Pseudotumor cerebri in a child with hyperimmunoglobulin E syndrome

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Hyperimmunoglobulin E syndrome (HIES) is recognized as a multisystem disorder with various connective tissue, skeletal and immunologic abnormalities. Central nervous system abnormalities have been considered a feature of HIES. Pseudotumor cerebri (PTC) is a condition characterized by increased intracranial pressure in the absence of any intracranial mass lesion or ventricular dilatation, with normal neurology and cerebral spinal fluid composition. PTC without papilledema is rarely reported in children. We describe an atypical presentation of PTC in a child with HIES.

Key words: hyperimmunoglobulin E syndrome, pseudotumor cerebri, children.

Hyperimmunoglobulin E syndrome (HIES) is a rare primary immunodeficiency characterized by eczema, recurrent skin and lung infections, elevated serum IgE, and various connective tissue, skeletal, and vascular abnormalities[1,2]. In the literature, several central nervous system (CNS) abnormalities in patients with HIES have been described, including occlusion of the cerebral artery, aneurysms, ischemic stroke, CNS vasculitis, lacunar infarcts, focal hyperintensities, CNS infections, and Chiari 1 malformations[2,3].

Pseudotumor cerebri (PTC) is characterized by an elevation in intracranial pressure in the absence of intracranial mass, inflammation or obstruction, with normal cerebrospinal fluid (CSF) contents and neurologic imaging results, and normal neurologic examination results except for abducens nerve palsy. However, atypical cases are described in the adult literature in which papilledema could be asymmetrical, unilateral, or even absent[4]. Here, we describe a child with HIES who presented with headaches and vomiting who was diagnosed as PTC without papilledema.

Case Report

A four-year-old girl presented to our hospital with complaints of progressively worsening headaches and vomiting for three weeks. Her parents were first-degree relatives. Two siblings had HIES, and the current patient had an extremely high serum IgE concentration (2900 IU/ml) and was diagnosed as HIES one year ago. There was no history of seizure, head trauma, loss of consciousness, or fever.

On physical examination, her vital signs including blood pressure were normal. There was no impairment in her consciousness. Both pupils were normal in size, shape and reaction. There were no features of neck stiffness or any cranial nerve abnormalities. Papilledema was not found on fundus examination. Snellen visual acuity and visual field grades could not be performed because of her young age. The remainder of the neurological examination was normal. An otolaryngologic examination revealed no abnormalities.

In laboratory investigations, full blood count, serum electrolytes, blood urea nitrogen (BUN), creatinine, bilirubin, alanine aminotransferase, aspartate aminotransferase, ammonia, and prothrombin time were within the normal limits. Her thyroid profile was normal. Serological tests were negative for hepatitis A-C viruses, Epstein-Barr virus, cytomegalovirus, *Toxoplasma gondii*, Rubella virus, *Mycoplasma pneumoniae,* and *Chlamydia pneumoniae*. Her lumbar puncture showed an increased opening pressure (480 mm water). The CSF was clear

with normal cell count, protein and glucose content. CSF culture for bacteria was negative. Her cerebral magnetic resonance imaging, cerebral angiography and venography were normal. The child was diagnosed as PTC. The patient was started on oral acetazolamide 25 mg/kg daily. After one week, the headache and vomiting had resolved significantly.

Discussion

The modified Dandy criteria used to diagnose PTC include headache, increased intracranial pressure (>250 mm water) with normal CSF constituents, no focal neurological deficits, normal neuroimaging results in an awake and alert patient, and papilledema[5]. Although headache is the most common symptom in PTC, transient visual obscurations, pulsatile intracranial noises and diplopia are also noted, though less frequently. The most important complication is visual loss.

Pseudotumor cerebri without papilledema, although well described in adults, is rarely reported in children[4,6]. Beri et al.[4] reported six children who were diagnosed as PTC without papilledema, like our patient. The pathophysiology for a lack of papilledema is not well-known. This could be attributed to congenital or acquired optic nerve sheath abnormalities, an interstitial elevation in intracranial pressure below the threshold for producing papilledema, or a resolution of papilledema because of the chronic nature of the disease. Lack of papilledema could also be attributable to an extensive trabecular meshwork within the nerve sheath[7].

Pseudotumor cerebri may be primary or occur secondary to certain conditions. In secondary cases, some conditions have been identified as causative agents, including certain medications, endocrine abnormalities, autoimmune disorders, anemias, and cranial venous outflow abnormalities[8]. To exclude underlying causes of secondary PTC, screening tests for CNS infections, cerebral focal lesion, stroke, cerebral sinus thrombosis, and endocrine abnormalities were performed. We could find no etiological reason for increased intracranial pressure.

Hyperimmunoglobulin E syndrome is a multisystem disorder with abnormalities of the immunologic, connective tissue, and skeletal tissue systems. There are also some morphologic abnormalities in connective tissue in many patients, including characteristic facies, scoliosis, joint hyperextensibility, retained primary dentition, craniosynostosis, osteopenia, and pathologic fractures[1,2]. There are a few previous reports of CNS abnormalities in HIES, mostly related to infections[2,3]. Freeman et al.[2] found neurologic abnormalities such as focal hyperintensities, ischemic stroke, lacunar infarcts, aneurysms of the cerebral artery, and Chiari 1 malformations. We found no CNS abnormalities in this patient except PTC.

In conclusion, PTC is a rare but important CNS complication of HIES. Early diagnosis is important, especially in atypic cases, for preserving visual functions and preventing unnecessary analgesic medications for headaches.

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