

Case report

Early-onset severe isoniazid-induced motor-dominant neuropathy: a case report

A. Zaoui,¹ A. Abdelghani,² H. Ben Salem,² W. Ouanes,¹ A. Hayouni,² F. Khachnaoui,¹ N. Rejeb¹ and M. Benzarti²

Introduction

Nervous system toxicity with current antituberculosis pharmacotherapy is relatively uncommon, although the frequency of the usage of antituberculosis therapy requires that physicians should be aware of such toxicity. Peripheral neuropathy is a rare adverse effect associated with isoniazid, and it occurs after the prolonged use of this drug [1]. This usually presents with paresthesias which can be accompanied by muscle aches, occasionally muscular weakness, and can progress to more severe symptoms such as ataxia [1]. Risk factors for developing neuropathy after isoniazid therapy include old age, slow acetylator status, diabetes, renal failure, alcoholism, malnutrition, HIV infection, chronic hepatic failure and pregnancy [1].

Here we report a case of acute isoniazid-induced peripheral neuropathy with predominant motor functional impairment associated with tetraplegia. To our knowledge, there has been no report of a patient who developed severe peripheral neuropathy barely 2 weeks after the initial administration of conventional doses of isoniazid. This atypical clinical course should be known in order to improve the outcome of adverse events due to antituberculosis treatment.

Case report

A 27-year-old man with a history of 3 months of cough, fever and sweating

was referred in March 2009 to the Department of Pulmonology at Farhat Hached Hospital of Sousse. The patient had no history of immunodeficiency, no diabetes, no renal failure, no hepatic failure, no HIV infection and he was a nonsmoker. Pulmonary tuberculosis was suspected and the investigation of sequential sputum samples confirmed the bacteriological diagnosis. Therapy was prescribed for the first 2 months of isoniazid, rifampicin, ethambutol and piazoline. The Tunisian regimen of antituberculosis treatment is: isoniazid 5 mg/kg per day + rifampicin 10 mg/kg per day + ethambutol 20 mg/kg per day + piazoline 30 mg/kg per day.

Two weeks after starting treatment, the patient complained of difficulty standing and rising from a chair. There was no burning, no pain and no numbness or tingling. Then muscle weakness in the lower limbs worsened and weakness of the upper limbs, hands and wrists developed. On examination, his body mass index (BMI) was 18 kg/m². Neurological examination revealed sensorimotor tetraparesis with a muscle testing of 0/5 in the lower extremities, 4/5 in the shoulders and elbows and 2/5 in the 2 wrists and hands. There were no deglutition or sphincter disorders or difficulty breathing. Achilles and patellar tendon reflexes were absent. Peripheral joints were free. There was no objective sensory finding and no cranial nerve lesions. Electromyography demonstrated impairment of bilateral peroneal nerve

function: evoked amplitude was markedly reduced, with slight slowing of nerve conduction velocity. The results of median sensory–motor, sural sensory and post-tibial motor nerve conduction studies were normal. Blood count, erythrocyte sedimentation rate, creatine phosphokinase, lactate dehydrogenase and protide were normal. Cerebrospinal fluid examination was negative. There was no cord compression on magnetic resonance imaging of the thoracolumbar spine. Computed tomography brain scan was normal.

A dose test of 300 mg isoniazid after 3 hours gave 1.2 mg/L which indicates rapid acetylator status. Peripheral neuropathy due to isoniazid was suspected and the drug was stopped. Pyridoxine at a dose of 50 mg was prescribed for 2 months and physiotherapy was initiated.

The patient was put on a 3-drug therapy for his pulmonary tuberculosis (rifampicin, piazoline and ethambutol) for 3 months followed by 6 months of rifampicin and ethambutol.

The physiotherapy aimed to prevent complications of supine positioning and consisted of articular mobilization and actively assisted muscle strengthening and functional work. After 7 months, there was progressive knee (2/5) and pelvic muscle (3/5) recovery. After 2 years follow-up, the BMI of the patient increased to 23 kg/m², he recovered muscle strength in the upper limbs to 5/5, lower limbs to 4/5 with recovery of his ability to walk up and down stairs

¹Department of Physiotherapy, Sahloul Hospital, Sousse, Tunisia.²Department of Pulmonology, Farhat Hached Hospital, Sousse, Tunisia (Correspondence to A. Abdelghani: ahmed.abdelghani@rns.tn).

Received: 16/3/11; accepted: 26/7/11

and he was able to independently undertake activities of daily living.

Discussion

Isoniazid-induced neuropathy is dose-related. Symptoms after initiation of treatment in patients receiving conventional doses rarely appear before 6 months. Isoniazid-induced neuropathy usually manifests as paresthesia that begins in the feet and can reach the hands and arms. The patient first complains of numbness or tingling of the feet, a burning sensation and pricking pain [1]. There has been no report to our knowledge of a patient who developed severe peripheral neuropathy barely 2 weeks after the initial administration of conventional doses of isoniazid and in the absence of predisposing factors. Furthermore, our patient developed

mainly motor neuropathy with dominant tetraplegia with sensory characteristics, unlike the typical peripheral neuropathy related to isoniazid. Therefore, isoniazid should not be dismissed as a possible cause in the event of rapid development of peripheral neuropathy with predominant motor symptoms after starting antituberculosis drugs, even in the absence of predisposing factors. It has been reported that smoking induces vitamin deficiency [2,3] but our patient had no history of smoking. The only possible explanation of this onset was his low BMI. Clinicians should be aware of the rapid onset of this side-effect.

Our review of literature showed that most cases of antituberculosis drug-associated psychoses were due to isoniazid [4–6]. A search on PubMed/MEDLINE found the following cases of isoniazid-induced complications:

isoniazid-induced lupus erythematosus presenting with cardiac tamponade [7]; 6 cases of pneumonitis [8]; 1 case of visual hallucinations [9]; 1 case of myopathy [10]; and 1 case of toxic neuropathy [1,11].

The rehabilitation is a part of the multidisciplinary management in this type of pathology. It aims to prevent decubitus complications, maintenance of cardiovascular endurance and recovery of muscle function, walking and autonomy.

Conclusion

Isoniazid can cause rapid onset of peripheral neuropathy with predominant motor symptoms and should be considered as a possible cause in cases presenting with such symptoms soon after starting the medication.

References

1. Steichen O, Martinez-Almoyna L, De Broucker T. Neuropathie toxique induite par l'isoniazide: pensez à la prévention [Isoniazid-induced neuropathy: consider prevention]. *Revue des Maladies Respiratoires*, 2006, 23(2), Pt 1:157–160.
2. Mashiyama ST et al. An assay for uracil in human DNA at baseline: effect of marginal vitamin B6 deficiency. *Analytical Biochemistry*, 2008, 372:21–31.
3. Traber MG et al. Burn and smoke inhalation injury in sheep depletes vitamin E: kinetic studies using deuterated tocopherols. *Free Radical Biology & Medicine*, 2007, 42:1421–1429.
4. Herrag M, Sajjai H, Alaoui Yazidi A. L'accès psychotique aigu secondaire à la prise d'isoniazide [Acute psychotic access following the administration of isoniazid]. *Revue de Pneumologie Clinique*, 2011, 67(2):118–120.
5. Alao AO, Yolles JC. Isoniazid-induced psychosis. *Annals of Pharmacotherapy*, 1998, 9:889–891.
6. Tiwari VK, Verma SM. Homicide by a tuberculous prisoner possibly having drug induced acute delusional psychosis. *Indian Journal of Tuberculosis*, 1997, 44:95–96.
7. Siddiqui MA, Khan IA. Isoniazid-induced lupus erythematosus presenting with cardiac tamponade. *American Journal of Therapeutics*, 2002, 9(2):163–165.
8. Nishizawa Y et al. A case of successful desensitization therapy for isoniazid-induced pneumonitis. *Nihon Kokyuki Gakkai Zasshi*, 2004, 42:649–654.
9. Maâlej S et al. Hallucinoze visuelle induite par l'isoniazide [Isoniazid-induced visual hallucinosis]. *Presse Médicale*, 2006, 35(3):425–426.
10. Chaouch N et al. Myopathie médicamenteuse à l'isoniazide [Isoniazid-induced myopathy]. *Revue de Pneumologie Clinique*, 2011, 67(6):354–358.
11. Argov Z, Mastaglia FL. Drug-induced peripheral neuropathies. *British Medical Journal*, 1979, 1:663–666.