gathered, and analyzed the data, reviewed the literature, and drafted the manuscript. YT and LG are second coauthors who helped in reviewing patient charts and contributed to the manuscript writing. MN helped with reviewing head up tilt table test, RP helped with reviewing neuroimaging, IB supervised the study and revised the article.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical Approval

There were no patient identifiers in the manuscript or tables, and no institutional review board approval was required as this was a retrospective case series.



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### Informed Consent

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### Trial Registration

Not applicable, because this article does not contain any clinical trials.

### Supplemental Material

Supplemental material for this article is available online.

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