

Cycloserine Induced Neurotoxicity: A Rare Case Report

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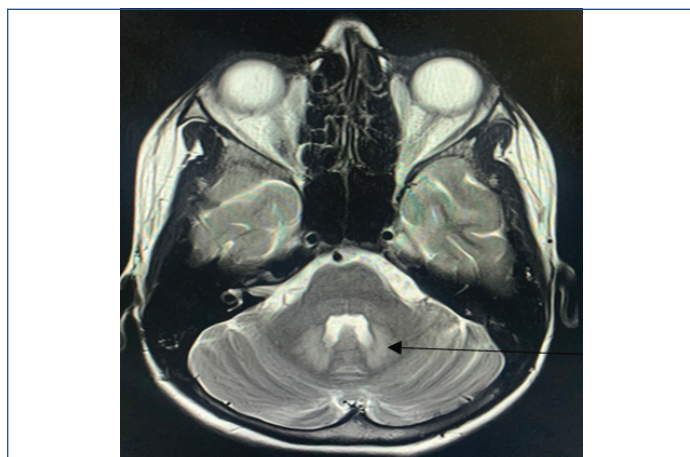
ABSTRACT

Cycloserine is one of the many drugs used in treatment of Multidrug Resistant Tuberculosis (MDR-TB). Neuropsychiatric complaints are common after cycloserine administration. Reports of neuroimaging in cycloserine neurotoxicity are rare. Authors hereby reports a case of 17-year-old female, who presented with hallucination and delirium since 2 weeks. She was a known case of pulmonary MDR-TB and was on Anti-Koch's Treatment category IV (AKT) for the same since last 12 months. On clinical examination, the patient was conscious and co-operative but disoriented. Magnetic Resonance Imaging (MRI) revealed, symmetric hyperintensities on T2 weighted images in bilateral dentate nuclei with restriction of diffusion, on diffusion weighted images. In addition, two well-defined T2 hypointense ring enhancing lesions were seen in right parietal and occipital regions. Patient's symptoms improved on stoppage of cycloserine. On follow-up MRI, 4 weeks after withdrawing the drug, there was complete reversal of MRI findings.

Keywords: Magnetic resonance imaging, Multidrug resistant tuberculosis, T2 hyperintensity

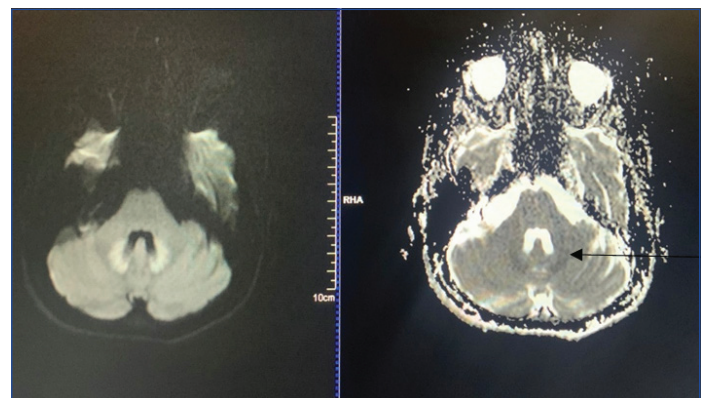
CASE REPORT

A 17-year-old female presented to the Outpatient Department of a tertiary care hospital with complaints of hallucinations and delirium since last 2 weeks. She was a known case of pulmonary Multidrug Resistant Tuberculosis (MDR-TB) and was on Anti-Koch's Treatment category IV (AKT) for the same since last 12 months. The drugs included in this category were kanamycin, ofloxacin, ethionamide, ethambutol, pyrazinamide and cycloserine [1]. There was no history of any neuropsychiatric complaints in the past. Lumbar puncture was not done as a part of current investigation as the patient did not have any meningeal signs. Other laboratory parameters like haemogram, liver function tests and serum electrolytes were within normal limits. Electroencephalogram (EEG) was normal and did not show any abnormal finding. On Magnetic Resonance Imaging (MRI), there were symmetrical areas of hyperintense signal in bilateral dentate nuclei on T2 Weighted Images (WI) [Table/Fig-1], with restriction of diffusion on diffusion WI and corresponding drop on signal on Apparent Diffusion Coefficient (ADC) maps [Table/Fig-2]. No evidence of signal dropout was noted on Susceptibility Weighted Images (SWI).

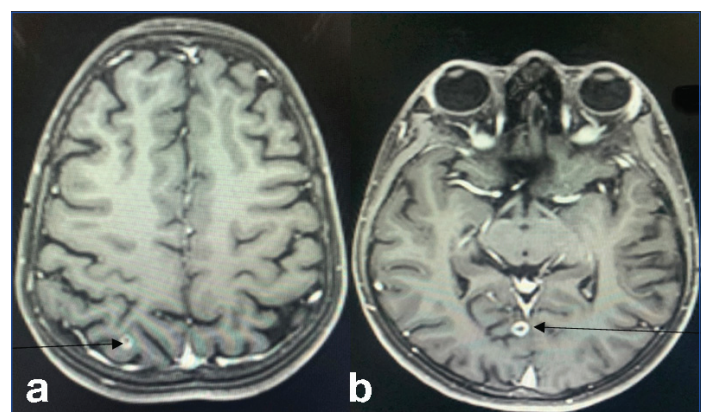


[Table/Fig-1]: Axial T2 weighted images showing hyperintense signal in bilateral dentate nuclei (black arrow).

There were two subcentimeter sized hypointense lesions on T2 WI which showed ring enhancement on postcontrast images in right parietal and occipital regions [Table/Fig-3a,b].



[Table/Fig-2]: Axial DWI and ADC maps ($600 \times 10^{-6} \text{ mm}^2/\text{s}$) showing restricted diffusion in bilateral dentate nuclei.

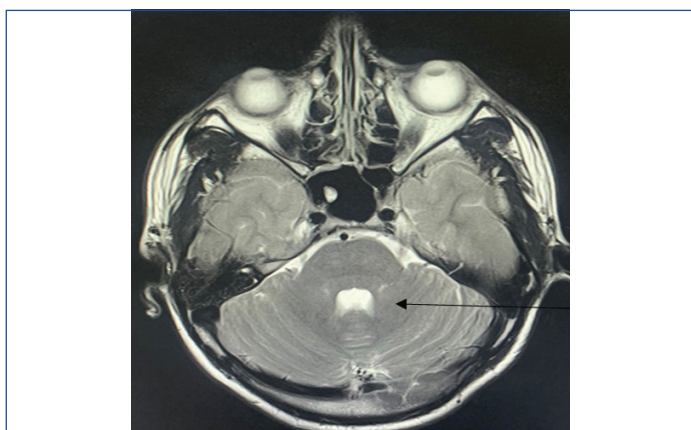


[Table/Fig-3]: Postcontrast axial images showing ring enhancing lesions (black arrow) in a) right parietal and b) occipital regions.

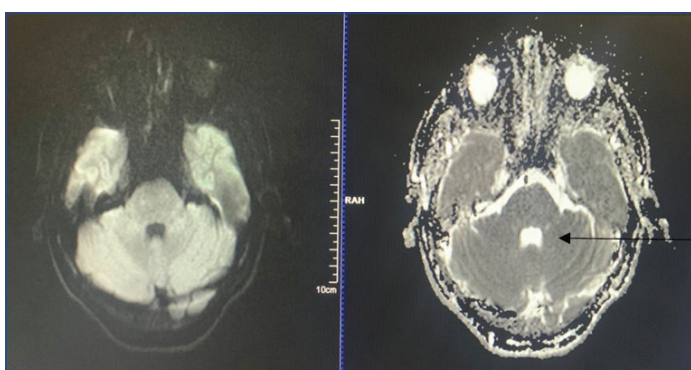
Findings on MRI were suggestive of tuberculomas with cycloserine neurotoxicity. Hence, cycloserine was withheld and clofazimine was added.

On follow-up MRI after 4 weeks, there was interval resolution of symmetrical hyperintense signal on T2 WI [Table/Fig-4] with no evidence of restricted diffusion [Table/Fig-5]. The ring enhancing lesions in right temporal and parietal region showed no significant interval change. Clinically, the patient showed improvement and there were no hallucinations, however the patient had low mood

even after withdrawing cycloserine. On last visit, patient was doing well and is on regular follow-up.



[Table/Fig-4]: Follow-up axial T2 WI showing complete resolution of hyperintense signal in bilateral dentate nuclei (black arrow).



[Table/Fig-5]: Follow-up of Axial DWI and ADC maps showing no restricted diffusion in bilateral dentate nuclei (black arrow).

DISCUSSION

N-methyl-D-aspartate agonist, Cycloserine, is used routinely to treat MDR-TB [2]. It is used as a second-line agent for MDR-TB therapy. Adverse drug reactions with cycloserine are mostly psychiatric like aggressive behaviour, hallucination, depression, disorientation, dizziness, drowsiness, suicidal tendency and neurological like headache, seizures and vision disturbances [3]. Cycloserine is associated with a higher incidence of psychiatric and neurological adverse drug reactions than other second-line drugs like kanamycin, ethionamide, ofloxacin and pyrazinamide [4]. However, these symptoms are reversible and disappear after stoppage of cycloserine. Pyridoxine was given daily also helps to prevent side-effects [5].

On MRI, cycloserine toxicity is demonstrated by hyperintense signal in bilateral dentate nuclei on T2 WI representing cytotoxic oedema and which show restricted diffusion with corresponding drop of signal on ADC maps [6]. These changes are reversible on MRI as well after stoppage of medication [7].

Similar case has been reported by Sharma S et al., where a young male who developed neurological symptoms during therapy for MDR-TB which included cycloserine [3]. The MRI of the brain

showed reversible bilateral symmetrical T2/FLAIR hyperintensities in dentate nuclei. Clinical and MRI findings were consistent with cycloserine toxicity. The patient's MRI findings and clinical symptoms resolved on stoppage of cycloserine.

A similar case has been reported by Kim S et al., where a young woman suddenly felt dizzy with graying out of her vision during her MDR-TB treatment. MRI revealed symmetrical high signal intensity in the dentate nuclei on Diffusion Weighted Images (DWI) and decreased ADC values [5]. After 2 weeks, a follow-up MRI was done after the stoppage of cycloserine, which showed the resolution of the high signal intensity in the dentate nuclei.

Another case has been reported by Kwon HM et al., where a 69-year-old female, developed hypersomnolence and asterixis during the therapy for tuberculous lymphadenopathy which included cycloserine. The MRI of the brain revealed hyperintense signal on T2WI in both thalami. On stoppage of cycloserine, there was resolution of patient's symptoms and the follow-up MRI after one month which showed marked reduction of the high signal intensities in both thalami [7].

In case reported by Jain M et al., reported a 24-year-old female diagnosed with primary MDR-TB at a tertiary hospital treated with cycloserine, supplemental pyridoxine and other drugs. The patient presented after two months with hypervigilance, labile mood, daytime somnolence and suicidal thoughts. The MRI of the brain showed T2 hyperintense signal in the dentate nuclei with restricted diffusion on DWI and decreased apparent diffusion coefficient values. Following cycloserine discontinuation, some symptoms and MRI findings resolved except persistent labile mood [2].

The present case highlights the importance of MRI in diagnosing the neurotoxicity caused by cycloserine and how it can help in timely management by withdrawal of the drug which leads to reversibility of symptoms.

CONCLUSION(S)

The major findings on MRI associated with cycloserine toxicity were hyperintense signal on T2 WI showing restricted diffusion on DWI and ADC maps in the dentate nuclei. Early diagnosis by using brain MRI and prompt discontinuation of the medication leads to reversibility of the brain findings on MRI and symptomatic relief as well.

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