



Isoniazid-Induced Systemic Lupus Erythematosus: A Case Report

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Abstract

Systemic lupus erythematosus (SLE) can be induced by various medications, such as hydralazine, procainamide, isoniazid, methyl dopa, chlorpromazine, quinidine, and minocycline. A patient was admitted complaining of fever with chills and rigor. After being diagnosed with tuberculous meningitis, the patient was given antituberculosis treatment. As the patient did not improve, detailed investigations were conducted, and elevated antinuclear antibody levels were found. The consulting physician diagnosed that the patient was suffering from SLE. As isoniazid is associated with an increased risk of developing SLE, it was suspected as the culprit drug. After withdrawing isoniazid from the antituberculosis treatment regimen, the patient improved and was discharged. Based on the WHO-UMC and Naranjo's causality assessment criteria, an association between the reaction and isoniazid was deemed probable. The reaction was moderately severe (level 4b) according to the modified Hartwig and Siegel scale.

Key Points

Isoniazid, an antituberculosis drug, can cause systemic lupus erythematosus (SLE).

Medications such as hydralazine, procainamide, methyl dopa, chlorpromazine, quinidine, and minocycline are known to cause SLE.

A suspected case of isoniazid-induced systemic lupus erythematosus was confirmed by the presence of serum antinuclear antibodies.

Care must be taken before administering antituberculosis therapy to check for a history of any allergy or drug-related reaction.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by the production of autoantibodies directed against nuclear and cytoplasmic antigens. SLE produces different clinical and immunologic abnormalities in several different organs [1]. The reported prevalence of SLE ranges from 14 to 60 per 100,000. The prevalence of SLE in India is comparatively low [2]. The severity of this reaction varies from a transient maculopapular rash to fatal toxic epidermal necrolysis. Significant levels of antibodies against single- and double-stranded DNA (dsDNA) with skin lesions are considered to be confirmatory in the diagnosis of SLE [3]. It is known that SLE can be induced by various medications, such as hydralazine, procainamide, isoniazid, methyl dopa, chlorpromazine, quinidine, and minocycline [4]. Management of SLE includes corticosteroid treatment and discontinuation of the causative agents [5]. Here we present a case of isoniazid-induced systemic lupus erythematosus.

Case report

A 14-year-old female patient was admitted to the medical ward with complaints of fever, body ache, and vomiting for 15 days. On admission, injections of ceftriaxone 2 g intravenously (iv) 12 hourly, mannitol 50 ml iv, dexamethasone 4 mg iv 8 hourly, ranitidine 50 mg iv 12 hourly, ondansetron 8 mg iv 8 hourly, normal saline 500 ml iv 8 hourly, and

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Ringer's lactate solution 500 ml iv 8 hourly were prescribed. Routine investigations were conducted, including a complete blood count, renal function test, Widal test, cerebrospinal fluid (CSF) examination, sputum examination, urine examination, culture and sensitivity test of blood and urine, stool examination, ultrasonography, HIV testing, and viral marker testing with magnetic resonance imaging (MRI). Relevant results of these investigations are listed in Table 1. The patient was prescribed antituberculosis therapy after being diagnosed with tuberculous meningitis based on brain MRI.

On day 2, the same treatment was continued along with the addition of an injection of 200 ml of O positive red cell concentrates to address the patient's low hemoglobin level. According to the MRI scan report and the CSF report, which were suggestive of tuberculous meningitis, a category 2 regimen (isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin, as per weight band) was started. (The patient had a past history of undergoing antituberculosis therapy started by a private physician, but the therapy was withdrawn after 3 months due to an adverse reaction: skin lesions on the head and both limbs.) The same treatment was continued on days 3 and 4. On day 5, the patient began to complain of fever, common cold, muscle weakness, joint pain, convulsion with multiple skin lesions, and multiple oral ulcers. Sodium valproate 200 mg every 8 hours orally (by tablet) was then prescribed for the convulsions.

The patient was referred to the pulmonary medicine and dermatology department regarding modifications to their antituberculosis therapy and to address the skin lesions after a positive antinuclear antibody (ANA) profile report was obtained (Table 2). They advised that the isoniazid should

be stopped for 15 days, and they prescribed clotrimazole mouth paint perorally, fluconazole 150 mg 24 hourly orally, and multivitamins along with the rest of the previous treatment, including corticosteroids. After 15 days, the patient had improved, and they were discharged with isoniazid omitted from their antituberculosis regimen.

Causality assessments were done using WHO-UMC criteria and Naranjo's scale. According to the WHO-UMC causality assessment criteria, an association between the reaction and the drug was probable [6]. Naranjo's score was 8 (probable) [7]. The modified Hartwig and Siegel scale showed that the level of severity for the reaction was moderate (level 4b) [8].

Discussion

Antituberculosis drugs such as isoniazid and rifampicin are among the drugs most widely used in antituberculosis therapy regimens. Used in either fixed-dose drug combinations or individually, they are effective, though drug-related complications occur frequently. In SLE, the immune system produces autoantibodies against the patient's own tissues [9]. Molecular mimicry between antibodies directed against infectious agents and self-antigens has been implicated in SLE [10]. Genetic differences in the cytochrome P450 system cause drugs to be metabolized differently among individuals, which in some cases can result in the generation of toxic metabolites that facilitate autoimmunity [11]. According to the literature, the disruption of immune regulation

Table 1 Relevant results from laboratory investigations along with reference values

Report	Result	Reference laboratory values
MRI scan	Tuberculous meningitis with granuloma	–
Hemoglobin	6 gm/dl	12–16 gm/dl
Total WBC	3000/ μ l	4500–11000/ μ l
Differential WBC count	80/14/02/04/00	50–80/14–44/2–5/1–5/0–1
RBC count	3.1 million/ μ l	4.2–5.7 million/ μ l
Packed cell volume	19.7%	37–47%
CSF sugar	34 mg/dl	50–75 mg/dl
Adenosine deaminase activity in CSF	22.4 μ l/min	< 10 μ l/min
Rheumatoid arthritis factor	Positive	Negative
C-reactive protein	Positive	Negative

Table 2 Antinuclear antibody profile report

Antinuclear antibody profile	Result	Inference
Antinuclear antibody (ANA) profile report from immunodot	Specific bands for histones, Sm, RNP 68 KD/A/C, Sm/RNP, SSA/Ro60KD, SSA/Ro52KD, SSB, ribosome PO antibodies	Associated with systemic lupus erythematosus, an autoimmune disorder

that leads to SLE is associated with an inhibitory reaction of isoniazid with complement component C4, which is likely to result in an inability to clear immune complexes [12]. In the present case, metabolites of isoniazid may have caused this reaction. To differentiate between drug-induced lupus erythematosus (DILE) and SLE, it should be noted that skin findings are less common in DILE than in SLE, and that DILE usually presents with a higher incidence of purpura and erythema nodosum. A literature review suggested that isoniazid was the culprit drug among those used to treat the present patient [5, 13]. The clinical presentation and ANA profile for this case are also similar to those reported by Jguirim et al. for a previous case of isoniazid-induced SLE [14]. A pharmacovigilance investigation suggested a probable causal relationship between this drug and the reaction in the present case. This case report reaffirms that SLE can be caused by isoniazid, albeit rarely.

Conclusion

Isoniazid can induce SLE by different mechanisms, as identified from the ANA profile. Therefore, care must be taken before administering antituberculosis therapy in patients with a history of any allergy or drug-related reaction.

Authors' contributions Dr. Jitendra H. Vaghela conducted the literature review and wrote the case description, abstract, discussion, and conclusion. Dr. Yogesh Solanki diagnosed the case and helped to retrieve clinically relevant information on isoniazid-induced SLE. Dr. Bhargav Purohit helped to search for relevant literature, scrutinized the case report, and provided guidance when writing the discussion and drafting the case report. Dr. Krishna Lakhani helped with the clinical diagnosis of the case, the treatment of the adverse event, provided guidance during the drafting of the case report, and helped to retrieve clinically relevant data.

Compliance with Ethical Standards

Conflicts of Interest Jitendra Vaghela, Yogesh Solanki, Krishna Lakhani, and Bhargav Purohit declare no conflict of interest.

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Informed Consent Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. A copy of the written consent may be requested for review from the corresponding author.

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