



Intracranial Hypotension Syndrome with Cortical Venous Thrombosis: A Rare Case

İntrakranyal Hipotansiyon Sendromunun Eşlik Ettiği Kortikal Venöz Tromboz: Nadir Bir Olgu

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Summary

A married woman aged 31 years who was a vegetarian presented with symptoms of fever with orthostatic throbbing headache, which she had for 7 days. Lumber puncture with manometry showed a low pressure of 40 mmH₂O. Magnetic resonance imaging of the brain showed prominent bilateral symmetric pachymeningeal enhancement with prominent engorged venous sinuses suggestive of intracranial hypotension syndrome. Magnetic resonance venography showed non-visualization of the left transverse and sigmoid sinus suggestive of cortical venous thrombosis. Spontaneous intracranial hypotension, though rare is a real risk factor for cortical venous thrombosis. A high degree of suspicion is needed for a timely diagnosis.

Keywords: Intracranial hypotension syndrome, cortical venous thrombosis, orthostatic headache

Öz

Ortuz bir yaşında, evli, vejetaryen kadın hasta 7 gündür devam eden ortostatik zonklayıcı baş ağrısı ve yüksek ateş yakınmaları ile başvurdu. Lomber ponksiyonunda manometri ile ölçülen açılış basıncı düşük saptandı (40 mmH₂O). Beyin manyetik rezonans görüntülemesinde intrakranyal hipotansiyon sendromunu düşündüren venöz sinüslerde belirgin angorjman ile bilateral, simetrik belirgin pakimeningeal kontrastlanma izlendi. Manyetik rezonans venografide kortikal venöz trombozu düşündüren sol transvers ve sigmoid sinüsün görüntülenemediği izlendi. Spontan intrakranyal hipotansiyon, nadir olsa da, kortikal venöz tromboz için gerçek bir risk faktörüdür. Zamanında tanı için yüksek derecede şüphe gereklidir.

Anahtar Kelimeler: İntrakranyal hipotansiyon sendromu, kortikal venöz tromboz, ortostatik baş ağrısı

Introduction

Intracranial hypotension may have variable clinical presentations, but has a rather uniform component of postural headache among its symptomatology. The aim of this case report was to highlight the clinical presentation of intracranial hypotension syndrome, which can mimic meningitis and result in inadvertent use of antibiotics or antitubercular treatment. The case report also focuses on ascertaining the relationship between intracranial hypotension and thrombus formation.

Case Report

A married woman aged 31 years who was a vegetarian presented with symptoms of fever with headache, which she had had for 7 days. Her fever was low grade, intermittent, and not associated with chills, rigors or rashes. The headache occurred bilaterally in the frontal area, was of moderate intensity, aching in nature, aggravated by sitting and bending forward, relieved by lying down, and associated with nausea and vomiting. Vomiting was non-projectile, non-bilious, and not blood stained. There was no history of seizures, weakness of any limb, loss of consciousness,

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urinary incontinence, photosensitivity or ear discharge. The patient had tuberculosis of the bone 3 years previously for which she had taken anti-tubercular drugs for 18 months. There was no significant past history or any other chronic disease. The family history was not contributory. The patient had normal menstrual cycles. She had two live births, the youngest child aged 3 years, both by normal delivery. There was no history of abortion and she was not presently taking any oral contraceptive pills.

On examination, the patient was conscious, oriented to time, place, and person. Her blood pressure was 104/70 mmHg and pulse rate was 90/min. There was no pallor, icterus, cyanosis, clubbing, pedal edema or lymphadenopathy. Respiratory, cardiovascular, abdominal and central nervous system examinations were unremarkable. Her fundus examination was also normal.

On investigation, her hemoglobin was 11 gm/dL, with a total leukocyte count of 8000/mm³, 64% polymorphs, 36% lymphocytes, and platelet count 180000/mm³. The erythrocyte sedimentation rate was 68 mm/hour. Her renal and liver function tests were normal. Her serum electrolytes, calcium, phosphate, serum proteins, and thyroid profile were also normal. Urine culture and blood culture were sterile and the Widal test was also negative. The malarial antigen card test and serology for leptospira and scrub typhus were negative. The antinuclear antibody assay, enzyme-linked immunosorbent assay for Hepatitis B surface antigen, anti-Hepatitis C virus, and Human immunodeficiency

virus were also negative. Her C-reactive protein level was raised. Lumbar puncture with manometry showed a low pressure of 40 mmH₂O. A cerebrospinal fluid (CSF) examination revealed a raised protein level 450 gm/dL, sugar level 72 mg/dL, with a corresponding blood sugar level of 120 mg/dL, the total leukocyte count was 178 cells/mm³, with 98% lymphocytes suspicious of tubercular meningitis. However, adenosine deaminase levels were normal and polymerase chain reaction analysis for Mycobacterium tuberculosis, Herpes simplex 1, 2, and enterovirus were negative. CSF culture and Gram stain were also negative. Complete urinalysis was normal and showed no albuminuria or pus cells.

Electrocardiography, chest X-ray, and ultrasonography of the abdomen were within normal limits. Noncontrast head computerized tomography was normal. Magnetic resonance imaging (MRI) of the brain showed prominent bilateral symmetric pachymeningeal enhancement with prominent engorged venous sinuses, prominent enhancement of the tentorium cerebelli, small ventricles, effaced sulci, prominent pituitary gland, no significant corpus callosum or cerebellar sagging, which was suggestive of intracranial hypotension syndrome (Figure 1). Based on characteristic MRI findings and low pressure CSF findings, a diagnosis of intracranial hypotension syndrome was made and the patient was started on conservative treatment with intravenous fluids and steroids. The patient had a mild improvement in symptoms. Further magnetic resonance venography showed non-

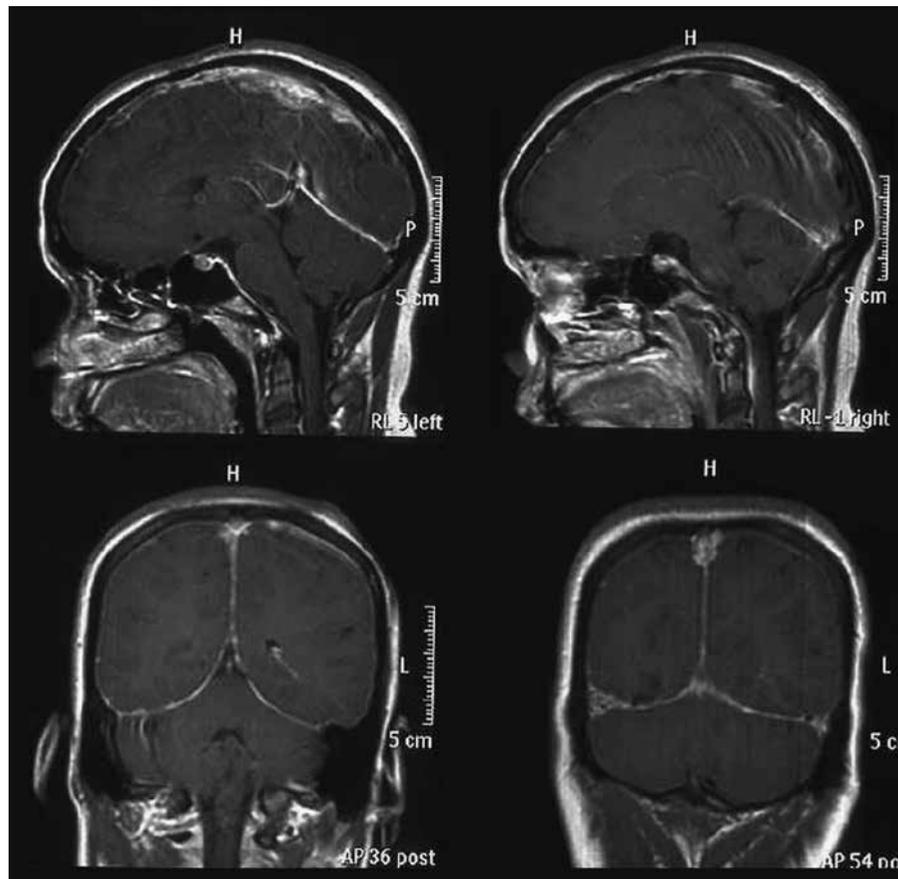


Figure 1. Magnetic resonance imaging brain findings suggestive of intracranial hypotension syndrome

visualization of the left transverse and sigmoid sinus, which was suggestive of cortical venous thrombosis (CVT) (Figure 2). Low-molecular-weight heparin was also added to the treatment and the patient was later transferred to warfarin. The patient began to recover from her symptoms. On repeated CSF examination, her proteins and sugar levels became normal with a total leukocyte count of 4 cells/mm³.

After around 2 weeks, the patient was discharged in a stable condition on oral anticoagulant warfarin. Oral anticoagulant was stopped after 6 months. Her coagulation profile including protein C, S, and factor V Leiden was normal 2 months after stopping anticoagulant therapy. A repeat MRI scan was performed after 6 months, which revealed a normal study, thereby ruling out any congenital anomaly.

Discussion

Spontaneous intracranial hypotension (SIH) is nowadays recognized with increasing frequency. SIH is an important cause of new-onset orthostatic headache, and is more common in females. Its incidence is estimated as five cases per 100 000. An orthostatic throbbing headache that occurs or worsens in the upright position and improves after lying down is a classic feature of intracranial hypotension syndrome. This syndrome is characterized by typical orthostatic headaches, low CSF pressure (<60 mmH₂O), diffuse pachymeningeal enhancement, sinus engorgement, subdural collections, and brain herniation on brain MRI imaging (1). These patients can be mistaken as having aseptic meningitis because they present with a similar manifestation of fever, headaches, and CSF findings of lymphocytic pleocytosis, elevated protein concentration, normal glucose levels, and negative culture results. The diagnostic

criteria of SIH as proposed by the International Headache Society is depicted in Table 1 (2).

Normally, CSF supports the brain such that its 1500-g weight amounts to only 48 g within the cranium. Depletion of CSF volume with downward displacement of the brain causes traction on pain-sensitive structures. The Monro-Kelly thesis proposes dilatation of intra-cranial pain sensitive vascular structures as the cause of headache, which could worsen in the upright position and by the Valsalva maneuver (1).

Table 1. Diagnostic criteria for spontaneous intracranial hypotension

A. Diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, fulfilling criterion D and with 1 or more of the following: <ol style="list-style-type: none"> 1. Neck stiffness 2. Tinnitus 3. Hypoacusia 4. Photophobia 5. Nausea
B. At least one of the following: <ol style="list-style-type: none"> 1. Evidence of low CSF pressure on MRI (e.g., pachymeningeal enhancement) 2. Evidence of CSF leakage on conventional myelography, CT myelography, or cisternography 3. CSF opening pressure <60 mmH₂O in the sitting position
C. No history of dural puncture or other cause of CSF fistula
D. Headache resolves within 72 hours after epidural blood patching
MRI: Magnetic resonance imaging, CSF: Cerebrospinal fluid, CT: Computed tomography

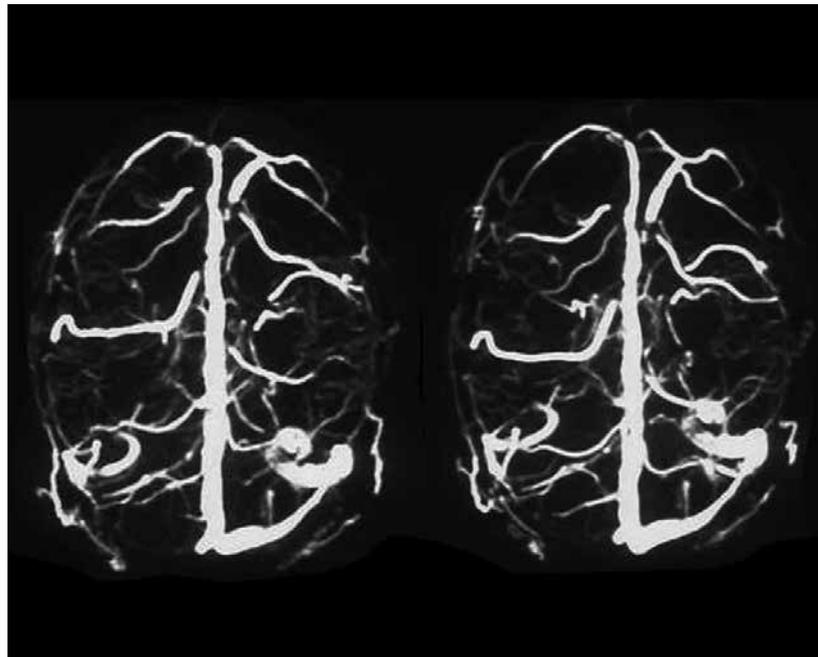


Figure 2. Magnetic resonance venography showed non-visualization of left transverse and sigmoid sinus suggestive of cortical venous thrombosis

Fever seen in patients with SIH might be explained by the release of pyrogenic cytokines by endothelial cells and astrocytes of the blood-brain barrier secondary to a drop in CSF pressure. These cytokines are the main mediators of the inflammatory response in infectious and non-infectious disorders (3). Another suggested mechanism for fever is impaired hypothalamic thermoregulation secondary to mechanical distractions and venous engorgement in cavernous sinus and diencephalic region. The main features of patients with aseptic meningitis and SIH were compared in a recently reported case series from Turkey (4). In SIH, all patients had headache, the important distinguishing feature being orthostatic headache. Out of 11 patients, fever was reported in seven patients, and neck rigidity was present in 5. Among the neurologic disorders, photophobia and phonophobia were most frequent followed by subtle cognitive deficits, amnesia, confusion, hyper-excitability, and syncope. Our patient presented with fever, headache, and irritability that mimicked meningitis, but low CSF opening pressure and characteristic MRI findings, which helped us make the diagnosis. The diagnostic criteria published by International Headache Society should be recommended to define or exclude SIH in the differential diagnosis.

CVT is a rare complication in SIH, which seems to constitute a rare (2.7%) local risk factor for thrombosis. Also, in a review performed in 2008, CVT was reported in only 2.1% of patients with SIH (5). Schievink and Maya (5) observed 141 patients with SIH and CVT was only seen in 3 (2.1%) as a complication. Haritanti et al. (6) reported one case of SIH in six patients with CVT (17%), Li and Lai (7) documented 1 in 11 (9%), Berroir et al. (8) reported two in 30 (7%) patients with CVT as a risk factor.

Little is known about the relationship between intracranial hypotension and cerebral blood flow. To our knowledge, there have been few reports regarding thrombus formation in SIH. Many hypotheses have been put forward to establish the cause of CVT in SIH syndrome. First, any loss of volume in the intracranial space has to be compensated by an increase in another because it is a closed compartment (Monroe-Kelly doctrine). Therefore, loss of CSF due to seepage results in expansion of the venous compartment, which is most expansile (9). Secondly, SIH leads to caudal displacement of the brain due to decreased CSF buoyancy (10), which stretches the venous sinuses resulting in endothelial injury (6). Thirdly, CSF loss leads to its decreased absorption, which causes increased viscosity (11). However, the presence of SIH should not prevent the search for other thrombotic risk factors.

The management of SIH is generally conservative with measures such as bed rest, caffeine administration, theophylline, adequate hydration, increased salt intake, CO₂ inhalation, and steroid therapy; however, in the event that leaks or tears are detected, epidural blood patch and surgery can be performed (12). The impact of medical management remains unknown because CVT in SIH is rare and no controlled therapeutic trials have assessed the role of anticoagulants.

To conclude, the varied manifestations of SIH along with its unfamiliarity with physicians leads to a delay in diagnosis and exposes the patient to risk of various medications and procedures. Symptoms of headache, especially orthostatic in nature with typical neuroimaging findings, could be a vital clue for suspecting it in the diagnosis. SIH, though rare, is a real risk factor for CVT. A high degree of suspicion leading to timely diagnosis and early management can reduce morbidity and financial burdens.

Ethics

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Deepak Jain, Ashima Mittal, Concept: Deepak Jain, Design: Deepak Jain, Data Collection or Processing: Ashima Mittal, Analysis or Interpretation: Deepak Jain, Literature Search: Deepak Jain, Ashima Mittal, Writing: Ashima Mittal, Deepak Jain.

Conflict of Interest: No conflict of interest was declared by the authors.

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