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Ethambutol Toxic Optic Neuropathy

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Abstract

This article presents a case of ethambutol toxic optic neuropathy determined during the routine examination of a 56-year-old female. Ethambutol is an established drug for the treatment of tuberculosis, but has significant side effects, notably optic neuropathy. The prognosis for vision restoration is unpredictable, with the possibility of permanent vision loss. Treatment cessation is the only option to limit ocular damage; therefore, the early recognition of optic neuropathy by ethambutol is essential.

Keywords: HIV, AIDS, TB, WHO.

Introduction

Tuberculosis, because of infection with Mycobacterium tuberculosis, is said to cause an estimated 1.7 million deaths annually, while almost 9 million people contract the disease each year.[1] A total of 1.4million people died from TB in 2019 according to WHO. The high numbers of deaths because of the disease occur despite mortality being preventable by timely and readily available and effective treatment.[2] However, the improvement in treatment and the eradication of the disease have been hindered by the high prevalence of the human immunodeficiency virus (HIV), persisting global poverty and the emergence of highly drug-resistant forms of TB.[3] Historically, there has been a reduction in the incidence of TB infections until the 1980s when the advent of HIV and acquired immunodeficiency disease syndrome (AIDS) saw a resurgence in TB infections, especially in the immunocompromised.[4]

Ethambutol (ethambutol hydrochloride) has been a long-established front-line drug in the treatment of TB, despite exhibiting toxicity.[5] A major toxic effect of ethambutol is optic neuropathy.[6] In combination with nephropathy, the optic neuritis is exacerbated because of the extended half-life of ethambutol[6] Optic neuropathy, especially retrobulbar optic neuropathy, resulting from ethambutol, is often unpredictable and dependent on treatment cessation, with variable resolution post-treatment.[7]

Case report

An Asian female, aged 56, presented to the outpatient department of her regional hospital on 13 January 2021, complaining of decreased vision at distance and near over the preceding 8months which was gradually progressive more from past 1-2months. She was facing difficulty with her current (progressive addition) spectacles, and reported no visual difficulties with them up until 1-2months prior. She had been diagnosed with extra pulmonary TB in May 2020 and placed on a

combination of four anti-TB medications (rifampicin, isoniazid, pyrazinamide and ethambutol). She was warned by her attending physician at the that the medication prescribed may have ocular side effects. Necessary investigations were done including red color desaturation test and subsequent to her diagnosis of ethambutol toxic optic neuropathy (ETON) she was placed on anti-tuberculous treatment which excludes ethambutol and pyrazinamide, for her continuing TB therapy, along with vitamin B and unspecified immunity booster vitamin supplements. There was no other family medical history.

Diagnostic data

Best-corrected visual acuity (BCVA) distance (Snellen chart at 6 m) was Right 6/18 and Left 6/9P. Near vision best corrected was N6 both eyes. Ocular motilities were full smooth and accurate in both eyes with a penlight target. A slit-lamp examination revealed no conjunctivalhyperaemia, and 3+/4 open angles (Van Herick), while an optic section indicated no lens opacification. Ophthalmoscopy revealed no disc or macular abnormalities in either eye. There was a gross central field defect on confrontation, theright eye more than the left, which was confirmed with a dense central pattern on the Amsler grid, again with the right eye more than the left. Generaliseddyschromatopsia was evident with red color being identified as pink. Intraocular pressure measured with a Non Contact Tonometer was Right 19 mmHg and Left 18 mmHg.

Differential diagnosis

Optic neuropathy is a frequent cause of vision loss, with diagnosis made on clinical findings.[8] The clinical history indicates the possible aetiology of the optic neuropathy, where rapid onset is typical of demyelinating, inflammatory, ischaemic and traumatic causes, and a slower course is indicative of compressive, toxic or nutritional and hereditary causes.[8] In order to accurately diagnose the disease, differential diagnoses need to be considered. Frequent causes of optic neuropathies include viral and bacterial causes, ischaemic optic neuropathies, demyelinating diseases, compressive or infiltrative optic neuropathies, Leber's hereditary optic neuropathy and toxic and deficiency optic neuropathies.[9]

Discussion

Toxic optic neuropathy (TON) is typically painless, progressive, bilateral and symmetrical with a classic central or centrocecalscotoma and decreased visual acuity, often with attendant colour vision deficiency. Toxic optic neuropathy is also caused by damage to the optic nerve through different toxins, including drugs, metals, organic solvents, methanol and carbon dioxide.[9] A similar clinical picture may also be caused by nutritional deficits, including B vitamins, folic acid and proteins with sulphur containing amino acids. Certain antimicrobial agents, antiepileptic drugs,[10] antiarrhythmic drugs, drugs used to combat alcoholism, skin-lightening creams (hydroquinolones), antimetabolites, cancer treatments (tamoxifen) and erectile dysfunction preparations (sildenafil,) have been associated with optic neuropathy.9Other drugs with potential, yet rare, vision-threatening neuropathy side effects include amiodarone, a potent antiarrhythmic agent that is used to treat ventricular arrhythmias,[11] the anticonvulsant medication vigabatrin[12] and even ibuprofen.[13]

The first-line treatment of TB, consisting of four anti-TB elements (rifampicin, isoniazid, pyrazinamide and ethambutol) is prescribed for an initial 8-week period, following which a sputum test is undertaken. If the sputum test is positive for TB bacillus, a further 4-week

course is normally prescribed. After the initial phase, a choice of several options for the continuation phase of either 4 or 7 months (a total of 6–9 months for treatment) is available.[14]

A visual prognosis with ETON is often devastating, with permanent visual field disturbances and colour vision deficiency.[15] There is no known treatment for this form of TON other than drug cessation.[16] This is in contrast to other causes of optic neuritis, where a post-treatment return of visual fields to normal after time is common.[15] In the case of ETON, vision restoration prognosis is unpredictable, often resulting in some permanent vision loss which could be partial or severe.[17] Treatment cessation appears to be the only option to limit ocular damage, and the early recognition of optic neuropathy is essential. Ophthalmic monitoring should be considered in all patients with ethambutol therapy.[18]

Because of the high prevalence of TB in developing countries, many patients undergoing treatment of the disease will present for routine eye examinations, possibly unaware of the potential side effects of their medication. An awareness of the side effects of TB treatment and prompt and accurate recognition of the signs and symptoms of ETON by eye care practitioners can potentially prevent complete vision loss in susceptible individuals. All patients presenting with unexplained vision loss should be screened for the adverse effects of all medications, even if used for short periods.[13] Colour vision evaluation and visual field testing using an Amsler grid should be a standard practice. Optical coherence tomography (OCT) is important in excluding other causes of vision loss because of neuritis or other aetiologies.[18]

Conclusion

The vast numbers of patients on TB treatment invariably result in such patients presenting for routine eye examinations. It is imperative that a thorough case history be conducted for each patient, including systemic and ocular disease history as well as prescribed medications. This is essential in being able to establish potential sight-threatening conditions because of drug toxicity, an important differential diagnosis in retrobulbar optic neuritis and every case of unexplained visual disturbance, even with the short-term use of medication.[13]

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