Minocycline-Induced Fulminant Intracranial Hypertension

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Objective: To describe the clinical course of an unusually severe case of minocycline-induced intracranial hypertension.

Results: Although the patient ceased minocycline treatment, there was ongoing and rapid worsening of symptoms and vision loss. Lumbar puncture, which normally acts as a temporizing measure to preserve vision, failed to prevent, and may even have precipitated, further deterioration in vision, necessitating surgical intervention with optic nerve sheath fenestration.

Conclusion: Minocycline can cause a fulminant syndrome of elevated intracranial pressure, with severe vision loss, even after the medication has been discontinued.

MINOCYCLINE HAS BEEN implicated in the development of elevated intracranial pressure (ICP), resulting in a syndrome that meets the most recent diagnostic criteria for idiopathic intracranial hypertension (IIH). It has been postulated that minocycline acts to reduce cerebrospinal fluid (CSF) absorption at the arachnoid villi, inducing elevated ICP. Most commonly, minocycline produces a benign condition that resolves spontaneously on discontinuation of the drug, with minimal, or no, visual loss. However, there are a few cases reported in the literature with severe papilledema and some vision loss requiring surgical intervention. Herein, we describe a unique case of minocycline-induced elevated ICP presenting as fulminant IIH with severe and progressive visual loss, despite withdrawal of the antibiotic.

REPORT OF A CASE

A nonobese 12-year-old girl presented with headaches and bilateral vision loss. Her medical history was significant for macrocephaly, diagnosed at age 1 year, with neuroimaging at that time showing “generous subarachnoid space,” which resolved within 4 months. Her family history was notable for a great uncle with hydrocephalus treated with a shunting procedure.

One month prior to presentation, the patient had started taking minocycline as an acne treatment. One week after commencing minocycline treatment, she developed mild headaches that progressively worsened and became associated with nausea. After only 3 weeks, she discontinued taking the minocycline, having herself decided that the antibiotic was making her unwell. However, her headaches continued to escalate. Two days later, she noticed postural transient visual obscurations and, shortly thereafter, reported decreasing vision bilaterally.

At evaluation 1 month after the minocycline treatment, and 1 week after its cessation, her body mass index was 20.1 (calculated as weight in kilograms divided by height in meters squared) and she had no history of recent weight gain. Her blood pressure was 95/75 mm Hg. Visual acuity was 20/30 OD and hand motions OS. There was a left relative afferent pupillary defect, bilateral abducens nerve pal-
sies, and severe disc edema in both eyes. Magnetic resonance imaging of the brain, with venography, showed normal intracranial contents, no hydrocephalus, bilateral transverse venous sinus stenosis, flattening of the posterior globes, and tortuous optic nerves in both eyes. Lumbar puncture (LP) demonstrated CSF opening pressure of 50 cm of water, with normal constituents. She was begun on 500 mg of acetazolamide twice daily and was admitted urgently to the hospital.

Immediately after the LP, her headaches resolved and the nausea dissipated. However, over the next 24 hours, her visual acuity rapidly worsened to hand motions OD and only light perception OS. Forty-eight hours after the LP, her visual acuity was reduced to light perception OU. There was a left relative afferent pupillary defect and a 50% abduction deficit in the left eye. She had severe bilateral disc edema with cotton-wool spots and peripapillary hemorrhages (Figure, A). Repeated LP showed a CSF opening pressure of 25.5 cm of water. She underwent bilateral sequential optic nerve sheath fenestrations 1 and 3 days later and also received a 5-day course of intravenous methylprednisolone. Acetazolamide treatment was maintained.

A week after the second optic nerve sheath fenestration, she remained free from headache and her visual acuity rapidly worsened to hand motions OD and only light perception OS. Forty-eight hours after the LP, her visual acuity was reduced to light perception OU. There was a left relative afferent pupillary defect and a 50% abduction deficit in the left eye. She had severe bilateral disc edema with cotton-wool spots and peripapillary hemorrhages (Figure, A). Repeated LP showed a CSF opening pressure of 25.5 cm of water. She underwent bilateral sequential optic nerve sheath fenestrations 1 and 3 days later and also received a 5-day course of intravenous methylprednisolone. Acetazolamide treatment was maintained.

A week after the second optic nerve sheath fenestration, she remained free from headache and her visual acuity had improved to 20/80 OD and hand motions OS. The abduction deficit had resolved. Funduscopic appearance had improved, with resolution of the hemorrhages. Goldmann visual fields showed a small central island of vision just inferior to fixation in the right eye and awareness of movement centrally in the left eye (Figure, B). She continued to improve over the following few weeks. Three months after her initial presentation, she was neurologically asymptomatic, visual acuity had stabilized at 20/50 OD and counting fingers OS, funduscoppy showed secondary optic atrophy, and Goldmann visual fields showed a 30° field temporally in the right eye and a small paracentral island of vision in the left eye (Figure, C).

**COMMENT**

Minocycline-induced elevation of ICP has been reported many times in the literature. What makes our case unusual is the severity of vision loss and the progressive worsening 2 weeks after discontinuation of the minocycline. In addition, this case raises the issue of why vision may acutely worsen following LP, despite resolution of other symptoms of elevated ICP. The half-life of minocycline is less than 24 hours; therefore, any consequences of a direct action of the medication on the body would be expected to resolve within a few days of stopping the medication. However, a study by Winn et al examining serial LPs in patients taking tetracycline-based medications (including minocy-
although the papilledema itself looked severe in 2 minocycline use have been reported.4,5 However, the rapid deterioration in our case necessitated surgical intervention, as has been recommended in the management of fulminant IIH.8

The severity of vision loss in this case is striking, despite the timely reduction in ICP, particularly when compared with other cases in the literature. Within a series of 12 patients from Chiu et al,2 symptoms of raised ICP developed within 2 weeks of starting minocycline treatment in 50% of cases. They documented no recurrences following cessation of minocycline and no patients with progressive visual deterioration. Final visual acuities in all patients were 20/20 OU or better. In 3 cases, a residual Humphrey visual field mean deviation of –5 dB in at least 1 eye was reported. Although acknowledging the potential for vision loss, this series documented a relatively benign course of the disease, with typical resolution of all symptoms and signs after discontinuation of the minocycline. A series reporting doxycycline-associated intracranial hypertension6 documented 1 case with visual acuity at presentation of 20/200 OD and 20/50 OS, but the visual acuity of all 7 patients in the series improved to 20/30 or better. However, 5 of the 7 patients had some permanent field loss, cautioning that medication-induced elevated ICP can still have visual consequences.

Rare cases of florid papilledema associated with minocycline use have been reported.4,5 However, although the papilledema itself looked severe in 2 cases,4 visual acuity remained at 20/20 OU, with no substantial visual field constriction. The most severely affected patient in that same series4 was a 23-year-old nonobese woman who had been taking minocycline for 3 months after a prior 4-month course of doxycycline and required ventriculoperitoneal shunting for persistent headache and worsening visual fields. However, the visual fields were only moderately affected, with a mean deviation of –4.02 dB and enlarged blind spots. The only other case in the literature with loss of vision was a 16-year-old girl who had taken minocycline for 6 weeks and had bilateral hemorrhagic papilledema and initial visual acuity of 2/10 OD and 5/10 OS.5 The CSF opening pressure was 90 cm of water and a lumboperitoneal shunt was performed. Visual acuity 1 week after the shunt had improved to 4/10 OD and 7/10 OS; the final visual acuity was not provided, although the authors indicated that the “clinical condition continued to improve.”

The cause of the severe and progressive visual deterioration in our case, despite the early cessation of the minocycline treatment and LP with documented reduction of the ICP, remains uncertain. Cerebrospinal fluid sequestration within the optic nerve sheath complexes may have resulted in localized ongoing high pressures even after LP. Indeed, persistent papilledema even after ventriculoperitoneal shunting has been reported, leading Killer et al10 to conclude that CSF flow may be bidirectional within the optic nerve sheath complexes, with poor flow from the subarachnoid spaces around the optic nerve to the intracranial subarachnoid space. This mechanism could explain further visual deterioration from papilledema following normalization of intracranial CSF pressure after LP. Killer et al10,11 hypothesized that there may be other local contributing factors in some individuals, such as narrowing of the subarachnoid space within the optic canal, inflammation and fibrosis causing compartmentalization of CSF, and accumulation of biologically active molecules within the optic nerve sheath complexes leading to cell apoptosis.

In our case, the rapid deterioration of vision was temporally related to the first LP. Progressive visual failure after shunting12,13 or craniotomy14 has been ascribed to the rapid decompression of long-standing elevated ICP in patients with chronic papilledema. However, we cannot explain how a standard uncomplicated LP could result in a drop in CSF pressure substantial enough to cause visual loss comparable with that seen with neurosurgical procedures.

The severity of vision loss, speed of onset, and presence of early optic nerve pallor in our case indicate a substantial element of ischemia affecting the optic nerve heads. Although no controlled trial has evaluated surgical treatments in IIH, there is general agreement that surgery is indicated in cases of progressive visual loss. Temporizing measures include repeated LPs, lumbar drain, and intravenous steroids. In 1 case series of fulminant IIH, surgery within 4 days after neuro-ophthalmic assessment was associated with partial improvement in visual function.8 Aggressive intervention is recommended in cases of elevated ICP and visual loss, regardless of whether there is an underlying precipitant such as minocycline.


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