

CASE REPORT

An unusual case of seizures in a 5-year-old Syrian female with abdominal tuberculosis: an isoniazid therapeutic dose side effect

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Abstract

Isoniazid (INH) is highly bactericidal against replicating tubercle bacilli and is involved in all antituberculous chemotherapeutic regimens. Several neurological adverse effects, following both therapeutic and overdose use of INH, have been reported in adults in the literature. Here, we present a case of a 5-year-old girl with intestinal Tuberculosis, who developed hemiclonic seizure as a side effect of INH therapeutic dose after 2 weeks of tuberculosis therapy.

INTRODUCTION

Isoniazid (INH) is the most widely used antituberculosis medication. The incidence of tuberculosis (TB) is ~10% under the age of 10 [1]. According to the World Health Organization (WHO) 2017, TB in children represented 11% of total TB cases and the prevalence was 0.38 per 100 000 in the pediatric group in Syria [2]. INH, the wonder drug in the war against TB, was first discovered in 1951. It is bactericidal, easily administered, inexpensive and relatively nontoxic in children. Almost 10% of children develop transiently elevated alanine aminotransferase (ALT) levels while taking Isoniazid, but the clinical toxicity is exceedingly rare [3]. Major adverse effects include hepatitis and peripheral neurotoxicity that is uncommon at conventional doses [4].

CASE REPORT

A 5-year-old female patient was admitted to the Pediatric Department with a 1-month history of prolonged fever

measured at 38.5–39°C at a rate of 4–5 times daily, partly controlled with antipyretic, associated with lack of appetite and weight loss of 4 kg. Although she was treated with various antibiotics, the fever continued to rise. In her medical history, there was diagnosed corrosive Esophagitis (caustic) and had several sessions of dilatation through the scope. The last one was about 8 months before admission. There was no family history of genetic disorders or contact with TB patients. The child underwent all the compulsory immunizations for her age.

On examination: Her body weight was 15 kg standard deviation (SD) (DS–1.8), the length was 100 cm (DS–1.3), temperature 38.3°C, oxygen saturation 98%, arterial blood pressure was 90/55 mm Hg, awake, breathing spontaneously, pale and there was bacillus Calmette Guerin (BCG) scar on her left shoulder. The abdomen was soft and the liver palpated 4 cm below the right costal margin. Other systems examinations were within normal limits.

Laboratory investigation reports were as in Table 1. The chest X-ray was normal. A Peripheral blood smear was as follows:

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Table 1: The laboratory data of the case

Test	Result	Test	Result
WBC ($10^3/\mu\text{l}$)	13.6	Uric Acid (mg/dL)	2.8
Neutrophils (%)	81	ALT	20
Lymphocyte (%)	14	AST	15
Hb (g/dl)	9.8	Na	135
PLT ($10^3/\mu\text{l}$)	626	K	4.5
Urea (mg/dl)	30	Wright test	negative
Creatinine (mg/dl)	0.5	Widal test	negative
ESR (1 h, 2 h)	(94, 127)	Urinalysis, Culture and sensitivity	normal
CRP (mg/dl)	33	Stool examination	normal
Ferritin (ng/ml)	1250	Calprotectin	normal
blood culture	no bacterial growth	occult blood test	normal
LDH (U/L)	148		

WBC: White blood cell, HB: Hemoglobin, PLT: platelets, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, LDH: lactate dehydrogenase, ALT: Alanine aminotransferase, AST: Aspartate Aminotransferase, Na: sodium, K: potassium.

leukocytes increased in neutrophils, erythrocytes different sizes shapes, and lack of pigment and platelets increased in number. Echocardiography was normal. The abdominal ultrasound showed liver heterogeneous (13–14) cm, spleen relatively large, increased thickness in the intestinal fold at the end of the ileum, many of the lymph nodes around aorta and its branches were detected, the largest is 2-cm diameter. Neck ultrasound showed a single lymph node submandibular region measured 10 mm, and several nodes along the right carotid path, the largest one measured 22 mm. Bone marrow puncture was normal. Tuberculin skin test (TST) was positive (10 mm) diameter after 72 h (Fig. 1). Contrast-enhanced computed tomography (CT) of the chest, abdomen and pelvis showed the enlargement lymph nodes in the abdomen and pelvis around the abdominal aorta and in the iliac fossa, with an increase in the thickness of the colon wall and the end of the terminal ileum. In a colonoscopy, there was a disturbing mucosa, diffuse abrasions, swollen follicular formations and absence of vascular pattern found in Sigmoid and terminal ileum, with loss of normal morphology and severely ulcerative formulations in Cecum and Bohan valve (Fig. 2).

The pathology of several biopsies from colons showed an inflammatory infiltrate of lymphocytes without follicular formations (Fig. 3). The cecum biopsies showed the presence of granulomatous formations with epidermal cells with several giant cells of the Langhans type (Fig. 4). The Differential Diagnosis includes Tuberculosis and Crohn's disease. The Ziehl Neelsen Stain (ZN) for bacillus was negative. We did not do the Culture because it was not available in our hospital. Upper gastrointestinal endoscopy was normal, the biopsies taken from the duodenum were normal. Antinuclear antibody, antineutrophil cytoplasmic antibodies, and TB polymerase chain reaction were negative. Anti-tubercular therapy was started with a regimen containing isoniazid, rifampicin, ethambutol and pyrazinamide for 2 months followed by isoniazid and rifampicin for 4 months. Vitamins B supplements were added to provide (1 mg/kg) vitamin B6. After 14 days of starting treatment of tuberculosis, the patient had hemiclonic seizure continued for 3 min. Phenytoin 15 mg/kg loading dose then complete with 5 mg/kg with stable in the seizure. CSF analyses, EEG, a CT of the brain were normal. The electrocardiogram, liver function tests and electrolytes were normal. Arterial Blood Gas (ABG) test was normal. INH levels and B6 levels were not available. The dose of INH was 15 mg/kg daily



Figure 1: TST positive test.

and this was not an overdose. The Seizure was a side effect of INH therapy after ruling out all other possible causes of seizure.

After about 3 weeks of treatment initiation, the child was in good general condition, remarkable clinical improvement, and weight gain of about 700 g. The girl was discharged with instructions to follow the treatment of Anti-tubercular therapy and vitamins.

We followed-up the patient for a year after the therapy and repeated the gastrointestinal endoscopy which was normal. The patient is healthy and does not have any symptoms of the disease now.

DISCUSSION

Abdominal tuberculosis (ATB) is a rare disease that can be challenging in diagnosis. ATB may be associated with abdominal pain (93%), episodes of intestinal obstruction (73%), fever (64%), and lack of appetite (52%), weight loss (47%) and diarrhea

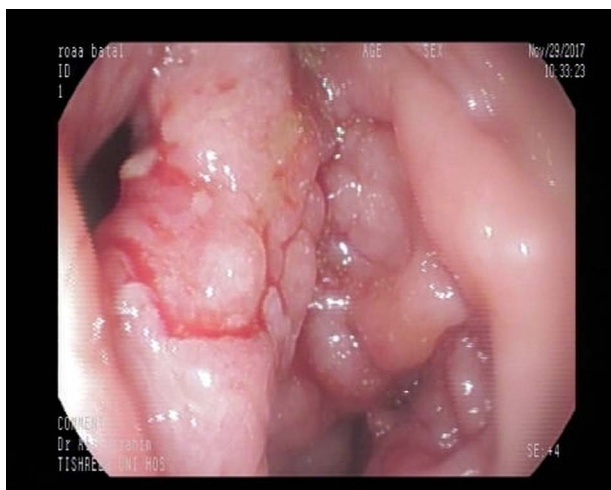


Figure 2: Colonoscopy showed ulcers in Bohan valve.

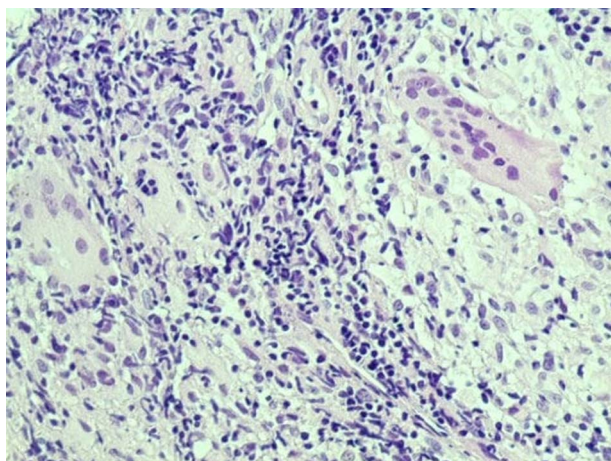


Figure 3: Colon biopsies pathology showed the infiltration of lymphocytes.

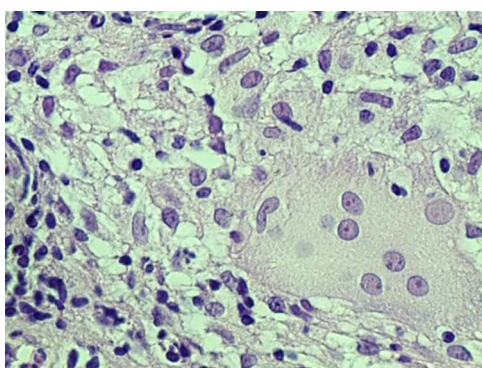


Figure 4: Colon biopsies pathology showed Langhans giant cells.

(12%) [5]. The culture of biopsy is the gold standard however it requires 3–8 weeks to provide conclusive results [6]. Six-month treatment consisting of rifampicin, isoniazid, ethambutol and pyrazinamide for 2 months, followed by rifampicin, isoniazid and ethambutol for 4 months is recommended as per accepted guidelines [7].

In our case, ESR elevation, positive TST, the enlargement lymph nodes in CT, besides the biopsies which revealed granulomatous lesions, diagnosis of ATB. We started antituberculous therapy, although PCR was negative.

INH is a first-line agent in the treatment of tuberculosis and is also used in preventive therapy. Its neurological side effects, including peripheral neuritis, dizziness and insomnia. Most reported INH-induced seizures occurred as a result of an overdose in suicide attempts or wrong taken by children [4]. Minns et al. [8] reported a case of a 10-month-old male infant was presented after being found with his father's INH.

The acute ingestion of INH at a dose above 30 mg/kg typically causes seizures, and INH ingestion of more than 80 mg/kg can rapidly cause death. Central nervous system effects occur due to vitamin B6 deficiency. The occurrence of seizures at conventional doses has rarely been reported. This report called by Tsubouchi et al. [4] in an 86-year-old woman who had convulsive seizures that occurred in association with the administration of a short-term therapeutic dose of INH. Puri et al. [9] also reported a case of a 65-year-old male who developed isoniazid induced seizures after the first therapeutic dose.

Three factors are influencing the risk of INH induced neuropathy. The first is the dose of INH used. The incidence of peripheral neuropathy is dose-related, with a large dose resulting in a high rate of adverse effects. The second factor is the patient's nutritional status. Money reported that the incidence of peripheral neuropathy is increased in malnourished patients. The third factor is the INH acetylation rate. Patients who acetylate INH slowly are at an increased risk of developing neuropathy [4].

In the case of INH toxicity, pyridoxine should be administered in a dose equivalent to the suspected amount of isoniazid ingested. If the amount of INH ingested is unknown, 5 g of pyridoxine should be given intravenously [9].

To date, our case has been the first case reported in the literature of seizures caused by INH in a child in a therapeutic INH. CSF analyses, EEG, a CT scan of the brain were normal. That denied meningitis to be the cause of the seizure. Our patient did not have any medical history of seizures. All other possible causes of seizures were ruled out by thorough clinical examination and relevant investigations.

Similar reaction can be expected in the future and patient should be monitored for the similar toxic effects during treatment.

CONFLICT OF INTEREST STATEMENT

All of the authors declare that they have no competing interests.

FUNDING

No funding was obtained for this study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This case report did not require review by the Ethics Committee Tishreen university hospital, Lattakia, Syria.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's parents for publication of this Case report and any accompanying

images. A copy of the written consent is available for review by the Editor.

AUTHORS' CONTRIBUTIONS

All authors have read and approved the manuscript.

AVAILABILITY OF DATA AND MATERIAL

All data generated or analyzed during this study are included in this published article.

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