

Spontaneous intracranial hypotension in Graves' disease

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ABSTRACT

Autoimmune thyroid disorders such as hyperthyroidism and hypothyroidism are rare causes of intracranial pressure alterations. We present a case of spontaneous intracranial hypotension associated with Graves' disease which was not reported previously in the literature. A 42-year-old woman was admitted to our institution because of a sudden developed headache, neck pain, nausea and vomiting. The headache was severe during standing and walking but improved within 15 to 30 minutes after lying down. Thyroid gland was grade 1b diffuse palpable and other physical examinations were normal. Autoimmune hyperthyroidism was diagnosed according to laboratory results. Gadolinium-enhanced magnetic resonance imaging revealed a hyperintensity that is consistent with thickened dura and subdural effusion. The patient was managed with bed rest, hydration, methimazole, methyl-prednisolone 16 mg/day of three days and then tapered gradually. After these medications the headache resolved. It should be kept in mind that encephalopathy associated autoimmune thyroid disease may be related with spontaneous intracranial hypotension.

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Introduction

Spontaneous intracranial hypotension (SIH) develops due to spontaneous spinal cerebrospinal fluid (CSF) leaks. Diagnostic criteria for headache disorders are described by an international classification [1]. It is clinically characterized by an acute or gradual onset of severe orthostatic headache which is relieved with supine position and may be co-exist with tinnitus, diplopia, photophobia, nausea, vomiting, vertigo, neck

stiffness, local back pain, facial numbness or weakness [2].

Extra thyroidal manifestations of Graves' disease include thyroid opthalmopathy, dermopathy and acropachy. In addition autoimmune thyroid diseases may be associated with neurological diseases. Key clinical features of "encephalopathy associated autoimmune thyroid disease" include alterations in

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consciousness, stroke-like events, seizures, tremor, and myoclonus [3]. Albeit rare, endocrine dysfunction (hyperthyroidism or hypothyroidism) is an established cause of benign intracranial hypertension. Reversible benign intracranial hypertension in a patient with autoimmune hyperthyroidism has been reported by Merkschlager *et al.* [4]. To the best of our knowledge, we report herein the first case in the literature presenting an association between Graves' disease and SIH.

Case Presentation

A 42-year-old woman was admitted to our institution due to sudden-onset headache, neck pain, nausea and vomiting. The headache was severe as long as the patient stands and walks but improved within 15 to 30 minutes provided the patient remained in lying position. There was no loss of vision or photophobia. She was afebrile without any history of spinal trauma, lumbar puncture, surgery, vigorous exercise or sneezing and straining. Based on the obtained anamnesis, she was diagnosed with Graves' disease two years ago which has been in remission state achieved eight months ago.

Blood pressure (125/75 mmHg) and pulse (84/min) were in normal limits. Skin was thin and moist. Thyroid gland was grade 1b diffuse palpable. Other physical examinations, including respiratory, cardiovascular, abdominal, and neuromuscular examinations were all normal. Optic fundus examination was normal.

The laboratory findings were as follows: serum freeT3 >32.2 ng/dL (1.80-4.60 ng/dL), free T4 >7.74 ng/dL (0.93-1.70 ng/dL), thyroid-stimulating hormone <0.01 μ IU/mL (0.27-4.20 μ IU/mL), TSH receptor antibody 219.94 U/L (14-100 U/L), anti-thyroid microsomal antibody 600 IU/mL (\leq 34 IU/mL) and thyroglobulin antibody 193.1 IU/mL (\leq 115 IU/mL). All other laboratory values were in normal range.

Gadolinium-enhanced magnetic resonance imaging (MRI) showed a hyperintensity suggesting thickened dura and subdural effusion. Imaging findings were in countenance with SIH (Figure 1).

Management of the patient involved bed rest, hydration, methyl-prednisolone 16 mg/day for three days which tapered gradually and the headache subsequently resolved. In addition to methimazole for thyrotoxicosis, radioactive iodine (I-131) treatment was also planned.

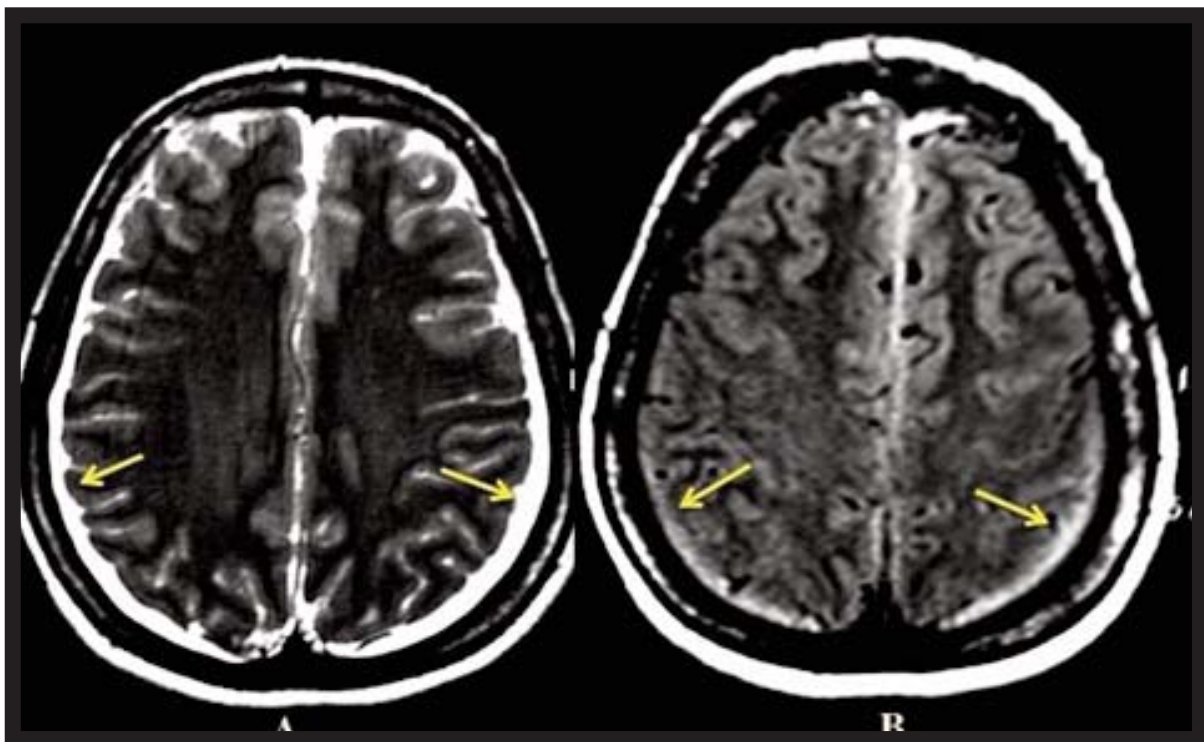


Figure 1. T2-weighted (A) and FLAIR (B) transverse images show hyperintensity of thickened dura and subdural effusion on both hemispheres (arrows).

Discussion

Intracranial hypotension is a clinical syndrome in which orthostatic headache is induced by low volume of CSF. Severe cases may provoke nausea, vomiting, photophobia, and decreased level of consciousness. Most probably, downward displacement of the brain exerting traction on the richly innervated dura causes orthostatic headache in SIH. A majority of the orthostatic headache cases exhibit a gradual onset with a range of severity from mild to debilitating. The headache of our patient was severe when she stood upright or walked but improved within 15 to 30 minutes after she rested in lying position [5]. Characteristics of the headache of our patient were compatible with SIH. Along with the postural headache, secondary symptoms such as posterior neck pain, nausea and vomiting, are common and attributable to meningeal irritation in approximately half of the patients, as in our patient. According to the 2004 International Classification of Headache Disorders at least one of the above-mentioned secondary symptoms, in addition to orthostatic headache, must be present in order to make the diagnosis of headache due to SIH [1]. SIH has an incidence of 5 per 100.000 of the population with a higher occurrence in women and mostly diagnosed in 4th to 6th decade of life [5].

Most often a leakage of CSF through a dural defect leads to SIH, which actually could be primary (idiopathic) or secondary. When it arises in secondary fashion cranial or spinal surgery, head or spine trauma and lumbar puncture may be the underlying reason. The reason of primary SIH is unknown but possible mechanisms include sagging of the brain, dilation of intracranial veins, and activation of adenosine receptors [5]. In 1938, Schaltenbrand [6] described a condition of low or negative CSF pressure with associated orthostatic headache, and postulated three possible causes as follows: low CSF production, high rate of CSF absorption, and CSF leakage. Typical MRI findings of pachymeningeal enhancement should suggest the benign SIH condition. Diffuse meningeal enhancement as detected by imaging studies in relation to intracranial hypotension was first highlighted as a phenomenon in an abstract from Mokri *et al.* [7] in 1991. The MRI changes include a marked degree of diffuse, smooth, contiguous dural thickening (2-8 mm) and enhancement, involving the supratentorial, infratentorial and cervical pachymeninges with no skip areas [8]. In our patient

characteristic MRI findings for SIH were noted.

Therapeutic approach recommends strict bed rest and use of epidural blood patch to seal the CSF leakage. Reports indicate positive outcomes attained by corticosteroid treatment and epidural saline infusion [2, 5]. Management in our case employed bed rest, hydration, methyl prednisolone (16 mg/day) for three days which was gradually tapered and the headache subsequently resolved. Methimazole treatment was initiated against thyrotoxicosis.

The likely association of autoimmune thyroid diseases (mostly Hashimoto and lesser Graves' disease) with neurologic diseases was mentioned in a systematic review published in 2006 [9]. Diagnosis of a neurologic disorder associated with thyroid autoimmunity is made upon the event of neuropsychiatric symptoms emerge in a patient with elevated anti-thyroid antibody levels in serum. Until now, no clinical, laboratory or neuroimaging findings that are specific for this entity could be defined. Key clinical features of "encephalopathy associated with autoimmune thyroid disease" are changes in consciousness, stroke-like events, seizures, tremor, and myoclonus [10]. The clinical picture of our patient, however, was not similar to any of these conditions.

A possible condition that might interfere with SIH is pseudotumor cerebri (PTC). PTC is characterized by an elevated intracranial pressure while CSF analysis is preserved as normal and cerebral MRI scans excludes any structural abnormalities. Neurological symptoms are headache, temporary visual disturbances, nausea and vomiting, as well as SIH and papilledema are expected common findings in adults. Reports have pointed out autoimmune thyroid disorders, hypothyroidism and hyperthyroidism causes of PTC [11, 12]. Our patient had neither papilledema nor features of intracranial hypertension on MRI images. Therefore, we did not think intracranial hypertension.

Conclusion

We aimed to present a case with concurrent SIH and Graves' disease. To the best of our knowledge, it is the first case in the literature presenting an association between Graves' disease and SIH. The likelihood of SIH contribution should not be

overlooked in case of encephalopathy associated with autoimmune thyroid disease. Further studies must be planned for explaining the possible relationship between these two conditions.

Informed consent

Written informed consent was obtained from the patient for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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