Isoniazid-induced Encephalopathy in a Patient with Pott's Disease with Chronic Kidney Disease: A Case Report

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Abstract

We report an isoniazid-induced encephalopathy in a man with chronic renal failure. Drug-induced encephalopathy is a common side effect of many drugs. Isoniazid (INH), a first-line drug for tuberculosis, can cause encephalopathy in patients with chronic kidney disease (CKD). For Pott's disease of the thoracic spine, he received rifampicin, INH, pyrazinamide, and ethambutol with pyridoxine and prednisolone. But the patient is free of pyridoxine for two and a half months. Subsequently, after treatment, the patient experienced recurrent episodes of altered consciousness, irrelevant conversations, and disorientation. After ruling out other causes, isoniazid-induced encephalopathy was suspected and confirmed by improvement of symptoms after discontinuation of high-dose isoniazid and pyridoxine.

Keywords: Chronic kidney disease, Isoniazid-induced encephalopathy, Tuberculosis

Introduction:

According to Global Tuberculosis Report 2019, approximately 10 million people were infected with tuberculosis and 1.2 million HIV-infected people died from tuberculosis in 2018.[1] In chronic kidney disease (CKD) patients, the incidence of tuberculosis is 10 times higher than in the general population due to decreased cell-mediated

immunity resulting from uremia.[2,3] In addition, adverse events associated with antituberculosis drugs are reported more frequently in patients with chronic renal failure.[4] Isoniazid, also known as isonicotinic acid hydrazide (INH), is an antibiotic used as one of the first-line drugs in the treatment of tuberculosis. The level of INH in the plasma depends on the genetically determined slow or fast acetylation process in the liver. Since INH is mainly excreted by the kidneys in free and acetylated forms, a reduction in INH dose may be required in patients with chronic renal failure.[5] The neurotoxic side effects of INH are well known. These can include peripheral neuropathy, optic neuritis, encephalopathy, dysarthria, and seizures, as well as psychiatric symptoms such as psychosis, obsessive-compulsive disorder, and mania.[6] The mechanism of these effects is inhibition of pyridoxine phosphorylation, resulting in reduced production of pyridoxal-5-phosphate, a coenzyme involved in neurotransmission.[3] In addition, reduced acetylation of INH in patients with chronic renal failure contributes to the prolongation of the drug half-life.[7] In 1961, Castaigne et al reported a case of INH-induced encephalopathy, which was one of the first drug-induced encephalopathies reported in the literature.[8]

Dialysis patients and slow acetylators transmitted by NAT2 polymorphisms are at increased risk of developing INH encephalopathy.[9]

We are presenting a case of INH-induced encephalopathy in a patient with CKD in the treatment of Pott's disease of the thoracic spine.

Case Study:

This 63-year-old Bangladeshi man with a known history of hypertension, diabetes, and chronic kidney failure presented with back pain, low-grade fever, weakness in both lower extremities, and urinary retention. Based on the clinical presentation, MRI of the thoracic spine and FNAC from the lesion, and other laboratory tests, he was diagnosed with Potts disease of the thoracic spine. He recommended a follow-up visit after 1 month. He was treated with isoniazid 300 mg/day, rifampicin 600 mg/day, ethambutol 400 mg, pyrazinamide 500 mg, pyridoxine 20 mg and prednisolone 60 mg after necessary adjustments for impaired renal function. At that time, his serum creatinine was 2.80mg/dl. Has was diagnosed as a case of DM within the last 25 years, hypertension for about 20 years & was on regular anti-diabetic (insulin) and antihypertensive drugs (Bisoprolol & Olmesartan) since last & half a year. During the last half of the month he developed an altered state of mind. In the past 13 days, symptoms have worsened with meaningless, excessive talking, trouble sleeping, restlessness, confusion, and bowel and urinary incontinence. These features are also fluctuating. There was no history of fever, headache, vomiting, loose motion, jaundice, hematemesis, melaena, weakness anywhere in the body, recent hypoglycemia, coughing, or loss of appetite. But Tab. Pyridoxine missed for the last 2 and half months. Adrenal insufficiency was ruled out based on normal ACTH and cortisol levels. But after two months of discharge, the patient missed pyridoxine. After this period, the patient complains of anorexia and excessive drowsiness, and sometimes an altered mental state, but continues to take anti-tuberculosis drugs without pyridoxine. Two and a half months later, the patient was hospitalized again because of irrelevant conversation, excessive talking, trouble sleeping, and confusion on waking. On examination she was pale, coma score 11, pitting oedema, pulse 84 bpm, blood pressure 120/80 mmHg, respiratory rate 16 bpm, disorientation in time, place and person, flapping tremor, bilateral planter – extensor was present, but there was no sign of meningeal irritation. At this time, her serum creatinine was 3.04 mg/dl, serum electrolytes, prothrombin time, SGPT, blood urea nitrogen and brain MRI were normal. After admission, the available symptomatic treatment was used, but the patient's condition did not improve. Other possible causes of encephalopathy were excluded. We discontinued anti-Koch after suspected INH-induced encephalopathy. After stopping the anti-Koch and adding a high dose of pyridoxine (80 mg/day), our patient experienced dramatic improvement and become oriented within four days.

Discussion:

Isoniazid-induced encephalopathy is usually diagnosed clinically by excluding other infectious causes or metabolic disorders. In this patient, the diagnosis is strongly supported by the full recovery (within four days) after stopping the drug. The clinical features and test results make the diagnosis

of other disorders such as sepsis, electrolyte imbalances, hypertensive encephalopathy, Wernicke encephalopathy, uremic encephalopathy, hepatic encephalopathy and cerebrovascular disease unlikely. Treatment with INH may increase the risk of developing pellagra by decreasing the conversion of tryptophan to niacin. Pellagra psychosis can be confused with INH-induced encephalopathy, which does not have typical dermatitis or diarrhea.[10] However, our patient showed complete resolution of symptoms after stopping INH alone, and no niacin replacement was required, making the diagnosis of pellagra less likely. Although this patient's INH concentration and plasma acetylator status were not determined, her Asian origin does not imply that she belongs to the slow acetylator phenotype. The mechanism of INH-induced encephalopathy is still unclear. This may be due to an INH-induced deficiency of pyridoxine and pyridoxal phosphate, which act as coenzymes for the production of synaptic transmitters.[6] Predisposing factors for the development of neuropsychiatric complications of INH are advanced age, diabetes, liver disease, alcoholism, malnutrition, hyperthyroidism, slow acetylators, brain damage, history or family history of mental illness, use of high doses of INH (>5mg/kg/day) and concomitant use of monoamine oxidase inhibitors.6, INH-induced encephalopathy can develop at any time from the first few days to 5 months after starting INH treatment. Rather, recovery is more predictable, usually within a week of stopping INH.[11] There are case reports describing the development of encephalopathy and cerebellar syndrome in patients with renal insufficiency while on regular pyridoxine.[12] Hence the role of pyridoxine in the prevention of Isoniazid-induced encephalopathy is uncertain, although the beneficial effect of pyridoxine on INH-induced peripheral neuropathy is well established.[6] However, some experts recommend a higher pyridoxine dose for prevention of INH-induced encephalopathy in patients with chronic renal failure.[8] However, our patient who took pyridoxine for the first 2 months showed no signs of encephalopathy. After discontinuing pyridoxine, he developed features of encephalopathy. Therefore, it can be concluded that the INH-induced encephalopathy in CKD patients can worsen when pyridoxine is omitted. Conclusion Isoniazid-induced encephalopathy should be considered in patients with chronic renal failure treated with INH when confusion and disorientation developed. Early recognition of such a diagnosis can be important, as stopping of drug with a high-dose pyridoxine therapy can lead to a full recovery.

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