CASE REPORT

# A probable case of isoniazid induced acneiform eruptions in a young female

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## SUMMARY

**Isoniazid (INH) induced acneiform eruptions are an uncommon cutaneous drug reaction, potentially due to under-diagnosis and under-reporting. Isoniazid results in drug induced acneiform eruptions among patients with slow acetylator phenotypes. Here we report a case of a young female with a background history of mild stable facial acne, presenting with acute acneiform eruptions on commencing multidrug anti tuberculosis regimen for disseminated pulmonary tuberculosis. The prompt initiation of treatment following recognition of what was a probable isoniazid induced acneiform eruption was key for symptom control. The acneiform eruptions were effectively treated, halting cosmetic implications which could pose significant psychological stress to her. Tuberculosis is highly prevalent in this study setting with an increased number of patients receiving treatment and a small percentage of them may experience this side effect. This case aims to improve awareness among primary care practitioners to recognize the benefit of early and targeted treatment for a highly probable isoniazid induced acneiform eruption to enhance symptom control, especially in a young patient.**

## INTRODUCTION

Isoniazid has been reported as a cause for drug induced acneiform eruptions with a small frequency estimated at 1.42-2.5%.[1,2] It is recognized as a drug with an undoubted causal relationship to acne.[2] Isoniazid induced acneiform eruptions are usually of an acute onset and can affect any age group. It presents with a monomorphic morphology which consists predominantly of inflammatory follicular papules or pustules, without comedones. Appearance is usually on the face and neck and may extend beyond the seborrheic areas.[2] This adverse cutaneous reaction to an antituberculous drug is usually troublesome but mild. Prompt clinical identification and diagnosis allows for symptomatic treatment with continuation of the drug without necessarily having to interrupt treatment. Most lesions will resolve spontaneously even when treatment is continued.[3] Early recognition and a prescription of appropriate therapeutic regimes in tandem with acneiform eruption severity is key to management to prevent permanent scarring which, among the younger age group, can lead to negative consequences such as poor self-image and social anxiety.[4]

We report a case managed as a clinically probable isoniazid induced acneiform eruption in a young female undergoing treatment for disseminated pulmonary tuberculosis.

## CASE REPORT

A 20-year-old female student was diagnosed with disseminated smear negative pulmonary tuberculosis involving the pleura and cervical lymph nodes in October 2020. She was commenced on a daily fixed 4-drug combination: AKURIT-4: rifampicin 150mg OD; isoniazid 75mg OD, pyrazinamide 400mg OD; and ethambutol 275 mg OD.

On day six of the full treatment regimen, she developed a generalized maculo-papular rash affecting her trunk, thighs and arms. She was prescribed a generous amount of regular emollient, without topical steroid, and oral chlorpheniramine at night. She continued to receive the full regime of anti-tuberculosis treatment for a further three weeks. However, the itchiness worsened and became extremely troublesome. This affected her functionally with poor quality of sleep and poor study performance. In response to this, the patient was admitted for a desensitisation procedure. The AKURIT-4 was stopped and during the desensitisation process, pyrazinamide was identified as the offending drug.

Following this, she was re-commenced on anti-tuberculosis treatment, with a new regime of isoniazid, rifampicin and ethambutol (HRE) and continued on regular moisturizers for her dry skin, over her back.

Thirteen days after commencement of anti-tuberculous treatment and one week into the new treatment regime (HRE) after desensitisation, she reported being distressed with an increasing appearance and severity of maculopapular and pustular lesions over her bilateral cheeks and to some extent, her forehead and chin.

The patient had a history of mild stable facial acne but never on treatment prior, as shown in (Figure 1). The patient expressed her worries about how this has affected her self-image while being in public and attending classes, which necessitated frequent use of face masks to hide the acne appearance. This affected her level of confidence socially and

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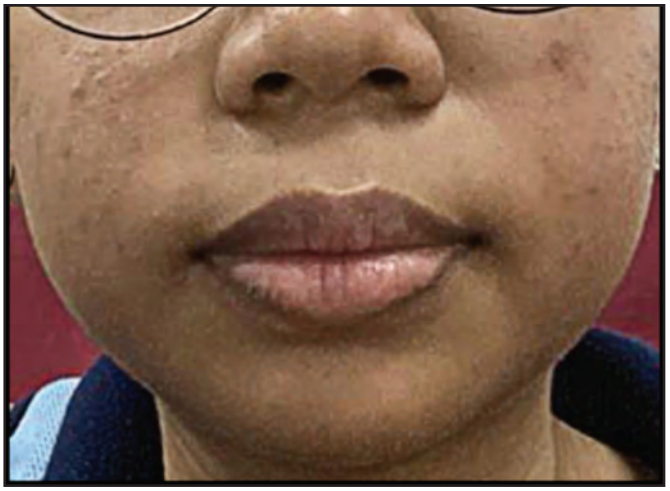

**Fig. 1:** Patient's facial acne at the onset of AKURIT-4

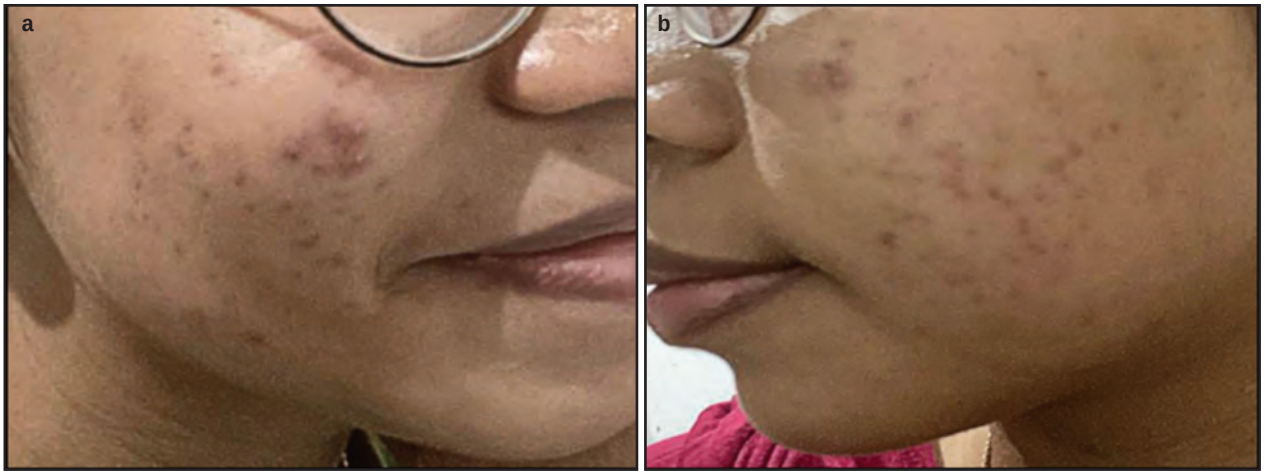


**Fig. 2:** Progress of the acneiform eruption with improvement on the papular and pustular lesions on the, (a) right cheek and (b) left cheek, following one-month treatment of topical adapalene and oral erythromycin

subsequently, her ability to focus and concentrate in her studies.

On examination, there were multiple monomorphic papules and pustules concentrated on her cheeks, clustering around old acne scars with no comedones noted. No acneiform lesions were identified on the trunk or elsewhere. Based on these presentations, a working clinical diagnosis of presumed isoniazid induced acneiform eruptions was made. Due to the severity of the acneiform eruptions, the patient was started on oral erythromycin 500mg four times a day for one month and adapalene cream while maintained on the isoniazid.

One month later, a marked improvement was observed in her acneiform lesions. The initial papules and pustular lesions had reduced in size and no new facial acneiform lesions were noted despite continuing the isoniazid (Figure 2).

She expressed her relief and happiness with this progress. Following this improvement, the patient regained her confidence to continue social interaction and improved in her daily function. At the last follow up, erythromycin was stopped and adapalene cream was maintained. The patient continued to receive regular follow-up for her symptom monitoring while continuing her maintenance phase with isoniazid and rifampicin, after completing 3 weeks of active treatment phase.

## DISCUSSION

Anti-tuberculous drugs are commonly known to cause diverse clinical patterns of cutaneous adverse drug reactions. Isoniazid has been commonly suggested to be associated with acneiform eruptions.[5-7] In this case, the patient initially presented with pyrazinamide induced generalized cutaneous exanthem involving the trunk, upper and lower limbs. After successful desensitisation and treatment, she was discharged well. However, she soon presented with facial acneiform lesions and was subsequently diagnosed as clinically probable isoniazid induced acneiform eruptions. The incidence of acneiform eruptions associated with isoniazid therapy remains low with a prevalence of 1.42% - 2.5%.[1]

It has been reported that isoniazid most easily results in acneiform eruptions in patients with slow acetylator phenotypes, which is commonly seen among the 2nd, 3rd, and 4th decade age groups.[1,2] Other potential causes of acneiform eruptions that should also be considered include the concomitant use of medications such as anticonvulsants, steroids, hormones, and the presence of metabolic abnormalities such as insulin resistance and metabolic syndrome, which were not present in this patient.

Isoniazid induced acneiform eruption can manifest as acute or up to 18-months following the exposure to isoniazid. In this case, the patient, who was in her 20s, manifested with an acneiform eruption approximately 3 weeks into exposure to isoniazid, which was given as part of a multi-drug regimen for disseminated pulmonary tuberculosis. Distinguishing between true acne vulgaris and acneiform eruptions requires a high index of suspicion. The skills to perform thorough history taking and clinical examination to evaluate the presentation of acneiform eruptions with temporal drug relationship is crucial to make a diagnosis. Acneiform eruptions have some common lesional patterns where they mimic pustular acne, with a monomorphic, inflammatory clinical pattern but with the absence of comedones.[6] The presentation is acute, commonly involving the seborrheic areas, and can aggravate pre-existing acne. Involvement of the arms, trunk, lower back, and genitalia are less common.6 In this case, isoniazid is suggested as the offending drug for developing acneiform eruptions with its sudden aggravation of stable facial acne.

The main management in severe adverse cutaneous drug reactions is to withdraw the culprit drug, as symptoms often improve following drug withdrawal. The current Malaysian Tuberculosis guidelines recommend discontinuation of anti-tuberculosis drugs in severe adverse cutaneous drug reactions.[3] In this case, her first cutaneous manifestation indicated mild adverse cutaneous drug reaction which could evolve to moderate or severe form if the drug culprit was not withheld. The patient had a period of severe generalized exanthems which was not responding to regular emollient and chlorpheniramine. She was admitted by the treating respiratory team for careful desensitisation. The anti-tuberculous medications were withheld, and individual anti-tuberculosis drugs were reintroduced sequentially under supervision, to identify pyrazinamide as the offending drug.

Fortunately, with her second troublesome cutaneous manifestation of acute acneiform eruptions, the clinical suspicion of a probable isoniazid induced acneiform eruption was identified early and treated symptomatically with erythromycin and adapalene cream,[7] without need for interruption of treatment. Her prompt management resulted in the resolution of symptoms. The patient's positive response to treatment against the acneiform eruptions falls in favour of isoniazid being the culpable cause of her drug induced cutaneous manifestation.

Managing drug-induced acneiform eruptions in an ongoing drug offender is often challenging. However, guidelines have reported that troublesome but not serious adverse drug reactions can be treated symptomatically without necessarily having to interrupt treatment.6 It requires for a clear and direct discussion between patient and medical professionals in making this decision due to the need for close supervision and monitoring of symptoms. This patient was given oral antibiotics as well as topical treatment as the acneiform lesions were inflammatory and had greatly impaired her quality of life. In cases of non- responders with a similar treatment regime, other systemic treatments like hormonal pills or oral isotretinoin are indicated.

Among the young, acne and acneiform lesions pose considerable negative self-image, reduced self-confidence, reduced self-esteem, and may lead to social isolation.4 Furthermore, the long term consequence of facial scarring could result in permanent negative psychological effects such as depression.[4] Therefore, early recognition of isoniazid as a culpable cause for acneiform eruptions with the anti-tuberculous drug regime is crucial for timely and optimal treatment execution to ensure compliance and adherence to medication with subsequent psychosocial well-being .

Moving forward, exploration and investigation of this young adult's slow acetylator status of isoniazid would be the objective line of ongoing management.

## CONCLUSION

In conclusion, recognizing isoniazid as culpable in mild yet troublesome cutaneous acneiform lesions with the anti-tuberculous drug regime is imperative to prompt clinical identification and initiation of optimally targeted treatment. Timely commencement of treatment for acneiform eruption in tandem with severity, ensures the continuation of the anti-tuberculosis regime without the need for interruption of treatment. This is particularly of importance in the young where acne and acneiform lesions pose disturbing negative influences on self-esteem and self-image which could lead to noncompliance in treatment. As a result, this improves physical and psychological impact of acneiform lesions. Recognition and awareness of this underdiagnosed and under-reported cutaneous drug manifestation to isoniazid will lead to enhanced primary healthcare outcomes in tuberculosis treatment, especially among the young.

Further exploration and investigation of this young adult's status of being a slow acetylator of isoniazid would be the next direction in management, moving forward.

What is new in this case report compared to the previous literature?

- Previous literature has implicated isoniazid as a cause for acneiform eruptions.
  However, isoniazid induced acneiform eruptions are often underdiagnosed and underreported.
- Timely and optimum treatment of isoniazid induced acne eruptions in tandem with severity will ensure compliance and continuation of the anti-tuberculosis treatment regime.
- This case report highlights the importance of early recognition and treatment of isoniazid induced acneiform eruptions to prevent interruption of the anti-tuberculous regime.

- Further exploration and investigation of this young adult's status of being a slow acetylator of isoniazid would be the next direction of objective management.

What is the implication to patients?

- Optimum and prompt treatment of drug induced acneiform eruptions will improve the physical and psychological impacts of acne especially among the young while ensuring compliance to the antituberculous regime.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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