CASE REPORT

Ethambutol optic neuropathy associated with enhancement at the optic chiasm

A 71-year-old woman was diagnosed with pulmonary *Mycobacterium avium* complex in 2006 and received multidrug treatment with ethambutol for 18 months between 2008 and 2009, with no ocular symptoms. Because of a progression in pulmonary nodules, ethambutol was restarted in 2015 at a total daily dose of 19 mg/kg along with rifampin and clarithromycin.

Nine months after the resumption of ethambutol, she noticed progressive visual blurring in both eyes. Ethambutol was discontinued by her pulmonologist, and she was examined in the neuro-ophthalmology clinic 1 month later. At that time, her best-corrected visual acuity was 20/125 OD and 20/200 OS with no improvement using pinhole. She correctly identified only 1 of 11 Ishihara color plates OD and zero color plates OS. Pupils were equal, round, and reactive to light without relative afferent pupillary defect. Extraocular movements were full and intraocular pressures were normal. Confrontation visual field testing suggested bitemporal field loss. The remainder of the external and anterior eye examinations were normal. Dilated fundus examination revealed mild temporal pallor in both eyes, with a cup-to-disk ratio of 0.3 bilaterally. There were no additional abnormalities on macular or peripheral retinal examination.

Humphrey SITA-Fast 24-2 visual fields confirmed predominantly bitemporal field loss, with a mean deviation of −3.96 dB OS and −8.44 dB OD (Fig. 1). Although the field defect was suspected to be caused by ethambutol toxicity, magnetic resonance imaging (MRI) of the brain was performed to exclude a structural lesion at the chiasm. This study showed increased T2 signal and mild enhancement of the optic chiasm (Fig. 2).

Laboratory testing showed a normal complete blood count, with normal folate, thiamine, B12, copper, and zinc levels. The aquaporin-4 antibody for neuromyelitis optica was also sent, given the enhancement at the optic chiasm, and was negative.

Over the following 6 months off ethambutol, she reported progressively improving visual acuity, colour

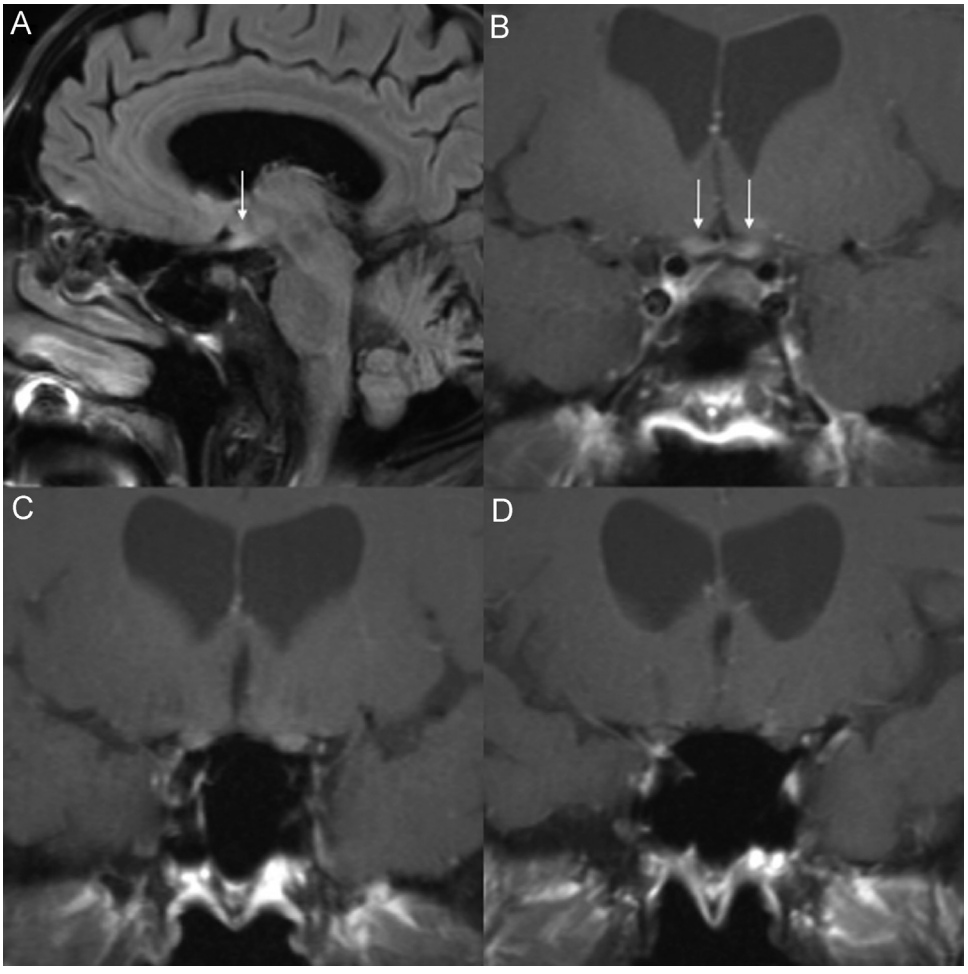

Fig. 1—(a) Sagittal T2-FLAIR MRI image of the optic chiasm showing increased FLAIR signal at the body of the optic chiasm (white arrow). (b–d) Coronal postcontrast T1-weighted MRI image of the optic chiasm showing contrast enhancement at the body of the optic chiasm extending into the proximal optic tracts bilaterally. T2-FLAIR, T2-weighted fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.

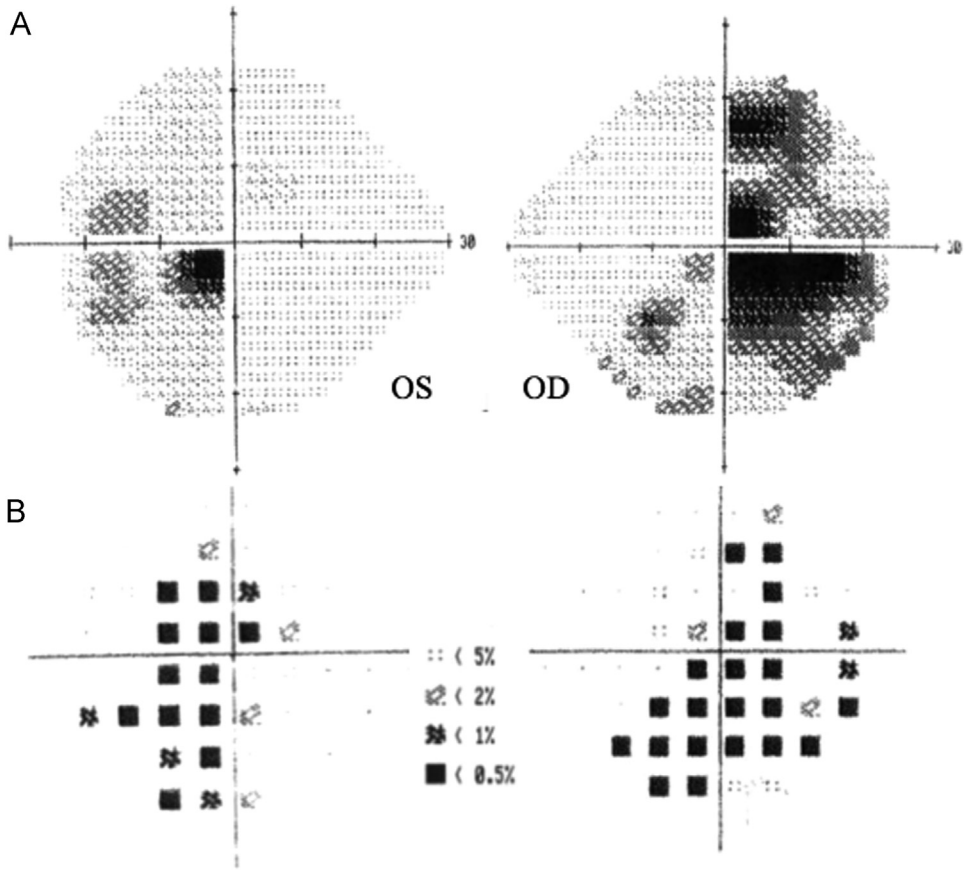

Fig. 2—Humphrey SITA-Standard 24–2 visual fields at presentation showing predominantly bitemporal visual field loss in both eyes using grayscale (a) and total deviation (b) plots. The mean total deviations were −3.96 dB OS and −8.44 dB OD.

perception, and peripheral vision. On repeat examination at her 6-month visit, her best-corrected visual acuity was 20/25 OD and 20/30 OS. She identified 6 of 11 color plates OD and 8 of 11 color plates OS. Confrontation visual fields were full, and there was no progression in her mild optic disc pallor in either eye. Humphrey SITA-Standard 24-2 visual fields showed a final mean deviation of −3.81 dB OS and −1.52 dB OD (Fig. 3). We did not repeat the MRI because she had clinically improved.

Discussion

Ethambutol optic neuropathy (EON) is a well-documented cause of medication-related optic neuropathy encountered worldwide, typically seen in the setting of the multidrug treatment of tuberculosis and *M avium* complex.[1] The toxicity is dose dependent, with the lowest risk occurring in those taking total daily doses of <15 mg/kg.[2] Recent studies have also identified older age, hypertension, renal failure, and dosing duration as risk factors for developing EON.[3–5]

EON classically presents with the gradual onset of decreased visual acuity, dyschromatopsia, and central or cecocentral visual field defects several months after the initiation of the medication, symptoms likely related to mitochondrially induced papillomacular bundle dysfunction.[1,2] However, bitemporal field defects with respect to the vertical midline have also been described in EON, a finding that has been histopathologically attributed to degenerative changes within the central portion of the optic chiasm and proximal optic tracts, leading to selective damage of the nasal crossing fibers.[6,7] Bilateral disc edema can sometimes be seen if the patient is examined early in the course of the ocular symptoms, but in many patients the only funduscopic finding is temporal optic disc pallor.

Most cases of EON have no MRI correlate. Rare exceptions include case reports of increased T2 signal in the chiasm and optic tracts in the setting of overdose[8] or more aggressive mycobacterial treatment.[9] To our knowledge, we are the first to report the presence of chiasmal gadolinium enhancement caused by ethambutol toxicity.

Our finding is important because the presence of chiasmal enhancement may inadvertently lead to a costly or invasive evaluation for autoimmune, inflammatory, or paraneoplastic causes of chiasmal neuritis. In addition, the subsequent empiric use of corticosteroids could complicate treatment of the primary mycobacterial infection.

The etiology of the chiasmal nerve enhancement in our patient is likely attributable to the morphological changes within the central crossing fibers previously reported in