CLINICAL VIGNETTE

Successful Azathioprine Desensitization in a 43-Year-Old Patient with Dermatomyositis

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Introduction

Dermatomyositis is a rare autoimmune disorder characterized by muscle inflammation and skin rashes. Azathioprine, a purine analog, is frequently prescribed as an immunosuppressive agent in the treatment of dermatomyositis, aiming to reduce disease activity and minimize steroid use. However, some patients may develop hypersensitivity reactions to azathioprine, necessitating its discontinuation. We present a case of a 43-year-old with dermatomyositis who experienced a severe rash upon dose escalation of azathioprine. The patient underwent a successful azathioprine desensitization protocol, allowing the continuation of this essential therapy.

Case

Clinical History: A 43-year-old female with a confirmed diagnosis of dermatomyositis presented to Allergy clinic due to reaction to azathioprine. Her diagnosis of dermatomyositis dated back three years, when she initially developed a rash on her face. She attributed the rash to sun sensitivity. Over the next few weeks it appeared on her arms, legs, chest, and upper back. In the subsequent weeks, she developed muscle weakness and difficulty rising from a seated position, leading to several falls.

Initial Treatment: She was initially treated with prednisone, mycophenolate and weekly IVIG infusions. The initial prednisone dose was 60 mg, gradually tapered until she was steroid-free. While her dermatomyositis was well-controlled with mycophenolate and IVIG infusions, she needed medication change due to her desire to become pregnant. Mycophenolate posed risks of first trimester pregnancy loss and congenital malformations.[1]

Azathioprine Hypersensitivity Reaction: Azathioprine was initiated at a daily dose of 50 mg daily, which she tolerated for several weeks until the dose was escalated to 100 mg. Within days of this dose increase, the patient developed diffuse hives over her upper and lower extremities, accompanied by pruritus, consistent with a hypersensitivity reaction. She was started on oral prednisone and oral diphenhydramine for symptomatic relief. Despite treatment, the rash persisted for three weeks, causing considerable discomfort and distress to the patient, even leading to the cancellation of a planned trip to Europe.

Referral and Desensitization: Subsequently, the patient was referred to Allergy for consideration of azathioprine desensitization.[2] Given the absence of suitable alternative medications, azathioprine desensitization was discussed with the patient, who agreed to proceed.

The patient underwent an outpatient azathioprine desensitization procedure in our office. She received premedication the night before and the morning of the procedure, including prednisone 40 mg, montelukast 10 mg, cetirizine 20 mg, and famotidine 20 mg. The desensitization was conducted using an oral suspension with a concentration of 10 mg/mL.

The desensitization protocol commenced with a minute dose of azathioprine 1 mg (1% of target dose) with dose increases every 20 minutes (Table 1). Over eight steps, the patient received a total of 100 mg over a 200-minute period. The patient tolerated the entire desensitization protocol without any signs of hypersensitivity or allergic reaction.

Follow-up: Following the successful azathioprine desensitization, the patient was instructed to continue azathioprine 100 mg via oral suspension daily. In addition, she was to take cetirizine 10 mg twice daily for 1 week then reduce to 10 mg daily. At follow-up one week later, patient had already reduced the cetirizine dose due to drowsiness with twice daily dosing but was tolerating the azathioprine oral suspension. She was subsequently transitioned to oral azathioprine at the same dose of 100 mg and advised to discontinue cetirizine after a few days. Currently, the patient remains on azathioprine 100 mg without any issues.

Discussion

Hypersensitivity reactions to azathioprine can pose a significant challenge in patients with autoimmune diseases, as this medication is often a crucial component of their treatment. Desensitization is a viable strategy to overcome these reactions and minimize need for alternative, potentially less effective therapies.[3] This procedure involves reintroducing the offending medication in gradually increasing doses while closely monitoring for any adverse reactions.

The slow and gradual reintroduction of the medication allows the patient's immune system to become accustomed to the medication, reducing the risk of an allergic response. Additionally, premedication consisting of steroid, antihistamine, and anti-leukotriene are given to further reduce the risk of a reaction. Depending on the severity of the reaction, a desensitization procedure can occur in either the inpatient or outpatient setting. Due to the mild nature of this patient's reaction, the azathioprine desensitization was successfully conducted in the outpatient office within a period less than 4 hours.

It is important to emphasize that medication desensitization only induces a temporary tolerance that is maintained as long as the medication is taken continuously but can recur if there is an interruption in therapy exceeding 48 hours. This was thoroughly explained to the patient, and she understood the importance of continuous therapy and the need to return to the allergy practice if there is a gap in treatment.

In summary, azathioprine desensitization proved to be a successful intervention in our patient with dermatomyositis, allowing her to continue the use of this essential medication. This case highlights the potential utility of desensitization protocols in managing hypersensitivity reactions to azathioprine, providing a viable option for patients with otherwise limited treatment options.

Table 1. Azathioprine desensitization protocol 10 mg/mL

1 mg (1%)	20 minute observation
2 mg (2%)	20 minute observation
4 mg (4%)	20 minute observation
8 mg (8%)	20 minute observation
10 mg (10%)	20 minute observation
15 mg (15%)	20 minute observation
20 mg (20%)	20 minute observation
40 mg (40%)	60 minute observation
Total 100 mg over 200 minutes Premedication regimen: Prednisone 40 mg, Montelukast 10 mg, Cetirizine 20 mg, Famotidine 20 mg administered night before and morning of the desensitization	

REFERENCES

1. **Dao KH, Bermas BL**. Systemic Lupus Erythematosus Management in Pregnancy. *Int J Womens Health*. 2022 Feb 15;14:199-211. doi: 10.2147/IJWH.S282604. PMID: 35210867; PMCID: PMC8859727.
2. **Lavaud F, Abdelli N, Thiefin G**. Successful desensitization for azathioprine skin rash in a patient with severe Crohn's disease. *Dig Dis Sci*. 1997 Apr;42(4):823. doi: 10.1023/a:1018828517366. PMID: 9125656.
3. **Kang SY, Seo J, Kang HR**. Desensitization for the prevention of drug hypersensitivity reactions. *Korean J Intern Med*. 2022 Feb;37(2):261-270. doi: 10.3904/kjim.2021.438. Epub 2022 Feb 28. PMID: 35123386; PMCID: PMC8925949.