

Intracranial Hypertension as an Acute Complication of Aseptic Meningoencephalitis with Leptomeningeal Contrast Enhancement on FLAIR MRI

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Key Words

Aseptic meningoencephalitis · Complications · Cerebrospinal fluid reabsorption · Intracranial hypertension · Lumbar drainage

Abstract

We report a case of a 19-year-old woman who developed intracranial hypertension as an unusual clinical complication of severe aseptic meningoencephalitis probably due to a diminished cerebrospinal fluid reabsorption capacity or leptomeningeal transudation as a consequence of blood-brain barrier dysfunction. These severe inflammatory changes were accompanied by prominent leptomeningeal contrast enhancement best visualized on fluid-attenuated inversion recovery magnetic resonance imaging. In such a prolonged course, a continuous lumbar drainage might be a temporary option to provide rapid symptom relief to the patient.

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Introduction

Acute aseptic meningitis is a common disease with a usually benign clinical course [1]. Although symptomatic intracranial hypertension is a well-recognized complication of bacterial meningoencephalitis, in aseptic meningoencephalitis it is a rather uncommon phenome-

non and has been systematically assessed in children only [2]. We report a case of aseptic meningitis complicated by severe intracranial hypertension and accompanied by a distinct leptomeningeal contrast enhancement on fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI).

Case Report

A 19-year-old woman presented with a 10-day history of continuous headache, mild photophobia and nausea; her medical and recent travel history were unremarkable as was the clinical examination. Cerebrospinal fluid (CSF) analysis (120 cells/ μ l; 85% lymphocytic and 15% monocytic cells; protein 1,031.6 mg/l; glucose and lactate within the normal range) was consistent with aseptic meningitis. Treatment with acyclovir was given until proof of negative CSF PCR for herpes simplex virus. One week after admission, the patient's condition worsened with a decline in cognitive functions and a generalized epileptic seizure. She was started on levetiracetam. A prominent sulcal and leptomeningeal enhancement was noted on FLAIR MRI after contrast involving both hemispheres and the cerebellum in the absence of focal parenchymal lesions. T1-weighted postcontrast MRI also showed a slight leptomeningeal enhancement (fig. 1). Repetitive broad serologic examinations (*Herpesviridae*, HIV, enterovirus, adenovirus, respiratory syncytial virus, measles, mumps, rubella, Tick-borne encephalitis virus, influenza, borreliosis, leptospirosis, *Chlamydia pneumoniae* and *trachomatis*, *Listeria monocytogenes*, *Legionella pneumophila*, *Mycobacterium tuberculosis*, *Treponema pallidum*, *Mycoplasma pneumoniae*, *Bartonella henselae* and *Haemophilus influenzae*) and viral full-genome sequencing could not identify a pathogen. In the absence of any eosinophilia, a fungal or parasitic etiology was unlikely, neither was there any hint at a systemic autoimmune disease. The patient complained about a progressive headache intensity with continuous nausea and repeated vomiting (an overview of the clinical course is given in fig. 2). Repeated MRI demonstrated an increasing severity of the leptomeningeal contrast enhancement. A CSF opening pressure of >60 cm H₂O was documented. In the further course, she developed a right sixth nerve palsy and metamorphopsia due to bilateral papilledema. Follow-up MRI demonstrated prominent optical nerves and an empty sella compatible with intracranial hypertension; venous thrombosis was ruled out. At this time, transcranial Doppler indicated vasospasms of the middle cerebral artery, which gradually resolved on nimodipine. In repetitive lumbar punctures, an opening pressure of >60 cm H₂O was measured; after drainage of 30 ml CSF and under oral therapy with acetazolamide, a rapid but short-lasting symptom improvement was achieved after each lumbar puncture. Over the course of 14 days, a maximum CSF cell count of 314/ μ l and a protein level $>2,000$ mg/l were found. CSF glucose and lactate were always within the normal range. Cytology varied between 80 and 97% of lymphocytes and between 3 and 20% of monocytes in the CSF. Increased blood-brain barrier (BBB) permeability was repeatedly demonstrated as illustrated in the Reibergram (fig. 3). We decided to place a temporary external lumbar drainage to reduce intracranial pressure (ICP) and to avoid further punctures. Subsequently, the patient became gradually headache free, and the sixth nerve palsy and the visual disturbances gradually resolved. After 7 days, the drain was removed, and another 10 days later, the patient was discharged and fully recovered over the course of the following 4 weeks. A follow-up CSF analysis including opening pressure and MRI findings returned to normal.

Discussion

This case of aseptic meningoencephalitis has several unusual features: a rather severe complication of intracranial hypertension – requiring temporary placement of an external lumbar drainage – and a persisting almost generalized BBB dysfunction as demonstrated on postcontrast FLAIR MRI and by CSF analysis for an extended period.

Reports on peri-infectious intracranial hypertension (ICHT) are much less frequent in aseptic meningitis compared to purulent meningitis. In a small case series of 3 patients between 14 and 28 years of age with aseptic meningitis, a course with papilledema and sixth nerve palsy has been described, and an elevated CSF pressure (30 cm H₂O) has been reported in 1 of these patients [3]. The further course was very benign, and no repetitive lumbar punctures were necessary. A presentation with headache, papilledema and an elevated CSF opening pressure of 46 cm H₂O requiring 3 additional lumbar punctures was reported in a 16-year-old female with cytomegalovirus-positive meningitis [4]. Another benign course with elevated ICP has been reported in a patient with acute Toscana virus meningoencephalitis. Despite a favorable clinical course after repetitive lumbar punctures, elevated ICP was associated with a hydrocephalus on imaging [5]. In an 8-year-old girl, chronic Epstein-Barr virus infection was complicated by cerebral involvement and elevated ICP but again with concomitant parenchymal abnormalities and, this time, without CSF pleocytosis [6]. On the other hand, elevated ICP in the absence of hydrocephalus on imaging is the leading criterion of idiopathic ICHT. Patients present with headache and papilledema, while CSF is unremarkable. Secondary intracranial hypertension has been described in a postinfectious context, e.g. in Lyme disease [7] and in peri-infectious aseptic meningitis in leptospirosis [8]. However, these patients presented with isolated symptoms of ICHT rather than meningitis. In the context of viral infections, intracranial hypertension has been reported in an 8-year-old child after measles but without CSF pleocytosis [9]. Secondary and severe ICHT treated by repetitive lumbar punctures was reported in a 15-year-old obese girl with chronic aseptic meningitis [10]. We faced a prolonged course of viral meningoencephalitis complicated by a continuously elevated ICP requiring repetitive lumbar punctures over a 2-month period. Since the patient showed a strong benefit from repetitive lumbar punctures, we chose to perform a continuous lumbar drainage for 1 week according to beneficial reports in bacterial meningitis [11]. This proved to be an effective symptomatic treatment and might be a useful means to treat ICP complications in meningitis patients. The elevated ICP could either be due to disturbed CSF reabsorption or leptomeningeal transudation due to leptomeningeal BBB dysfunction.

Despite the absence of parenchymal lesions and, furthermore, the absence of a hydrocephalus, MRI provided important information by revealing contrast enhancement in the sulcal space in a leptomeningeal pattern on postcontrast FLAIR MRI. This phenomenon has been recently reported in several leptomeningeal pathologies including subarachnoid hemorrhage, meningitis or meningeal carcinomatosis [12, 13]. Mainly due to the suppression of the CSF signal, postcontrast FLAIR images show a higher sensitivity in the delineation of meningeal pathologies [14]. Leakage from damaged pial vessels, leading to focal extravasation of the contrast agent into the CSF adjacent to the brain, is the most likely pathophysiological explanation for leptomeningeal enhancement on FLAIR images [15], indicating blood-CSF barrier disruption and matching the finding of an increased albumin CSF/serum ratio in the CSF analysis. CSF and MRI results suggest that a BBB disturbance, as frequently seen in aseptic meningitis, may cause raised ICP. Since we did not identify a pathogen, we can only speculate about the mechanism of such a prolonged BBB disturbance, e.g. a BBB-toxic agent, activation of chemoattractants or an overwhelming immune reaction.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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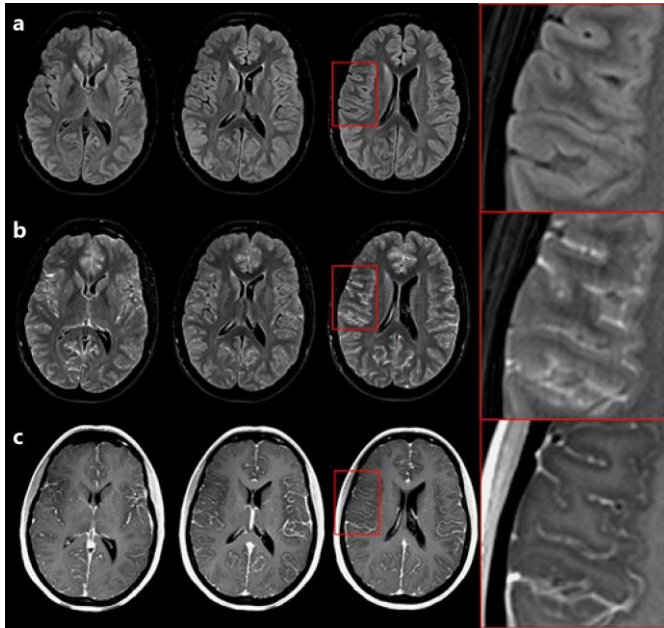


Fig. 1. Signs of BBB disruption on MRI and in CSF analysis. Native FLAIR (a), postcontrast FLAIR (b), and postcontrast T1-weighted (c) MRI: postcontrast FLAIR images show a prominent leptomeningeal enhancement with hyperintensity in the sulcal spaces in the absence of any parenchymal lesions; T1-weighted postcontrast images also show a mild leptomeningeal enhancement pattern (enlarged detail on the right).

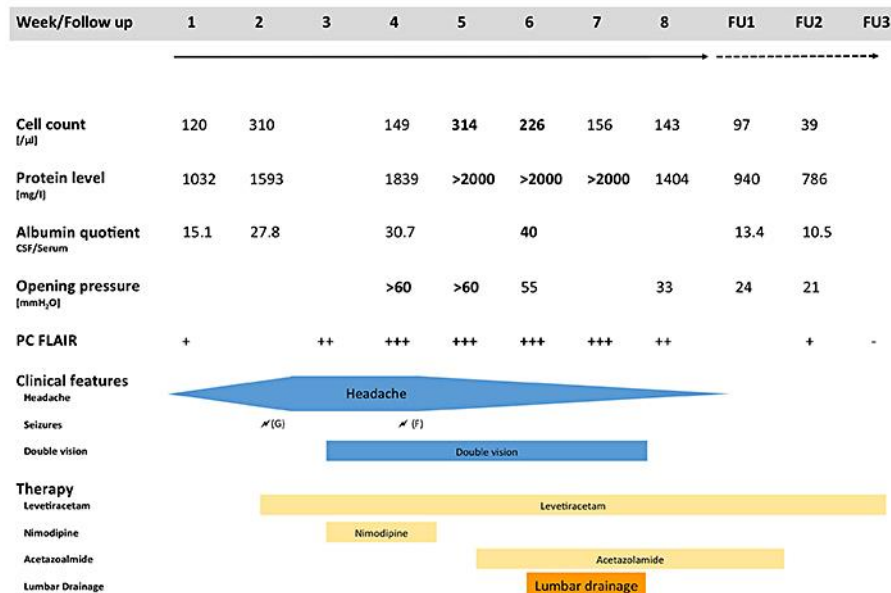


Fig. 2. Overview of the clinical course with concomitant investigations and therapeutic approaches during 8 weeks of hospitalization and further follow-up. PC FLAIR = Postcontrast FLAIR; FU = follow-up; G = generalized seizure; F = focal seizure.

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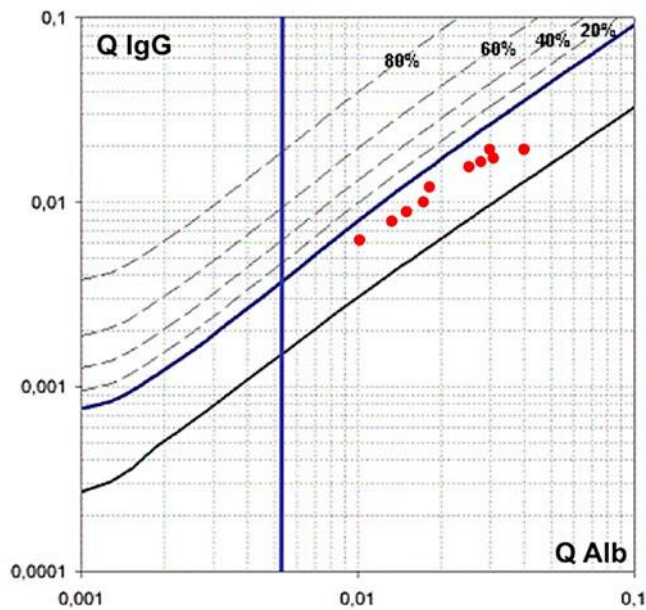


Fig. 3. Signs of BBB disruption in the CSF analysis. The Reibergram (CSF/serum quotient diagram) illustrates the BBB dysfunction at every spinal tap (one red dot represents one CSF analysis). The vertical blue line indicates the age-adapted threshold for the albumin CSF/serum quotient (Q Alb). Dots to the right of the line signal a BBB dysfunction. The horizontal blue line represents the threshold for intrathecal IgG synthesis, which was not found (all dots are below the line).