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BILATERAL DENTATE NUCLEUS T2/FLAIR HYPERINTENSITY IN A PATIENT OF CHRONIC KIDNEY DISEASE: A RARE MANIFESTATION OF ISONIAZID INDUCED CEREBELLAR TOXICITY

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ABSTRACT Isoniazid is the mainstay of anti-tubercular therapy. Used in isolation or in combination with other anti-tubercular drugs, it is generally well-tolerated. While hepatotoxicity are reported, neurotoxicity in patients of chronic kidney disease remains uncommon. We report a case of rare radiological manifestation of cerebellar toxicity due to isoniazid in a patient with chronic kidney disease.

KEYWORDS : Isoniazid, Dentate Nucleus, T2/FLAIR Hyperintensity, MRI

INTRODUCTION

Isonicotinylhydrazide (INH) is an anti-tubercular drug often used together with rifampicin, pyrazinamide, and either streptomycin or ethambutol for active tuberculosis.[1,2] It is usually taken per oral but can be given intramuscular.

Isoniazid neurotoxicity usually manifests with seizures, encephalopathy, and peripheral neuropathy; however, cerebellar ataxia is rare.[3]

The first signs and symptoms of isoniazid toxicity may appear within 30 minutes to two hours after ingestion and may include nausea, vomiting, rash, fever, ataxia, slurring of speech, peripheral neuritis, dizziness, and stupor[4].

In this report, we present a case of isoniazid induced cerebellar toxicity in a patient with chronic kidney disease in the form of bilateral dentate nucleus T2/FLAIR hyperintensity on MRI.

CASE REPORT

A 81-year-old woman, a known case of chronic kidney disease (CKD) presented with history of cough and fever from last four months. Fever was low grade, intermittent and was associated with poor appetite. Cough was dry and associated with pruritic pain. She had no abdominal complaints. The examination showed dull note on percussion on left side of chest with decreased breath sounds on auscultation. There was no hepatosplenomegaly and breast examination was normal. Neurological examination was unremarkable.

She was evaluated for fever and cough. Her hemoglobin, total leukocyte count and platelet counts were 8.5 g/dl, 5880/µl, and 1.5 lakhs/µl, respectively. The kidney function tests revealed serum urea of 43 mg/dl and serum creatinine of 6.90 mg/dl. The serum sodium and potassium levels were 136 mmol/l and 4.8 mmol/l, respectively. The liver function tests and thyroid function tests were normal. Blood cultures were sterile. X ray showed left sided moderate pleural effusion (Figure 1). Ultrasound abdomen showed left sided moderate pleural effusion and bilateral echogenic kidney however size of kidney appeared normal. There was no hydroureteronephrosis.

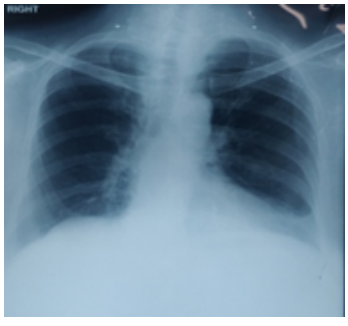
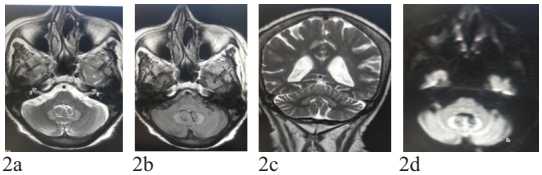


Fig 1: Chest x ray PA view shows pleural effusion on left side

Pleural tapping was done and was sterile. In view of low grade fever, dry cough and pleural effusion,she was empirically initiated on antitubercular therapy with four drugs (isoniazid [INH], rifampicin, pyrazinamide and ethambutol) with appropriate dose adjustments for her kidney function. Two months after initiation of antitubercular drug patient developed pruritis, ataxia and psychosis. Magnetic resonance imaging (MRI) brain showed T2W/FLAIR hyperintensity and diffusion restriction in bilateral dentate nuclei with no evidence of hemorrhage , abscess or tuberculoma (Figure 2). As there was no other obvious explanation of the sudden development of cerebellar ataxia, INH induced toxic encephalopathy was considered and INH was withdrawn. Three days after withdrawal of INH, patient's condition started to improved.



2a 2b 2c 2d

Fig 2: Signal change in the bilateral dentate nucleus. Axial T2W MR image(Fig 2a) and T2W FLAIR image(Fig 2b) and Coronal T2W image(Fig 2c) shows hyperintensity in dentate nuclei which shows restriction on DW image (Fig 2d)

DISCUSSION

Isoniazid is a bactericidal antitubercular drug that interferes with pyridoxine metabolism leading to deficiency of this vitamin. Adverse effects occur in about 5% of patients on INH, who are also on adequate doses of pyridoxine (10–50 mg/day). Common neurotoxicity of INH is that of peripheral neuropathy that is usually mild and reversible. Due to its hepatic clearance if toxicity happens is generally manifested with hepatotoxicity and so no dose modification is generally required in patients with kidney disease and is used extensively in patients with CKD, on dialysis and following a renal transplant.[5]

Altered consciousness secondary to encephalopathy as Central nervous system toxicity due to INH is described in literature but cerebellar ataxia is very rare.[6]

Severe neurotoxicity presenting with encephalopathy and seizures has been described with INH overdose in children which requires treatment with intravenous pyridoxine.[7]

Our patient was given with 40 mg/day of pyridoxine along with INH 300 mg once a day. She was not treated with higher doses of pyridoxine as the neurological features were not severe, and they responded to withdrawal of the drug. Cerebellar ataxia due to INH has been described in the past in children.[8]

In developing countries, where tuberculosis is prevalent, INH toxicity should be included in the differential diagnosis of bilateral dentate nuclei hyperintensity, among other causes such as metronidazole[9] or methyl bromide toxicity,[10] as well as enteroviral infections,[11] or atypical Wernicke's encephalopathy.[12]

SUMMARY

In summary, we describe a patient with CKD developing cerebellar ataxia and MRI findings of B/L dentate nuclei lesions after the commencement of INH. The neurological features completely resolved after withdrawal of INH. Clinicians should be aware of this rare complication of INH therapy

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