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Case Report

Azathioprine Induced Pancreatitis - An Uncommon Phenomenon.

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Abstract

Introduction: Azathioprine (AZA)-induced pancreatitis (AIP) is a known, though relatively uncommon, idiosyncratic drug reaction causing inflammation of the pancreas, often seen in patients with Inflammatory Bowel Disease (IBD) (Crohn's/UC) or autoimmune conditions, manifesting as abdominal pain, nausea, and vomiting, typically resolving quickly after stopping the drug but requiring medical attention for diagnosis and management. It's an unpredictable reaction, not strictly dose-dependent, linked to certain genetic markers (HLA alleles), and emphasizes the need for monitoring when using AZA.

Case Report: We report a case of fifty-two-year-old female, a known case of--- on dermatological follow up and was started on tablet azathioprine 50 mg twice daily after food for last six months. She suddenly presented with acute pain abdomen which was epigastric and radiated to back. On evaluation, serum amylase and lipase were massively raised, leukocytosis, mild transaminitis but renal function test, complete lipid profile, blood sugar was normal and viral screen was negative. The ultrasonogram abdomen showed bulky pancreas with overlying intestine dilated with gaseous distension. The computed tomography abdomen done on 5th day revealed mild interstitial pancreatitis with CTSI score of 6/10. She was managed symptomatically with analgesics, antibiotics, intravenous fluid and other supportive therapy. After one week, she was discharged under hemodynamically stable condition and was pain free, passing normal stools and accepting orally well. There was no other risk factor identified for pancreatitis. She was advised not to take azathioprine and after regular follow up for last two years, she is totally asymptomatic without any kind of symptoms.

Conclusion: Azathioprine is used in patients with complex dermatologic conditions and/or resistant to conventional treatments. It has been approved for diseases like lupus, dermatomyositis, and pemphigus vulgaris. Thus, dermatologist should adequately educate the patient receiving azathioprine about its adverse effects and themselves remain vigil about these undesired effects which improve and resolve when azathioprine is decreased or interrupted. It is always recommended to start at the lowest possible dose in order to improve tolerance and to avoid permanent discontinuation of a drug that can be extremely beneficial for the patient.

Keywords: Pancreatitis, Azathioprine, Computed tomography scan, Amylase, Lipase

INTRODUCTION

Azathioprine is an immunosuppressant medication used in dermatology to treat a variety of severe inflammatory and autoimmune skin conditions, particularly those unresponsive to conventional therapies. It is frequently used as a steroid-sparing agent to minimize the long-term side effects of oral steroids. Azathioprine is used in treatment of Pemphigus Vulgaris, Systemic Lupus Erythematosus (SLE) & Cutaneous Lupus, Dermatomyositis, Atopic Eczema (Dermatitis), Bullous Pemphigoid, Pyoderma Gangrenosum, Chronic Actinic Dermatitis, Cutaneous Vasculitis, Psoriasis, Intractable Pruritus. Azathioprine is a pro-drug that is converted in the body into active metabolites which disrupt DNA synthesis, primarily in rapidly dividing immune cells like T and B lymphocytes. This process suppresses the overactive immune system, thereby reducing the inflammation that causes skin disease symptoms. Treatment with azathioprine requires careful monitoring due to potential side effects. Acute pancreatitis occurs in around 2% of inflammatory bowel disease patients exposed to azathioprine or 6-mercaptopurine and is an important limiting toxicity of these thiopurine antimetabolites. Factors determining the risk of pancreatitis are unknown: the risk is not related to dose, though it may occur more commonly in individuals with Crohn's disease than in other disorders [1]. Acute pancreatitis (AP) has become increasingly recognized in children, with an incidence estimated to be 1 in 10,000, approaching the lower range in adults [2-6]. Several risk factors are known for AP, including biliary, anatomic, trauma, drugs, genetic risk factors,

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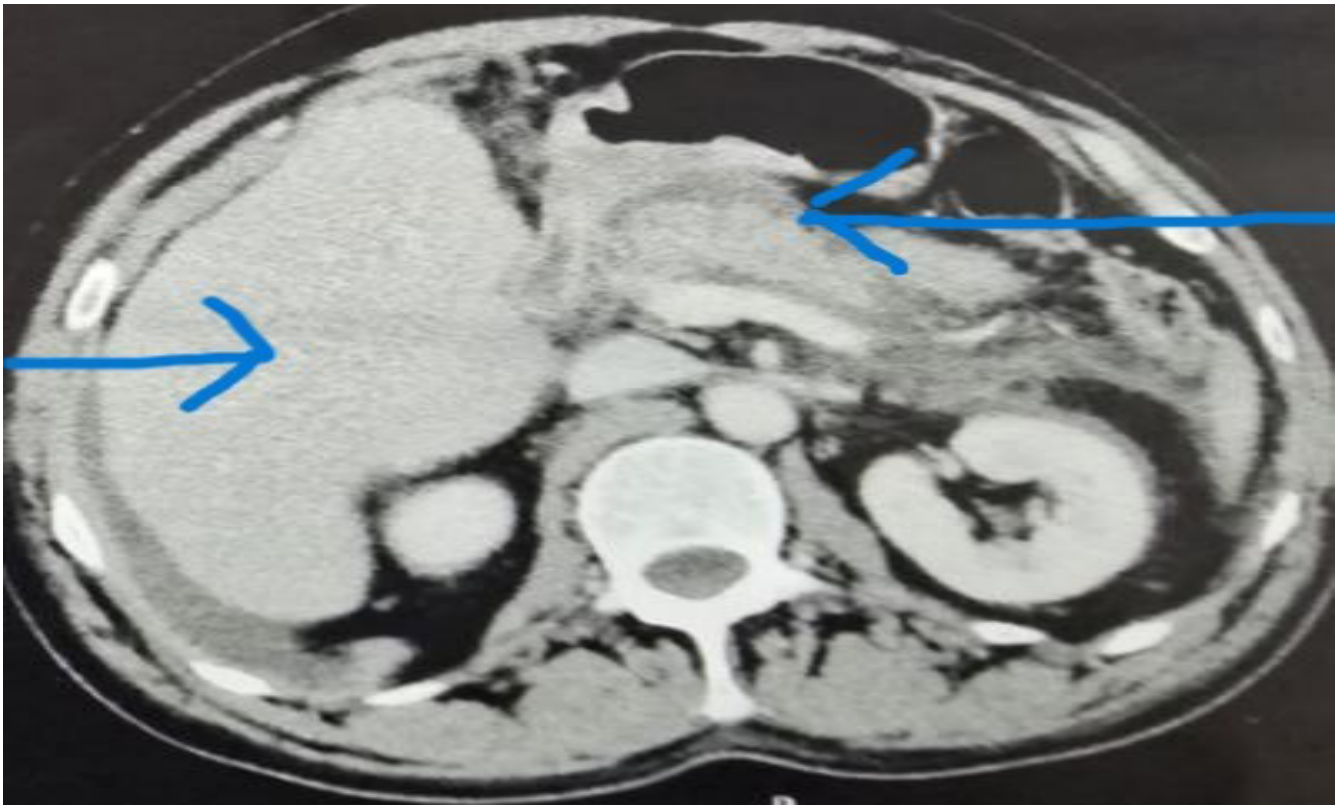
immune system-mediated, and metabolic disturbances [7-8]. Among these risk factors, drug-associated pancreatitis (DAP) has higher prevalence in pediatric than adult studies [9-11]. The drugs like azathioprine, cimetidine, interferon-alpha, methyldopa, metronidazole, olsalazine, and oxyphenbutazon all had a definite causal relationship with acute pancreatitis whereas doxycycline, enalapril, famotidine, ibuprofen, maprotiline, mesalazine, and sulindac had a probable causal relationship with acute pancreatitis [12]. Well-recognized dose-dependent adverse events associated with AZA and 6-mercaptopurine (6-MP) include myelosuppression and hepatotoxicity, which often resolve with dose reduction. These adverse events rarely necessitate termination of therapy [13]. Idiosyncratic adverse drug reactions (i.e. intractable nausea, malaise, fever without leucopenia, arthralgia and acute pancreatitis), while more common in frequency than dose dependent reactions, often demand discontinuation of the offending medication [14]. One review showed with moderate certainty that the use of AZA to induce remission and maintain medical induced remission in Crohn's disease (CD) was probably associated with increased occurrence of pancreatitis [15]. A delayed type II or IV allergic reaction or immune-mediated genetic disposition has been postulated, with the former supported by the fact rechallenge of AZA results in recurrence of symptoms [16].

CASE REPORT

We report a case of fifty-two-year-old female, a known case of Pemphigus vulgaris on dermatological follow up and was started on tablet azathioprine 50 mg twice daily after food for last six months. She suddenly presented with acute pain abdomen which was epigastric and radiated to back. The pain was associated with non- passage of flatus and faeces. On evaluation, serum amylase and lipase were massively raised, leukocytosis, mild transaminitis but renal function test, complete lipid profile, blood sugar was normal and viral screen was negative. The ultrasonogram abdomen showed bulky pancreas with overlying intestine dilated with gaseous distension. The computed tomography abdomen done on 5th day revealed mild interstitial pancreatitis with CTSI score of 6/10. She was managed symptomatically with analgesics, antibiotics, intravenous fluid and other supportive therapy. After one week, she was discharged under hemodynamically stable condition and was pain free, passing normal stools and accepting orally well. There was no other risk factor identified for pancreatitis. She was advised not to take azathioprine and after regular follow up for last two years, she is totally asymptomatic without any kind of symptoms.

Figure 1. CECT scan abdomen Showing Pancreatitis (large blue arrow).



CONCLUSION

Azathioprine is used in patients with complex dermatologic conditions and/or resistant to conventional treatments. It has been approved for diseases like lupus, dermatomyositis, and pemphigus vulgaris. Thus, dermatologist should adequately educate the patient receiving azathioprine about its adverse effects and themselves remain vigil about these undesired effects which improve and resolve when azathioprine is decreased or interrupted. It is always recommended to start at the lowest possible dose in order to improve tolerance and to avoid permanent discontinuation of a drug that can be extremely beneficial for the patient.

Conflict Of Interest

No conflict of interest and prior permission from patient and relatives was taken before publishing the case report.

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