Intracranial Pressure Returns to Normal About a Month After Stopping Tetracycline Antibiotics

Tetracycline antibiotics are used widely, especially for the treatment of teenage acne vulgaris. Raised intracranial pressure with fulminant papilledema can occur as a rare, idiosyncratic adverse effect.1-3 The diagnosis is often delayed because obesity, a diagnostic clue associated with pseudotumor cerebri, is usually absent. Consequently, patients may have advanced visual field loss and impending blindness. To guide treatment, it would be useful to know how long intracranial pressure remains elevated after halting the use of tetracycline-class antibiotics.

Eight patients were treated by a single neuroophthalmologist (J.C.H.) from 1991 to 2006 for pseudotumor cerebri caused by tetracycline antibiotics. In 4 cases, lumbar punctures were performed after stopping the use of the antibiotic. Measurement of the opening pressure (performed in the lateral decubitus position) revealed how long it takes for intracranial pressure to return to normal. All of the patients had negative magnetic resonance imaging results and normal cerebrospinal fluid results.

Report of Cases. Case 1. A 15-year-old girl with an 8-month history of minocycline hydrochloride use had neck pain, obscurations, peripheral visual field loss, and diplopia. She had bilateral papilledema and an opening pressure of 49 cm H2O. Minocycline use was discontinued and acetazolamide treatment was started. Three weeks later, there was still severe papilledema and visual field loss. A spinal tap yielded an opening pressure of 17 cm H2O. Acetazolamide treatment was discontinued and follow-up examinations showed eventual resolution of the papilledema.

Case 2. An 18-year-old woman received minocycline for 2 months. This was stopped when she developed headache. Examination 2 weeks later showed florid papilledema and bilateral abducens nerve pareses. A spinal tap yielded an opening pressure of only 22 cm H2O, presumably because minocycline use had been stopped 2 weeks earlier. Treatment was commenced with acetazolamide but was discontinued 3 weeks later when her papilledema showed marked improvement.

Case 3. A 16-year-old girl had received tetracycline for 4 months. She developed headache, obscurations, and advanced visual field loss (Figure 1). Examination revealed bilateral papilledema. The opening pressure was 60 cm H2O. Tetracycline use was discontinued and treatment with acetazolamide was started. Four subsequent spinal taps were performed to lower intracranial pressure by removing cerebrospinal fluid. The pressure returned to normal 3 weeks after stopping tetracycline treatment (Figure 2). A final measurement was obtained a week after discontinuing acetazolamide use to make sure that her intracranial pressure did not rebound. Fundus examination 6 weeks after cessation of tetracycline use showed residual papilledema, although her intracranial pressure had presumably normalized.

Case 4. An 18-year-old woman received doxycycline for a month. She developed headache, diplopia, and papilledema. The doxycycline use was stopped and acetazolamide was started. A spinal tap performed 19 days later yielded an opening pressure of 49 cm H2O. Two subse-
Comment. The elimination half-life of tetracycline antibiotics is less than 24 hours, even for minocycline, the longest-acting drug in this class. Therefore, one might expect intracranial pressure to return to normal within a few days of stopping tetracycline antibiotics. If so, treatment to lower intracranial pressure would be useful for only a narrow time window after halting antibiotics.

In fact, intracranial pressure remains elevated longer than one would predict from the brief elimination half-life of tetracyclines. Mochizuki et al described a 16-year-old girl treated with minocycline whose intracranial pressure remained elevated for several weeks. This case, combined with our 4 cases, indicates that raised intracranial pressure persists for 2 to 5 weeks after stopping the use of tetracyclines. During this interval, patients should be monitored closely and treated aggressively to prevent permanent visual loss. One should not intervene surgically, however, without verifying that intracranial pressure is still elevated, as it can return to normal before papilledema resolves.

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Bradyopsia in an Asian Man

Bradyopsia is a rare retinal disorder, first described in 3 unrelated Dutch families. Patients with bradyopsia have difficulty tracking moving objects and adapting to sudden changes in luminance levels owing to a defect in the photoreceptor deactivation mechanism within the phototransduction cascades. Homozygous mutations in either the regulator G-protein signaling 9 (RGS9) or RGS9 anchor protein (R9AP) gene that encode the photoreceptor GTPase accelerating protein and its anchor protein, respectively, have been identified in patients with bradyopsia. We report a case of bradyopsia in an Asian man with characteristic electrophysiological and genetic findings. This study was approved by the institutional review board of the Singapore Eye Research Institute.

Case Description. A 19-year-old Chinese man sought care because he had reduced vision in bright lights and from a young age had difficulty tracking moving objects. He had no noteworthy medical history. His refractive error was +0.50–2.25 × 160 OD and +1.25–3.50 × 15 OS. Best-corrected visual acuity was 20/25 (6/7.5) OD and 20/30 (6/9) OS, and he had normal color vision. Examination results of both anterior and posterior segments were unremarkable. His parents, elder brother, and younger sister were asymptomatic and had normal ophthalmic examination results.

The full-field electroretinogram (ERG) showed normal scotopic responses (Figure 1). The maximal ERG responses were normal but only for the initial flash. Responses from the subsequent flashes were reduced with a 20-second interstimulus interval but normal with a 60-second interstimulus interval. The scotopic red-flash ERG responses indicated the presence of cone system function. However, the photopic ERG and 30-Hz flicker were undetectable. The ERG findings of the patient's family members were normal (data not shown).

Both the RGS9 and R9AP genes of the patient and his family were screened for mutations by direct sequencing after informed consent was obtained. This showed a novel compound heterozygous mutation in the single-exon gene R9AP. The mutation in the paternal allele was a 2-base pair deletion (c.277-278delAT) (Figure 2). The maternal allele had a deletion of an undefined size that encompassed at least the entire coding region of R9AP. Hemizygosity was observed in the patient and his mother for 2 single-nucleotide polymorphisms located 2 kilobases apart in the 5’ and 3’ untranslated regions of the R9AP gene, confirming that this genomic deletion encompasses the entire coding region of the R9AP gene. Real-time quantitative polymerase chain reaction performed on genomic DNA also confirmed that only 1 copy of the R9AP gene was present in both the mother and the patient relative to the father and a normal control (data not shown).

Comment. To our knowledge, this is the first report of bradyopsia in an Asian family.