Unusual Presentation of Acute Lymphoblastic Leukemia Masquerading Idiopathic Intracranial Hypertension

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Abstract- Idiopathic intracranial hypertension (IIH) is defined as increased cerebrospinal fluid (CSF) opening pressure and abnormal fundoscopy when other causes of increased intracranial pressure are ruled out. We present a patient with a primary diagnosis of IIH who had undergone a lumboperitoneal shunt. Later she was treated with shunt revision, anti-tuberculosis drugs, and intravenous immunoglobulin. Acute lymphoblastic leukemia (ALL) was diagnosed after bone marrow biopsy. The initial response to chemotherapy was promising. Careful history taking, avoidance of unnecessary repetition of diagnostic procedures, avoidance of a tunneled vision, and a strong clinical suspicion is important to see the hidden causes underlying a difficult case of pseudotumor cerebri. Acute lymphoblastic leukemia and carcinomatous meningitis should be sought in IIH patients with abnormal presentation and unusual response to the known treatments.

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Introduction

Idiopathic intracranial hypertension (IIH) or primary pseudotumor cerebri (PTC) is a syndrome of increased intracranial pressure (ICP) typically seen in an overweight woman of childbearing age (1). It is most commonly manifested by headache, visual disturbance, tinnitus, and papilledema (2). Neurological deficit, such as bilateral abducens nerve palsy is common (3). Cerebrospinal fluid (CSF) analysis and neuroimaging should be normal (4). Diagnosis is made by documentation of papilledema and elevated opening pressure at lumbar puncture (LP). Optical coherence tomography (OCT) has been shown to have a good correlation with optic nerve and peripapillary changes (4). Thrombosis or stenosis of the lateral sinus may be either a cause or an effect of intracranial hypertension, and a mechanism of the vicious cycle may be present (5,6). Standard of treatment is weight loss and using acetazolamide, and if treatment is failed, surgical options including lumboperitoneal shunt, ventriculoperitoneal shunt, and optic nerve fenestration could be considered (4).

It is very important to investigate other causes of intracranial hypertension. In this paper, we introduce an unusual case that first has been diagnosed as IIH and treated with lumboperitoneal shunt, and despite developing new symptoms, the correct diagnosis was not made until after one year.

Case Report

A 24-year-old woman was consulted with dense paraplegia and sphincter dysfunction but no sensory dysfunction. She had been previously undergone three operations of lumboperitoneal shunt after diagnosis of IIH. The sequence of symptoms are as follows; 12 months ago, sciatica-type pain in lower extremities that responded to conservative therapy; 10 months ago, blurred vision and sixth nerve palsy that was responded to a few lumbar punctures; 9 months ago she underwent lumboperitoneal (LP) shunt which is revised two times, one and two months later. After the first operation, lower extremities' weakness made her use a crutch.

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However, when asked retrospectively, she mentioned that the progressive weakness of the lower extremities had, actually, been started before the first operation. She densely paraplegic since last two months; complete sphincter dysfunction is present. In examination, there is no sensory deficit. During the period that she underwent two revision surgeries, she has been hospitalized for more than two months. Meanwhile, several diagnostic and therapeutic actions have been taken. She has been taking anti-tuberculosis medication for 2 months, which was discontinued later. She had been also subjected to intravenous immunoglobulin (IVIG) therapy, but no constant positive response occurred. One episode of leukopenia has been mentioned, and when consulted with a hematologist, it has been treated with granulocyte colony-stimulating factor (GCSF). Moreover, during revision surgery, thickening of cauda equina and arachnoiditis were mentioned. Nerve conduction studies in the same phase detected severe L3 to S1 root lesion. On whole neuraxis magnetic resonance imaging (MRI), there was no pathological finding except for a 1-2 mm tonsillar herniation, mild to moderate L4/L5 disc bulging, a misplaced LP shunt catheter at T12/L1 level and intrathecal fullness compatible with intraoperative observation of arachnoiditis (Figure 1 a-d).

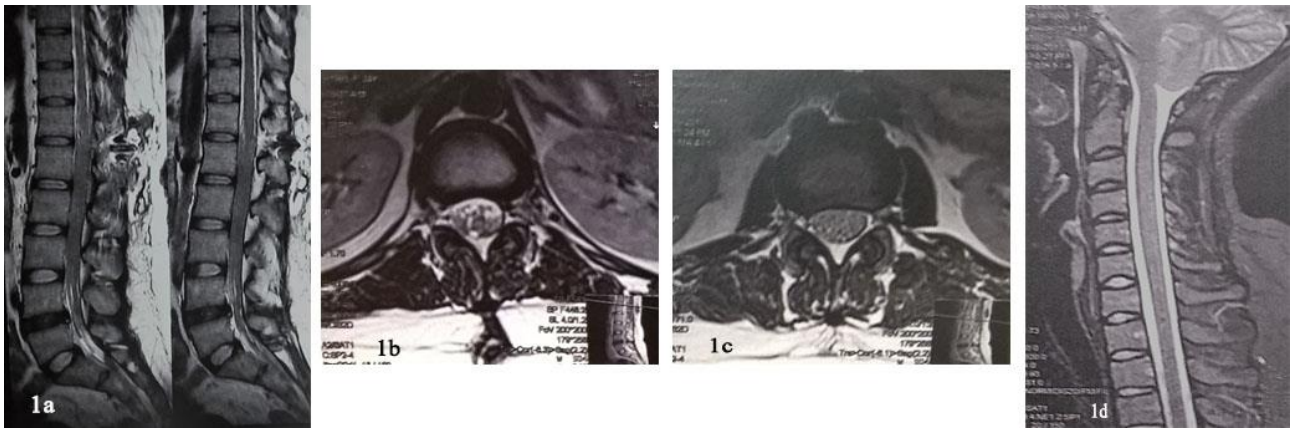

Figure 1. We can see sagittal (a) and axial views (b, c) of lumbosacral MRI that shows an entrance point of LP shunt at level of conus. Cervical (d) MRI of the patient revealed a 1-2 mm tonsillar descends

During the course of hospitalization in our center, lower cranial nerve deficits occurred, leading to dysphagia and necessitated intubation of the patient. Nerve conduction studies reported active polyradiculopathy and cranial nerve involvement, and also, the anterior Horn Disease or Diffuse meningeal involvement was suggested. At the same time, a modest drop in platelet and hemoglobin persuaded us to do an open bone marrow biopsy. Finally, the diagnosis of ALL was confirmed. A rapid response was observed after the start of chemotherapy.

Discussion

Diagnosis of IIH or primary PTC in a patient with headache and visual problems is usually made by the detection of papilledema and a raised CSF opening pressure in the absence of secondary causes. Unusual presentations have been reported in the literature; a very rapid course of visual deterioration and blindness in one week or one month have been reported (7,8). Some patients may have symptoms and signs very similar to PTC while they have normal CSF pressures (9,10). The involvement of multiple cranial nerves, other than the 6th cranial nerve, is reported rarely in PTC (11,12).

There are also reports that mention challenges in the diagnosis of PTC, association with Chiari syndrome, undiagnosed optic nerve sheath meningioma, pseudotumor cerebri syndrome secondary to anemia, and undiagnosed pancraniosynostosis were among the reported diagnostic challenges (13,14,15,16). We present a case of undiagnosed hematologic malignancy in a patient who first has treated surgically for PTC.

According to this case three different scenarios can be proposed as the most probable etiologies; first, raised intracranial pressure secondary to ALL also reported by Russell *et al*., (17); in this scenario, presence of symptoms from nearly one year ago prompts a slow progression of ALL, so that the CNS manifestations have occurred months before the hematologic manifestation. CNS involvement at the presentation time is uncommon in the setting of ALL occurring in 5 to 7%

of patients (18). Neoplastic meningitis occurs in 5-15 % of leukemia patients, an in this condition; if it is left untreated, survival would be 4 to 6 weeks (18). So, according to the natural history of ALL and neoplastic meningitis, this scenario could not be postulated. Moreover, multiple samples of CSF did not contain any clue in favor of neoplastic meningitis.

Second, the coincidence of ALL in a patient with a background of PTC; this is a possible scenario, but the presence of progressive weakness in the lower extremities before and after the diagnosis of PTC is against this suggestion. Weakness cannot be explained by pure PTC (4).

In the third scenario, we assume the presence of a Guillain- Barre-like syndrome. It is suggested by the presence of progressive weakness, first involving the lower extremities and then the cranial nerves and lack of sensory symptoms. Association of Guillain-Barre with PTC or with ALL has been reported elsewhere (19,20). However, it is not a classic ascending paralysis because the upper extremities were unaffected. Besides, we did not have characteristic electrophysiologic features of Guillain-Barre. A controversial response to IVIG cannot prove anything.

When MR imaging is reviewed, it is evident that the insertion point of the LP shunt is in T12-L1 space at the level of conus, which is an inappropriate location and suggested an intra-operative conal injury at first glance. However, sensory-sparing nature and later, the progression of the disease to involve the lower cranial nerves made this diagnosis less likely. It is not clear if ALL is a comorbidity that is added to PTC, or it is the cause of PTC. It is also possible that in a background of PTC, ALL has been developed and has changed the picture of the disease in a confusing fashion. It was quite challenging to convince hematologists to start chemotherapy because they usually do not consider intubated patients for treatment. However, apart from paralysis of cranial nerves, the general condition of our patient was not so bad, and after the start of chemotherapy, she rapidly recovered and was extubated.

It is very important to be aware of secondary causes of raised intracranial pressure, and also it is necessary to consider comorbidities that may change the scenario of PTC. The last point is that we can start chemotherapy in an apparently ill patient if there is a background of carcinomatous meningitis.

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