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A rare case of Ethambutol toxicity - Early diagnosis and treatment

[1]Dr. Rashmi Rajur, Senior resident department of general medicine TNMC Mumbai.

Corresponding Author: Dr. Rashmi Rajur, Senior resident department of general medicine TNMC Mumbai.

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Abstract

Here we are presenting a young 26-year female with tubercular meningitis. Who developed vision loss after starting antitubercular treatment. Ethambutol is the drug responsible for vision loss. Early diagnosis of vision loss and stopping the drug helped in improvement of vision and prevented permanent vision loss.

Introduction

In developing countries like India tuberculosis is most prevalent disease. Tuberculous meningitis (TBM) is a manifestation of extrapulmonary TB, developing in 1%–5% of the approximately 10 million cases of TB worldwide [(1)(2)(3)]. Mycobacterium tuberculosis bacilli enter the host by droplet inhalation, the bacilli may then seed to the central nervous system (CNS) and result in three forms of CNS TB: tuberculous meningitis, intracranial tuberculoma, and spinal tuberculous arachnoiditis [(4)].

Multidrug antitubercular therapy is considered the mainstay of treatment in tuberculous meningitis, however the optimal duration is unclear, and the efficacy of drugs may be limited due to variable CSF penetration [(5)]. Anti-tubercular drugs have many side effects. One of the anti-tubercular drug that is Ethambutol may cause occular toxicity resulting in vision loss. However this incidence is very low [(6)(7)]. Early detection and treatment of Ethambutol toxicity has a good outcome.

Case report

A 26-year-old female came with complaints of altered sensorium and fever since 2 days. Patient also had headache and vomiting 2 days back. There was no history of loose stools, cough, convulsions and urinary incontinence.

On examination, patient pulse rate was 116 bpm, blood pressure 120/70 mmHg and spo2 97%. Temperature was 38.9 °C. Cardiovascular, respiratory and per abdominal examination was normal. On Central nervous system examination Patient was drowsy and disoriented. Neck rigidity was present.

Based on history and physical examination meningitis was suspected and CSF studies were done. MRI brain also done. These were consistent with tubercular meningitis. The patient was started on antitubercular treatment. After 5 to 7 days of antitubercular treatment

the patient gradually improved. Patient became conscious and oriented. But after 1 month the patient vision was decreased. Hence repeat MRI brain was done which showed Ethambutol toxicity. Hence Ethambutol was withheld and after 15 to 20 days vision improved and MRI brain showed resolution of Ethambutol toxicity.

Occular examination

Visual acuity: Right eye: Finger counting at 3 feet

Left eye: Finger counting at 2 feet.

Occular motility: Normal. No ptosis and no nystagmus.

Pupils: Bilateral equal and reactive to light

Investigations

The blood investigations were hemoglobin 11.2 g/dL, Whole blood count 14.5/ microliter, Platelet count 223460 / microliter, Serum creatinine 0.8 mg/dl, Serum urea 28 mg/dl, Serum sodium 138 mEq/L, Serum potassium 4.3 mEq/L, Total bilirubin 1.1 mg/dL, SGOT 38 U/L, SGPT 42 U/L, HIV Non-reactive.

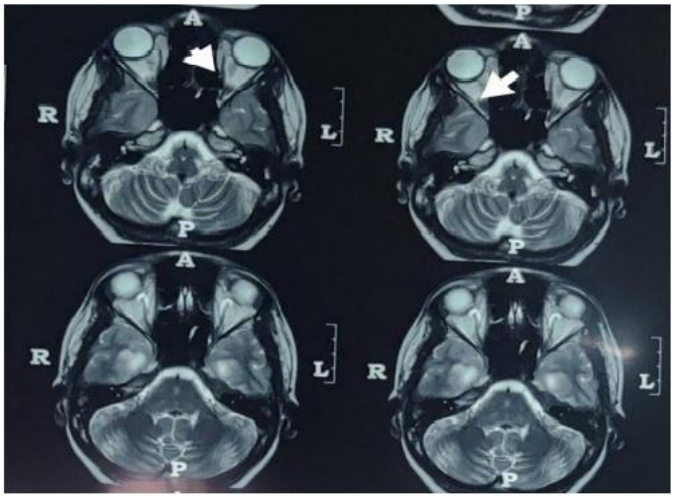
The CSF studies were, CSF cytology 340 cells with 84% lymphocytes, 16% neutrophils, CSF protein 70 gm and CSF ADA levels 28.6 IU/L.

MRI brain after 1 month of starting Ethambutol

Multiple disseminated enhancing tubercular foci in bilateral cerebral and cerebellar hemisphere. Basal exudates and nodular leptomeningeal enhancement in both the peri- mesencephalic, suprasellar, parasellar and middle cerebellar artery cisterns and bilateral sylvian fissures and around the optic chiasma and intracranial portion of both the optic nerves, along the anterior surface of pons, me dull, sulcal spaces of both the cerebellum and fronto – parietal lobes consistent with meningitis, likely Tubercular in etiology.

T2/STIR hyperintense signal in bilateral optic tract, optic chiasma and visualised proximal part of optic radiation.Optic chiasma appears bulky. These suggest ethambutol toxicity.

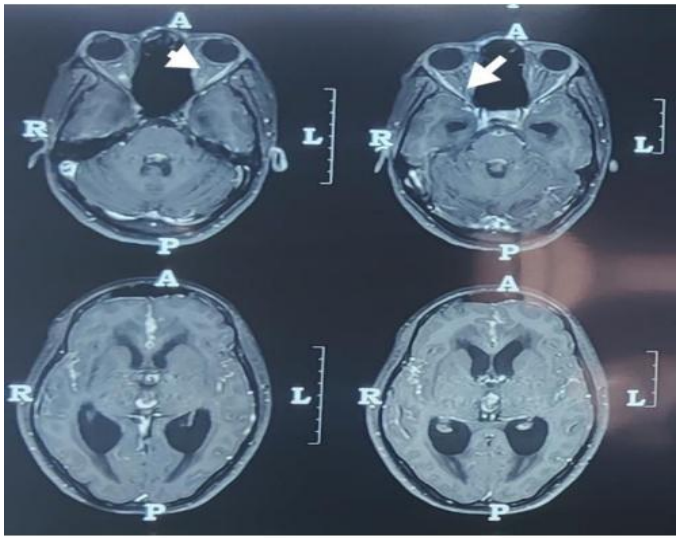
Figure 1:



MRI brain after 4 weeks of stopping Ethambutol

As compared to previous scan there is mild reduction in T2/STIR hyperintense signal in the intracanalicular portion of the bilateral optic nerves and chiasma.

Figure 2:



Discussion

Tubercular meningitis, is a specific type of bacterial meningitis caused by the Mycobacterium tuberculosis infection of the meninges. The treatment of TB meningitis is isoniazid, rifampicin, pyrazinamide and ethambutol for two months, followed by isoniazid and

rifampicin alone for a further ten months [8]. Steroids help reduce the risk of death. They can be used in the first six weeks of treatment [9]. The drugs used in treatment of Tubercular meningitis may have many adverse effects. Ethambutol use may lead to permanent vision loss by inducing a dose- and duration-dependent optic neuropathy. However, ethambutol continues to be used because of its anti-mycobacterial action with relative systemic safety [10]. The toxicity typically occurs between 3–5 months of usage, though it may present as early as within 1 month and as late as 12 months of use [11].

Earlier, Ethambutol ocular toxicity was considered as reversible, but over time, this concept has changed to one of variable or partial recovery with increased emphasis on early detection and management [12]. Typically, patients present with subacute, bilateral, and painless symmetric loss of central vision, though visual involvement may be asymmetrical or sequential [13][14].

In the early stages of ethambutol toxicity, the pupillary responses are preserved and normal, but in advanced cases, relative afferent pupillary defects or sluggish reactions may be seen.

The fundus exam is often normal in the initial stages, or a small peripapillary hemorrhage and hyperemic discs may be observed. If not managed early, ethambutol toxicity would eventually lead to optic disc pallor [15]. Visual fields typically show a cecocentral or bitemporal defect.

Dyschromatopsia may be the earliest sign of toxicity, and blue-yellow color changes are the most common [16]. Only treatment for Ethambutol toxicity is to stop the drug. Recovery may take weeks to months.

Conclusion

Ethambutol toxicity can cause a permanent vision loss, if it is not diagnosed and treated early. Hence the patients on antitubercular treatment should be tested for vision regularly because the only treatment for Ethambutol toxicity is to discontinue Ethambutol as early as possible.

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