

## Azathioprine induce hyperimmunoglobulin syndrome

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### ABSTRACT

This case was reported on the adverse effect of azathioprine drug toxicity and the importance of early recognition of the signs and symptoms of azathioprine toxicity. This case report involves a 60-year-old female patient who took excessive intake of tablet azathioprine for more than 6 months. The patient was diagnosed with hyperimmunoglobulin syndrome (HIES). Azathioprine is commonly used in the treatment of severe atopic dermatitis by suppressing immune responses and reducing inflammation, itching, and rashes. However, its immunosuppressive action may predispose patients to rare disorders. Hyperimmunoglobulin E (IgE) HIES is a rare primary immunodeficiency characterized by elevated IgE levels, recurrent skin infections, and eczema-like symptoms. This report presents a rare case of HIES in a 60-year-old female with a history of hypertension, diabetes mellitus, and asthma, associated with prolonged azathioprine use. Clinical features, laboratory findings, and treatment regimens are discussed.

**Key words:** Atopic dermatitis, Azathioprine, Elevated immunoglobulin E levels, Hyperimmunoglobulin E syndrome, Immunosuppressive therapy

Azathioprine is an immunosuppressive medication frequently prescribed to manage autoimmune and inflammatory conditions [1]. Although effective, it may cause serious adverse reactions when used long-term [2]. Hyperimmunoglobulin E (IgE) syndrome (HIES) is an immunological disorder marked by extremely elevated IgE levels, recurrent skin infections, and eczema dermatitis [3]. The estimated global incidence is 1–2 per million [4]. This condition affects both genders across all ethnicities, with most reported cases originating from the United States and Europe [5]. Azathioprine-related hypersensitivity and immune reactions are uncommon, occurring in approximately 1–2% of treated patients. Most reactions are mild, such as nausea, fever, or transient skin rashes, and resolve after dose adjustment or drug withdrawal. However, severe allergic or immunologic complications, including drug-induced HIES, are extremely rare, with only a few isolated cases described in the literature worldwide. Because of this rarity, such reactions are often under-recognized, underscoring the importance of careful monitoring and prompt reporting during long-term azathioprine therapy.

Azathioprine is commonly used to control autoimmune diseases, but sometimes it can affect the

immune system in unusual ways. Usually, the side effects of azathioprine include fever, skin rash, or liver problems, but very few reports mention increased IgE levels with long-term use. We are presenting this case to create awareness among doctors and pharmacists about this unusual reaction and to remind them to check immune markers such as IgE during long-term treatment with azathioprine.

### CASE REPORT

A 60-year-old female with comorbidities presented with chronic itching, rashes, papules, and plaques lasting for 3 years. She was admitted to a hospital with a past medical history of hypertension, type 2 diabetes, and asthma. At the age of 43, she suffered from asthma. On consulting the clinician, they prescribed the tablet Astymin, which she has been taking for the last 17 years. After a few years, she started experiencing hypersensitivity reactions (rashes, itching, and papules), for which she consulted the physician. The clinician prescribed the drug azathioprine (dose 50 mg). She used the drug for 6 months. After prolonged use of the drug azathioprine for 6 months, the severity of rashes increased.

Upon examination, the patient had fever, itching, and red rashes mainly on the trunk and arms. There was no liver or spleen enlargement and no swollen lymph nodes. On local examination, multiple erythematous, raised,

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and scaly plaques were observed over the anterior trunk, upper limbs, and lower legs. The lesions were oval to irregular in shape, measuring approximately 2–5 cm in diameter, with well-defined margins and mild scaling on the surface. The rashes were dry, non-blistering, and slightly itchy (Fig. 1). These signs suggested a possible allergic reaction to azathioprine, so an IgE test was done to confirm it.

The laboratory examinations showed the raised IgE levels (increased to >2,000 IU/ML), Blood sugar: 160 mg/dL, and liver function test: <50 U/L. Due to an increase in levels of IgE, the patient experienced a severe allergic reaction.

Based on laboratory findings, the patient was diagnosed with HIES. The clinician prescribed medication as maintenance therapy for the hypersensitivity reaction and comorbidities. Her routine medications included amlodipine 5 mg once daily for hypertension, metformin 500 mg twice daily for type 2 diabetes, metrogyl was given to treat the diabetic skin infection from prolonged rashes, and capsolone was used as an immunosuppressive agent to manage skin disorders related to hypersensitivity reactions. Vitamin C supplementation was provided to support blemish healing and reduce hyperpigmentation. Triamcinolone was prescribed to control allergic reactions and manage inflammatory skin conditions. Glycerin and liquid paraffin were recommended to keep the skin hydrated and reduce dryness. Lycoderm cream (1:1) was applied to relieve itching and reduce rashes on the affected skin areas.

## DISCUSSION

This case highlights a potential link between prolonged azathioprine therapy and the onset of HIES [1,6]. While azathioprine is effective for autoimmune management, its immunosuppressive effects may trigger secondary immunodeficiency disorders, including HIES [7]. Proper diagnosis involves clinical evaluation, laboratory tests, and differential diagnosis to exclude other dermatologic and immunologic conditions [8].

Management includes cessation of the offending agent, immune modulation, and symptomatic treatment using corticosteroids, antihistamines, and supportive care [1-11]. The differential diagnosis for elevated IgE and rash includes atopic dermatitis, drug-induced hypersensitivity, parasitic infection, and immunodeficiency disorders. However, these were excluded based on the patient's history, laboratory data, and clinical course.



**Figure 1: Multiple erythematous, raised, and scaly plaques were observed over the upper limbs**

Several case reports have described rare hypersensitivity or immune-mediated reactions linked to long-term azathioprine therapy. Although azathioprine is commonly used in autoimmune conditions and transplant patients, its immunologic adverse effects remain uncommon but clinically important.

In one report by Dave *et al.*, a 45-year-old male developed elevated serum IgE levels, generalized itching, and erythematous rashes after chronic azathioprine use for autoimmune hepatitis [4]. Our patient's symptoms improved markedly after azathioprine withdrawal and initiation of corticosteroids and antihistamines, confirming a drug-induced secondary HIES. Another case by Amato *et al.* (1993) described an immunologic alteration following azathioprine therapy, including increased IgE and abnormal lymphocyte activity [2]. Although true HIES secondary to azathioprine is exceedingly rare, these studies emphasize the need for early recognition, drug withdrawal, and supportive treatment to prevent serious outcomes.

## CONCLUSION

Prolonged use of azathioprine can lead to allergic reactions (rashes, itching, and papules). This leads to an increase in IgE levels based on the levels at which HIES was diagnosed. This case emphasizes the importance of routine monitoring of patients on immunosuppressive therapy. Early diagnosis and comprehensive treatment can significantly improve a patient's quality of life.

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