Increased ICP as the First Sign of Pediatric-Onset Multiple Sclerosis: A Case Report and Brief Review of the Literature

Sir,

Pediatric-onset multiple sclerosis (POMS) is a demyelinating disease manifesting in children aged <18 years and represents 3–5% of all multiple sclerosis (MS) cases.[1,2] The association between intracranial hypertension and demyelinating disease dates back to 1994.[3] A wide range of pathological conditions from sinusitis to brain lesions can lead to increased intracranial pressure (ICP) in pediatric patients.[4] Although increased ICP has been reported in adult MS, there has been only one such case in pediatric MS.[3,5] In the present article, we report a previously healthy child that presented with increased ICP as the first sign of POMS.

A 12-year-old Caucasian girl presented to the Accident and Emergency Department complaining of progressive blurry vision, intermittent frontal headache, and malaise gradually deteriorating for the past 20 days. Ten days earlier, she had been examined by an ophthalmologist who assessed her vision and performed a fundoscopy that revealed bilateral papilledema, suggestive of increased ICP. A brain magnetic resonance imaging (MRI) was performed which showed sinusitis that was treated with a 10-day course of clarithromycin and steroid nasal spray.

At presentation, the neurological examination was unremarkable, a repeat fundoscopy showed persistent bilateral papilledema and repeat brain MRI demonstrated edema of the lining of the sphenoid sinus, mild subarachnoid space dilatation around the optic nerve, and white matter abnormalities, with one left brainstem T2-bright focus 10 mm in diameter [Figure 1] and no gadolinium-enhancing lesions. There was no hydrocephalus. Her clinical and imaging findings were not compatible with sinus venous thrombosis, and magnetic resonance venography was not obtained. Lumbar puncture showed an opening pressure of 42 cm H_2O. Cerebrospinal fluid (CSF) examination was normal, showing

no oligoclonal bands, nor increased cells, lymphocytes, immunoglobulin G (IgG) index, and IgG/albumin ratio suggestive of an old exacerbation.

The patient did not have any other predisposing risk factors for the development of intracranial hypertension except previous sinusitis. Her family history was positive for autoimmune diseases. (Paternal grandmother has Hashimoto's disease.) CSF and blood workup was negative for viral infections, Lyme disease or mycoplasma pneumonia infection, antinuclear antibodies, thyroid–parathyroid function abnormalities, antithyroid autoantibodies, B12, folic acid and copper deficiency as well as elevated urine copper.

Because of the presence of symptomatic intracranial hypertension, the patient was started on IV acetazolamide (15 mg/kg/day); IV methylprednisolone pulses (30 mg/kg/day up to 1 g/day) for 5 days, because of the deterioration of vision acuity; and IV ceftriaxone (75 mg/kg/day) for 7 days, because of the possible correlation between intracranial hypertension and sinusitis complications. Oral prednisone tapering was continued for 10 days.

After 6 months, the patient returned for reevaluation. Physical examination was unremarkable, and there were no new findings in brain MRI. She remained asymptomatic for 13 months from the first evaluation; however, she presented again with a 40-day history of intermittent leg numbness bilaterally. Brain MRI was indicative of demyelinating disease. The CSF evaluation was unremarkable, and CSF opening pressure was <25 cm H_2O. She was started on IV methylprednisolone (1 g/day) for 5 days and was subsequently switched to a tapering dose of oral prednisone for 10 days. She was discharged with resolved leg numbness.

Six months later, she was admitted anew to our department, complaining again of leg numbness in both legs. MRI scans showed multiple new white matter abnormalities at her brain and a gadolinium-enhancing lesion at her cervical spinal cord. The old, left brainstem T2-bright focus was still present. Because of the presence of symptomatic inflammatory lesions, the patient was started, again, on IV methylprednisolone (1 g/day) for 5 days and then switched to a tapering dose of oral prednisone. The numbness gradually resolved, and she was discharged.

Considering the *2017 revisions of the McDonald criteria*, an MRI scan performed 6 months later showed new white matter abnormalities at left ventricle, pons, medulla with post-gadolinium enhancement in these areas as well as gadolinium-enhancing lesions at her cervical spine. Interferon beta-1a was initiated in the outpatient setting [Figure 2].[1]

Thereafter, she is being followed in the Pediatric Neurology Clinic, remaining asymptomatic with a further decrease in the number of brain MRI-enhancing lesions with no further relapses to date.

The pathophysiological correlation between demyelinating diseases and elevated CSF pressure is not fully understood. Various mechanisms have been suggested, such as central nervous system (CNS) inflammation, autoimmune mechanisms, or deregulation of CSF flow dynamics, according to the Monro–Kellie hypothesis, after CNS demyelination which may result in elevated ICP in few patients with demyelination.[6-8]

Combining the findings from many studies, we concluded that since increased ICP may be the result of an autoimmune mechanism and MS may follow another autoimmune disorder, these two pathological entities may be linked.[7,9] Female preponderance in adolescent patients is notable for autoimmune disease, including MS and causes of intracranial hypertension.[1,9] In addition, family history of MS patients may be "positive" of autoimmune diseases with their relatives suffering from other autoimmune disorders that could potentially lead to increased ICP in those patients.[10] These findings and correlations raise the suspicion of a possible "chain autoimmune mechanism" that led to the pathogenesis of MS in our patient.[9]

Our patient presented with a clinical history and laboratory and imaging findings indicative of intracranial hypertension

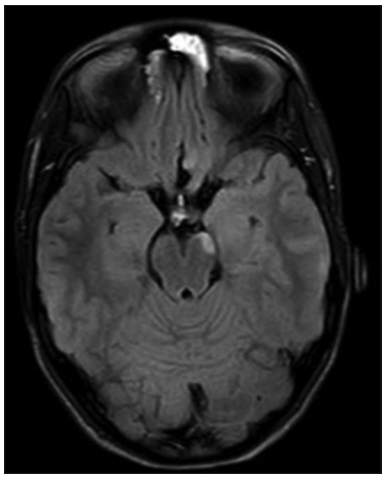

Figure 1: Magnetic resonance imaging (MRI) axial T2W-FLAIR image. Note left brainstem bright foci

Figure 2: Magnetic resonance imaging (MRI) axial T2W-FLAIR image. Note T2-bright foci at the right side of the pons

confirmed with increased CSF opening pressure. Because of the presence of white matter abnormalities consistent with demyelinating disorder, the patient was periodically reevaluated and acute relapses and MRI findings were consistent with the diagnosis of definite MS.

In summary, when children present with signs of increased ICP and a family history of autoimmune disease there should always raise suspicion of an autoimmune mechanism that could potentially lead to secondary demyelination and in our case, particularly, MS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Otallah S, Banwell B. Pediatric multiple sclerosis: An update. Curr Neurol Neurosci Rep 2018;18:76.
2. Boiko A, Vorobeychik G, Paty D, Devonshire V, Sadovnick D. Early onset multiple sclerosis: A longitudinal study. Neurology 2002;59:1006-10.
3. Newman NJ, Selzer KA, Bell RA. Association of multiple sclerosis and intracranial hypertension. J Neuroophthalmol 1994;14:189-92.
4. Aylward SC, Way AL. Pediatric intracranial hypertension: A current literature review. Curr Pain Headache Rep 2018;22:14.
5. Williams BJ, Skinner HJ, Maria BL. Increased intracranial pressure in a case of pediatric multiple sclerosis. J Child Neurol 2008;23:699-702.
6. Narula S, Liu GT, Avery RA, Banwell B, Waldman AT. Elevated cerebrospinal fluid opening pressure in a pediatric demyelinating disease cohort. Pediatr Neurol 2015;52:446-9.
7. Markey KA, Mollan SP, Jensen RH, Sinclair AJ. Understanding idiopathic intracranial hypertension: Mechanisms, management, and future directions. Lancet Neurol 2016;15:78-91.
8. Mokri B. The Monro-Kellie hypothesis: Applications in CSF volume depletion. Neurology 2001;56:1746-8.
9. Langer-Gould A, Albers KB, Van Den Eeden SK, Nelson LM. Autoimmune diseases prior to the diagnosis of multiple sclerosis: A population-based case-control study. Mult Scler J 2010;16:855-61.
10. Nielsen NM, Frisch M, Rostgaard K, Wohlfahrt J, Hjalgrim H, Koch-Henriksen N, *et al*. Autoimmune diseases in patients with multiple sclerosis and their first-degree relatives: A nationwide cohort study in Denmark. Mult Scler 2008;14:823-9.

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