Intermittent Third Nerve Palsy with Cryptococcal Meningitis

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In the several days before death, two AIDS patients with cryptococcal meningitis and increased intracranial pressure (ICP) experienced episodic unilateral third nerve palsies seemingly related to transient peaks in ICP. While cryptococcal neuritis may have predisposed the nerves to pressure effects, CT scans showed no evidence of tentorial herniation. These cases raise the possibility that severe elevations of ICP can precipitate third nerve paresis on rare occasions.

Key Words: Third nerve palsy—Cryptococcal meningitis—Increased intracranial pressure—AIDS.

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Meningitis is a well-recognized cause of third nerve damage. Possible mechanisms include direct invasion or vasculitic infarction of the nerve, midbrain infarction and abscess, and tentorial herniation. The following patients with terminal cryptococcal meningitis showed unusual intermittent oculomotor nerve pareses that appeared to be related to increased intracranial pressure (ICP) in the absence of tentorial herniation.

CASE REPORTS

Case 1

A 21-year-old man with acquired immunodeficiency syndrome (AIDS) was admitted following 2 weeks of headache. Physical examination was normal, aside from elevated blood pressure, and his computed tomographic (CT) scan showed no abnormalities. Lumbar puncture results included a resting pressure of 370 mm cerebrospinal fluid, no cells, a protein value of 20 mg/dL, and a glucose level of 50 mg/dL. Cryptococci were seen on India ink preparation, cerebrospinal fluid cryptococcal antigen titers were positive, and amphotericin therapy was begun.

Two days after admission, he experienced a sudden increase in headache severity, became lethargic, and developed severe left third nerve paresis. Repeat CT scan was again read as normal, but showed mild diffuse cerebral swelling when carefully compared to the initial and subsequent studies. Within minutes of administering intravenous mannitol, the third nerve palsy disappeared. On two further occasions in the next 36 hours a complete isolated left third nerve palsy with a 6-mm fixed pupil appeared and resolved within 30 minutes after mannitol administration. In the following 12 hours he became progressive obtunded and died.
Case 2

A 34-year-old AIDS patient was admitted because of 3 weeks of headache, myalgias, and weight loss. Eye movements and pupillary functions were normal, but papilledema was present. Early the next morning, following sedation with morphine in the emergency room, he developed a third nerve palsy manifested by a dilated, fixed pupil and severe ptosis. These signs cleared as the effects of the morphine wore off, but later that morning he became transiently obtunded with increased headache and right ptosis, a 7-mm fixed right pupil, and a 4-mm fixed left pupil. An enhanced CT scan was normal. That afternoon, a third episode of severe right third nerve paresis manifested by right ptosis, nearly complete adduction paresis (vertical movements could not be assessed) and a 6-mm fixed pupil (left pupil 3 mm and reactive) was accompanied by difficulty seeing and hearing and increased lethargy. The episodes lasted from 15 to 40 minutes.

A lumbar puncture showed a resting pressure greater than 550 mm cerebrospinal fluid, 16 monocytes, a protein value of 34 mg/dL, and a glucose level of 37 mg/dL. Budding yeast was abundant on Indian ink preparation and Cryptococcus neoformans later grew from multiple cultures. Treatment with amphotericin and dexamethasone was initiated. The patient became progressively obtunded and experienced a cardiac arrest 40 hours after arriving at the hospital.

DISCUSSION

Third nerve pareses develop in varying patterns; most advance steadily to a maximum, many show saltatory progression, and a few demonstrate spontaneous temporary improvement. Repeated rapid development of a severe third nerve palsy followed by resolution within the hour, as seen in our patients, is a highly unusual event.

Cryptococcal meningitis, a common secondary infection in AIDS, is often associated with marked elevations in ICP (1,2). The three 10- to 40-minute episodes of severe third nerve paresis that each of our patients experienced were accompanied by increased headache and mild to severe obtundation. Most episodes coincided with events that suggest fluctuations in intracranial pressure: morphine precipitation, relief after mannitol, and simultaneous obtundation with hearing and visual loss similar to symptoms seen with plateau waves (3). In one episode, the opposite pupil was smaller but also fixed, suggesting midbrain involvement in that instance. CT scans of both patients were obtained at the time of the episodes and eliminated tentorial herniation as a cause of the oculomotor nerve palsy.

Increased intracranial pressure (IICP) is not an accepted cause of oculomotor nerve paresis. Third nerve damage associated with tentorial herniation is sometimes loosely said to be due to “pressure,” but the proximate cause is brain shift and compression of the third nerve and midbrain. The experimental Cushing response to IICP may include late serial pupillary dilation, but the effects of midbrain distortion and terminal midbrain ischemia confound any possible direct effect of pressure upon the third nerve (4,5). Similarly, in older reports of third nerve palsies associated with remote intracranial tumors (6), the effects of brainstem distortion and meningeal tumor spread cannot be discounted.

Benign intracranial hypertension (BIH) provides the purest clinical example of IICP. Abducens nerve palsies are commonplace, but rare involvement of other cranial nerves has been reported with benign intracranial hypertension. Reports of possible third and fourth nerve palsies include instances of diffuse ophthalmoplegia of uncertain localization and patients with minor vertical diplopia which may be secondary to the horizontal dissociation from abducens pareses (7). However, a case of apparent benign intracranial hypertension, (8) in which a complete third nerve palsy was preceded by episodic pupillary dilation and decerebrate posturing, suggests that pressure-induced midbrain and oculomotor effects might have occurred in that patient.

Rapid fluctuations of sixth nerve function, similar to the intermittent third nerve pareses in our patients, have been observed in a case of cryptococcal meningitis with severe IICP (9). The 5- to 15-minute episodes of bilateral abducens pareses in that patient were accompanied by headache, obtundation, tinnitus, decreased hearing, facial sagging, a sluggish response in one or both pupils, and an elevation in blood pressure, suggesting a brainstem effect of transient intracranial pressure elevation (3,4).

That the intermittent third nerve pareses in our two patients were strictly the result of IICP is unlikely; predisposing infectious invasion of the nerves was probably present. However, the episodes are unusual in themselves and raise the possibility that, under exceptional circumstances, elevated ICP may precipitate third, as well as sixth, nerve pareses.
REFERENCES


