Association of Multiple Sclerosis and Intracranial Hypertension

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Abstract:
Three patients fulfilled the diagnostic criteria for both multiple sclerosis and pseudotumor cerebri. Although coincidence is possible, intracranial hypertension may be a manifestation of demyelinating disease.

Key Words: Pseudotumor cerebri—Idiopathic intracranial hypertension—Raised intracranial pressure—Multiple sclerosis—Demyelinating disease.

Multiple sclerosis and idiopathic intracranial hypertension (pseudotumor cerebri) are both diseases found with higher frequency among women in their childbearing years. We report three patients in whom these two diseases coexisted clinically. Although coincidence is possible, several features of these cases raise the possibility of an association between these two clinical entities.

CASE REPORTS

Case 1
At age 31, a previously healthy, thin white woman experienced intermittent paresthesias from the waist down. A myelogram was normal. She did well until age 39 when she experienced daily episodes of vertigo lasting 30–45 minutes for several months, followed by left-sided numbness that lasted 4 weeks, then gradually resolved. Workup included magnetic resonance imaging (MRI) with periventricular white matter abnormalities consistent with demyelinating disease and normal four-vessel cerebral arteriography. Two lumbar punctures with the patient relaxed revealed opening pressures of greater than 300 mm of water, no white blood cells, normal protein levels, and no oligoclonal bands. At age 40, she developed ataxia. Neurologic examination revealed bilateral disc edema, normal visual acuity, and left-sided ataxia. She was diagnosed with multiple sclerosis and treated with prednisone, 60 mg/day, for 4 days, but this was discontinued secondary to insomnia. Several subsequent lumbar punctures all had elevated opening pressures (none lower than 290 mm of water), no white blood cells, and normal protein levels. Oligoclonal banding was documented on at least one occasion. She was treated with acetazolamide. Approximately 3 months after the disc edema was first appreciated,
Case 2
At 45 years of age, a previously healthy, thin white woman developed numbness of her left hand and difficulty in holding objects. She underwent carpal tunnel surgery, but the numbness and clumsiness of the left hand persisted intermit-
tently. She also complained of some problems with her right lower leg, causing her to trip when she walked, as well as some intermittent pain in the neck and both arms. When she was 47 years old, an MRI demonstrated several bright T2 periventic-
tricular white matter lesions compatible with de-myelinating disease. At age 49, she began to com-
plain of early morning occipital headaches that would frequently wake her from sleep, occasional episodes of horizontal diplopia, and bilateral, seconds-long, transient visual obscurations. Neuro-
ophthalmic examination revealed vision of 20/25 —
ons-long, transient visual obscurations. Neuro-
ophthalmic examination revealed mild bi-
lateral disc edema but normal visual function. The lumboperitoneal shunt was revised and symptoms resolved.

Case 3
At 26 years of age, an obese white woman, complaining of 2 years of severe headaches, was noted to have bilateral disc edema. Two computed tomography (CT) scans of the brain were normal. Lumbar punctures on three separate occasions documented opening pressures of 250–350 mm of water. The cerebrospinal fluid was otherwise completely normal, including normal protein levels, <5 white blood cells, and no oligoclonal bands. She was diagnosed with pseudotumor cerebri and treated with a regimen of prednisone 20 mg every other day, acetazolamide 250 mg twice per day, and furosemide 20 mg/day. Her headaches persisted, and 6 months after the initiation of therapy she also complained of progressive blurred vision in the left eye, diplopia, and decreased sensation of the left hand. On examination, visual acuity was 20/30 OU. There was a 0.3 log unit left relative afferent pupillary defect. Ophthalmoscopic examination revealed bilateral optic disc pallor, left worse than right. There was decreased hearing on the right. She had patchy decreased sensation of the left hand. Gait was wide-based and unsteady. Repeat lumbar puncture revealed an opening pressure of 280 mm of water, 1 white blood cell, normal protein and glucose, and no oligoclonal bands. Sedimentation rate was 38, thyroid function tests were normal, ANA, RPR, ACE levels, and Lyme titers were negative. MRI of the brain demonstrated multiple, nonenhancing, bright T2 periventricular lesions consistent with demyelinating disease. Her acetazolamide dosage was increased, and her prednisone and furosemide was discontinued. The patient’s symptoms gradually improved. Follow-
up lumbar puncture 3 months later revealed an opening pressure of 210 mm of water and normal cerebrospinal fluid. Approximately 6 months later, the patient complained of "blind spots in the left eye," vertigo, increased difficulty with balance, and numbness over the distal left upper extremity and the occipital area of the scalp. Repeat MRI demonstrated periventricular white matter lesions without change. Lumbar puncture revealed an opening pressure of 180 mm of water, and the cerebrospinal fluid was positive for oligoclonal bands.

DISCUSSION

These three patients had papilledema, documented elevation of intracranial pressure, otherwise unremarkable cerebrospinal fluid, and no evidence of hydrocephalus or encephalopathy, all compatible with the diagnosis of idiopathic intracranial hypertension or pseudotumor cerebri (1,2). They also had experienced episodes of neurologic dysfunction separated in time and space, best localized to lesions in central nervous system white matter, consistent with demyelinating disease and the diagnosis of multiple sclerosis (MS) (3-5). In further support of the diagnosis of MS, all three patients had MRI periventricular white matter abnormalities, and two had oligoclonal bands in their cerebrospinal fluid (3). While no feature alone is specific for MS, case 1 would meet the criteria for clinically definite multiple sclerosis (3). Why intracranial hypertension was seen among the initial findings in a 45-year-old man presenting with his first manifestations of multiple sclerosis is somewhat expected. However, our three patients demonstrated neither the clinical features nor the neuroimaging findings characteristic of this form of demyelinating disease.

Buiter and Gilligan (14) reported a 32-year-old man with laboratory-supported definite multiple sclerosis and obstructive hydrocephalus secondary to the mass effect of a plaque of acute demyelination in the brainstem. Our patients showed no evidence of hydrocephalus or potentially obstructing plaques. The theory that a small, neuroradiologically undetected plaque in some way transiently obstructed normal cerebrospinal fluid circulation was used by David and colleagues (15) to explain why intracranial hypertension was seen among women ages 15 to 44 years, the Russian literature refers to cerebrospinal fluid hypertension in the setting of MS exacerbation as if it were a commonly accepted association (6). A total of 40 patients, 29 women and 11 men, ages 24-44, were studied during an exacerbation of MS. All of them had raised intracranial pressure (220-380 mm of water) and symptoms of headache, nausea, and sometimes vomiting and changes in mentation. In 33 patients there was widening of the third ventricle by "echoencephalography." Although most patients had an increased number of T lymphocytes in the cerebrospinal fluid, no specific details are given regarding the number of white blood cells or the protein lev-

els within the spinal fluid. No mention is made of papilledema. The authors hypothesize that, during the flares of multiple sclerosis, the increased IgG and oligoclonal bands cause changes in the osmotic and oncotic pressures within the cerebrospinal fluid, thereby disturbing the blood brain barrier and elevating the intracranial pressure.

Other theories to explain a causal relationship would need to explore ways the multiple sclerosis process could decrease cerebrospinal fluid resorption or increase production. None of our three patients had elevated spinal fluid protein levels or significant cellular content. It would be highly unlikely that raised intracranial pressure alone would cause the episodic neurologic symptoms and signs as well as the MRI findings in our cases. However, it is conceivable that autoimmune triggers could result in both diseases. Finally, the treatment of presumed demyelinating disease frequently involves the use of corticosteroids, agents whose use as well as whose rapid withdrawal have been associated with raised intracranial pressure. All of our patients had papilledema noted prior to any corticosteroid treatment.

The association of demyelinating disease and intracranial hypertension may be missed in patients with concurrent or presumed papillitis. Alternatively, those patients with multiple sclerosis and optic atrophy secondary to previous episodes of optic neuritis may fail to exhibit disc edema even if the intracranial pressure is elevated. Although lumbar puncture is often performed on patients with suspected demyelinating disease, the opening pressure may not be measured or recorded. The examining physician might assume that an elevated pressure reflects poor relaxation, a spurious measurement, or an incidental finding, rather than a manifestation of the disease process under investigation.

REFERENCES