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CASE REPORT

Mycoplasma meningitis resulting in increased production of cerebrospinal fluid: case report and review of the literature

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Abstract
Purpose We report a case of increased cerebrospinal fluid (CSF) production in a child with concomitant mycoplasma meningitis.
Materials and methods This 4-year-old boy presented with a 2-week history of body aches, malaise, and headaches. He developed sudden onset of obtundation, apnea, left eye deviation, and bilateral dilated and unreactive pupils. A ventriculostomy was placed initially for a poor neurologic examination in the setting of likely meningitis. Initial intracranial pressure was high, and CSF production was supraphysiologic for the first few days of empiric, broad-spectrum treatment. Mycoplasma meningitis was diagnosed. The ventriculostomy was weaned after adequate treatment for mycoplasma meningitis.
Results and conclusions At 4 months follow-up, the child remains shunt-free with only mild cognitive–linguistic impairment. Untreated mycoplasma meningitis may cause raised intracranial pressure (possibly as a result of increased CSF production) and result in a poor neurological examination. In this setting, CSF diversion in the form of an external ventricular drain may be beneficial to preserve neurologic function during treatment with antibiotics.

Keywords Cerebrospinal fluid · Ventriculostomy · Pediatric neurosurgery

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Introduction

There are many known causes of decreased cerebrospinal fluid (CSF) production including CSF infection, ouabain, acetazolamide, hyperosmolality, hypothermia, atrial natriuretic hormone, vasopressin, serotonin receptor agonist, and dopamine D1 receptor antagonist [3]. Few entities, however, are known to increase the production of CSF. Such entities include choroid plexus papilloma, choroid plexus hypertrophy, cholera toxin through cyclic adenosine monophosphate (cAMP), and adrenergic stimulation via cAMP [2–4, 15, 16].

CSF is formed as an ultrafiltrate of plasma with possibly a secretory component. CSF is produced by the choroid plexus, but up to one third of CSF is extrachoroidal in origin. In adults, CSF is produced at an average rate of 0.35 ml/min or approximately 500 ml/day. Animal studies have shown that the formation of CSF from choroid plexus is between 0.2 and 0.5 ml min^{-1} g^{-1} choroid plexus [3].

We report what we believe to be the first documented case of increased CSF production in a child with mycoplasma meningitis.

Case report

J.M. is a 4-year-old boy who presented with a 2-week history of body aches, malaise, and headaches. Four days before presentation, he developed occasional emesis and nocturia. He was admitted to the pediatric service, and an initial workup revealed a peripheral white blood cell count of 40,000, C-reactive protein of 2.08, sedimentation rate of 51, and a sodium level of 129. A head computed tomography (CT) without contrast was benign. On hospital day 2, he developed sudden onset of obtundation, apnea,

left eye deviation, and bilateral dilated and unreactive pupils. He was transferred to the intensive care and loaded with Dilantin for suspected seizure. Antibiotics and antivirals were started empirically for meningitis.

On our initial evaluation, he was obtunded and nonvocal. His pupils were 6 mm and unreactive. He had intact corneal and oculocephalic reflexes and would briskly localize all four extremities. He had nuchal rigidity and increased reflexes throughout, with upgoing toes and clonus at both ankles. A repeat head CT was benign and unchanged. A magnetic resonance imaging (MRI) was performed and found to be within normal limits (Fig. 1).

The initial diagnosis was meningitis, and the neurology and neurosurgery services were consulted. In the setting of a poor neurologic examination and cranial neuropathy (unreactive pupils), we elected to place a ventriculostomy [12]. Initial pressure was around 40 cm water but quickly decreased with spinal fluid diversion. With a decreased intracranial pressure, his neurologic examination improved, and he began to regain consciousness and follow commands.

Despite antibiotics and an improved exam, his peripheral white blood cell count increased to 87,000, with 86% neutrophils. Blood cultures had no growth. Initial CSF studies revealed 330 white blood cells, 1,085 red blood cells, glucose of 158, protein of 74, and a negative Gram stain and culture. CSF cytology was negative for malignancy. Encephalitis panels were performed for cryptococcus, eastern equine, California, St. Louis, Western Equine, herpes simplex 1 and 2, cytomegalovirus, measles, mumps, varicella, and B. Henselae, all of which were negative. Mycoplasma pneumonia polymerase chain reaction was positive.

MRI of the brain with and without contrast was obtained and showed increased fluid attenuation inversion recovery signal in the left thalamus, right thalamus, left extreme capsule, right caudate head, and bilateral frontal lobe subcortical white matter. No enhancement was seen. The differential diagnosis included mycoplasma meningitis and acute disseminating encephalomyelitis. The patient was treated for both acute disseminating encephalomyelitis and mycoplasma meningitis with prednisolone and azithromycin.

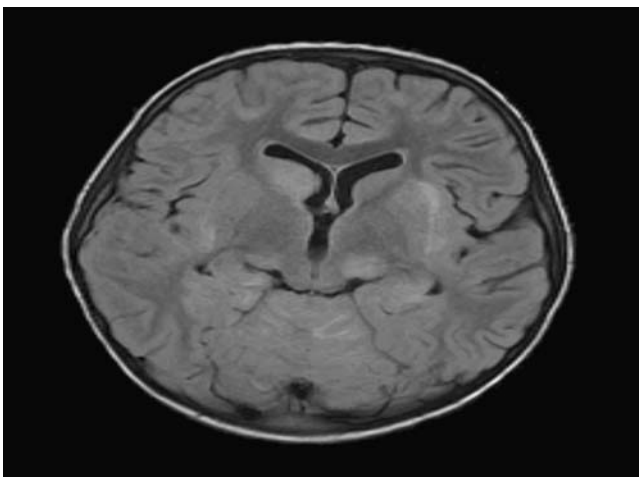

Fig. 1 Axial MRI of the patient reported herein

After initial ventriculostomy placement, this patient had a high volume output of CSF, 550 and 481 cm^3 recorded on 2 consecutive days at a drain height of 15 cm water. With steroids and antibiotics, this patient improved neurologically. His CSF output decreased to less than 100 ml output per day at a drain height of 15 cm water, and we were able to wean and discontinue his ventriculostomy after 2 weeks of CSF diversion. His peripheral and spinal white blood cell counts both normalized with time.

After inpatient physical therapy, he was discharged home nearly 1 month after admission, shunt-free, without headaches, on a regular diet, able to ambulate on his own, and nearly at his neurological baseline. He was discharged on a prednisone taper and oral Levaquin.

Discussion

Mycoplasma pneumoniae is known to have possible neurologic manifestations including meningoencephalitis, aseptic meningitis, myelitis, stroke, and polyradiculopathy [1, 6, 10, 13, 14]. Neurologic complications are rare, comprising 0.1% of all *M. pneumoniae* infections in one study [14].

Recently, a case of idiopathic intracranial hypertension diagnosed via lumbar puncture in a patient with mycoplasma meningitis has been reported [11]. This patient's papilledema and diplopia resolved with steroid treatment. There is also a report of a neonate with *Mycoplasma hominis* meningo-encephalitis that required ventriculostomy and subsequent ventriculoperitoneal shunt placement [7]. We found no mention in the literature of ventriculostomy being used to divert CSF in a patient with *M. pneumoniae* meningitis.

The mechanism of central nervous system (CNS) involvement in patients with mycoplasma pneumonia is thought to be through direct extension into the blood stream, cytokine-mediated effects on the CNS, vascular injury, and hypercoagulable states [14]. Mycoplasma meningitis is thought to occasionally cause acute disseminated encephalomyelitis and Guillain–Barré syndrome [14].

There are previous in vivo and in vitro experiments with rats and hamsters demonstrating that intracranial injection of mycoplasma pneumonia causes communicating hydrocephalus with a large number of *M. pneumoniae* visibly attached to ependymal cells, likely because these cells are ciliated and resemble ciliated respiratory epithelium [8, 9]. In such studies, it has been shown that there is a negligible

degree of inflammation produced within the ventricles but that the cilia on the infected ependyma are dysfunctional. The authors of these studies theorized that the hydrocephalus could be due to CSF stasis or an imbalance in CSF secretion and absorption either because of the ependymal dysfunction or toxic substances produced by the infectious organism.

Typical CSF production in a 70-kg male patient is 450 to 500 cm/day or about 20 ml/h, with approximately 150 cm^3 total volume in the body at any given time [3]. Our patient (17 kg) had recorded outputs of 550 cm^3 in 1 day. We attribute this increased production of CSF to his mycoplasma meningitis. Yasuda et al. [17] studied 100 children with hydrocephalus who were treated with extraventricular drainage and found that the average CSF production in children less than 15 years of age was 5 ml/h with a maximum of approximately 10 ml/h. Increases in age resulted in more CSF production. Therefore, our patient at four years of age produced at least 50 ml more CSF in one day than the average adult male and probably four times the quantity for age matched controls. To our knowledge, increased production of CSF has not previously been attributed to *M. pneumoniae*. In vivo studies in rats and hamsters provide evidence that there may be an imbalance in CSF secretion and absorption due to ependymal infection. We have not found evidence that CSF production has been studied in the setting of mycoplasma meningitis.

It is useful to note that previous case reports describe patients with symptoms that can be attributed to increased intracranial pressure, but only one report hypothesized that these patients have increased intracranial pressure [11]. Socan et al. [13] described a series of patients with mycoplasma meningoencephalitis in which a subset of patients was treated with mannitol and furosemide therapy "for probably cerebral edema." In this group, some patients had poor outcomes, including death. Hydrocephalus was not mentioned in the case report, and neurosurgical intervention was not obtained. Guleria et al. reported symptoms of persistent headache with difficulty concentrating and thinking in some patients [5]. Other patients presented with papilledema and somnolence, and there are multiple reports of death from presumed mycoplasma encephalitis. No patient was diagnosed with hydrocephalus, and there is no mention of neurosurgical intervention. Tsiodras et al. described cases of ataxia and stroke due to mycoplasma encephalitis [14]. There is one report of a neonate with *M. hominis* meningo-encephalitis requiring a ventriculostomy and ventriculoperitoneal shunt, but the details of CSF output and reason for shunting are not elaborated upon in the case report [7].

To our knowledge, no author has reported the use of ventriculostomy for diagnosis and therapy in a patient with *M. pneumoniae* meningitis. It is interesting to note that Oliver et al. [12] reported an approximately 5% chance of herniation after lumbar puncture in children with bacterial meningitis, and in these children, a preprocedure head CT was almost always normal. Moreover, most patients who herniated after lumbar puncture had a neurological deficit at the time of lumbar puncture.

Conclusions

We document one case of increased CSF production caused by mycoplasma meningitis in a 4-year-old boy. Animal data previously reported describe a possible mechanism for this increased CSF production. It may be prudent to consider mycoplasma-diagnostic tests in situations of possible viral meningitis [13] In addition, the placement of a ventriculostomy with CSF diversion may be needed in patients initially diagnosed with mycoplasma meningitis, and careful observation may be warranted for patients with untreated or partially treated mycoplasma meningitis.

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