ISONIAZID THE CULPRIT BEHIND TOXIC OPTIC NEUROPATHY

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ABSTRACT

Literature regarding toxic optic neuropathy (TON) due to isoniazid (INH) is scarce. This diagnosis is often missed, leading to unnecessary delay in institution of corrective measures. Often, this delay can worsen the patient’s vision, with a high likelihood of development of serious damage to the patient’s vision. We report a case of a 49-year-old gentleman, afflicted with meningeal tuberculosis, who developed visual disturbances following the administration of antitubercular therapy. The patient’s vision improved dramatically following INH’s withdrawal. This case highlighted the need to keep INH as a possible cause for TON, especially if vision does not improve following ethambutol’s withdrawal. Further, this case attests to the need for thorough and periodic visual examinations in patients receiving antitubercular therapy.

Keywords: Optic neuritis, Antitubercular treatment, Reversible visual disturbance, Pyridoxine deficiency.

INTRODUCTION

Tuberculosis caused by Mycobacterium tuberculosis is an airborne infection in 80% of cases [1]. It is a contagious infection affecting wide range of population in low income and developing countries with India being highest burden country in the world [2]. Various drug regimens are used to treat tuberculosis which includes isoniazid (INH), rifampicin, pyrazinamide, INH, and streptomycin used as first-line agents. Adverse drug reactions due to tuberculosis are very common as these drugs are given for a longer period ranging from 6 months to 2 years depending on the course of illness and diagnosis at the first place. Optic neuropathy, due to antitubercular drugs, has rarely been attributed to INH. An extensive literature search revealed only a handful of cases, where INH has been implicated as the causative agent for optic neuropathy [3,4]. Given that ethambutol is the more commonly associated antitubercular agent with optic neuropathy [5], the odds of overlooking INH as the offending agent is extremely high. The resultant delay in arriving on the appropriate diagnosis could manifest in serious damage to the patient’s vision, maybe even optic atrophy. Further, given that the incidence of tuberculosis overall and particularly, meningeal tuberculosis is extremely high, especially in the developing nations like India [6], it is of imminent signiﬁcance that a greater awareness of the INH induced ocular disturbances be created within the scientiﬁc community. Hence, with the aim of contributing to the existing literature, we report a case of INH induced toxic optic neuropathy (TON) in a tubercular patient in a tertiary care hospital in southern India.

CASE REPORT

Informed consent was taken from the patient. A 49-year-old gentleman, devoid of any other comorbidity, was diagnosed and initiated on the first line antitubercular treatment for tubercular meningitis since October 30th, 2015. During the gentleman’s follow-up visit on January 23rd, 2016, he complained of sudden, painless blurring of vision of 4 days’ duration. Examination revealed features of abnormality of color vision and perimetry revealed central scotoma. A recent fundoscopic examination revealed worsening of the inflammation of the optic nerve and visual acuity also was markedly reduced. Hence, in light of the worsening of the ophthalmological symptomatology, a decision to withdraw INH was taken. Further, a second line anti-tubercular agent, i.e., injection amikacin 750 mg and moxifloxacin 400 mg once daily was started. Subsequently, during the patient’s stay in the hospital over the next 10 days, there was drastic improvement in patient visual symptoms. The lack of change in the magnetic resonance imaging picture, before and post withdrawal of INH, further conﬁrmed it to be a case of INH induced TON.

DISCUSSION

TON is one of the most underdiagnosed ophthalmologic conditions apparently diagnosed when the stage of irreversible vision loss is reached. Impairment of vision defines it due to damage caused to the optic nerve. Anterior pathway of eye is highly susceptible to damage via various toxins encountered in the workplace, eating some foods, ingesting toxins, and due to drugs without sex predilection across all populations. Reduced color vision, papillo macular bundle damage and central or cecocentral scotoma usually forms a triad in diagnosing TON. Various etiologies cause TON with both toxins and nutritional factors in tandem playing a synergistic role. It usually presents as bilateral, symmetrical painless loss of vision. Dyschromatopsia is usually the first presenting sign gradually leading to generalized loss of color perception. Loss of visual acuity usually starts as a relative scotoma slowly leading to total loss of vision with peripheral visual sparing. The one exception to this is acute loss of complete vision seen in cases of methanol poisoning. Various causes of TON are illustrated in Table 1. Pathogenesis behind TON is mainly impairment of vascular supply either to the optic nerve or to the papillo macular bundle. The optic nerve is highly susceptible to this ischemic damage due to its unusual configuration leading to accumulation of toxins; this remains unproven as of date. However, the common generalized mechanism accepted till date is mitochondrial damage and disturbance of physiological hemostasis [7].

Antitubercular medications are known to cause various side effects, and ophthalmic adverse effects have also been reported over the years. Ethambutol and INH causes optic neuropathies but TON due to ethambutol is very common when compared to INH. Ethambutol causes optic neuropathy in about 1-15% patients treated with it for tuberculosis. Proposed mechanism of ethambutol-induced TON is mainly through its zinc chelating property and its said to be due to the influx of calcium ions into the mitochondria leading to excitability [7]. It is usually dose dependent and optic neuropathy reverses itself on discontinuation of the drug. In a recent systemic review, as per literature, it was found that the incidence of ethambutol induced ocular
In our case, the patient complained of vision abnormalities within 3 months of initiation of antitubercular therapy. Initially, ethambutol was suspected as the offending agent, and the drug was discontinued. Subsequently, the gentleman’s vision worsened. Hence, INH was suspected as the next possible cause for the visual deterioration and discontinued. The patient improved drastically on stopping INH. The patient’s visual acuity was 20/20 in both eyes. Therefore, ethambutol was not considered as the cause of TON.

In conclusion, as toxicity was 22.5 per 1000 persons treated with INH compared to the toxicity of ethambutol (19.9 per 1000 persons treated), INH is a safer option in the treatment of tuberculosis. However, it is important to monitor the patient’s vision periodically to prevent the occurrence of TON. If TON occurs, INH should be discontinued immediately to prevent permanent visual damage.