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CASE REPORT

Azathioprine Induced Acute Pancreatitis in a Patient with Lichenoid Dermatitis

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Abstract

Acute pancreatitis (AP) is an inflammatory condition, characterized by elevated levels of amylase and lipase, with manifestation of acute abdominal pain and acute with high mortality and morbidity rates. The most common causes of AP other than gallbladder stones and alcohol include hypercalcemia, infections, hypercalcemia, and drugs. One such drug associated with AP is azathioprine. Azathioprine for dermatologic lesions are used as steroid sparing immunomodulatory agents. Here in, we report such an unusual case of azathioprine induced acute pancreatitis.

Keywords: Lichenoid dermatitis, drug-induced acute pancreatitis, azathioprine, idiosyncrasy DIP

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Introduction

Acute inflammation of the pancreas, commonly known as acute pancreatitis, stands as a significant cause for hospital admissions globally related to gastrointestinal issues. The death rate associated with this condition hovers around 5% [1], although this figure can fluctuate based on the severity of the disease and the patient's overall health condition. The origins of this ailment are diverse, with gallstones and alcohol consumption being the primary culprits. However, other factors such as high lipid levels in the blood, infections, elevated calcium levels, certain medications, and autoimmune responses also play a role. Medication-induced acute pancreatitis represents roughly 2% of these cases and is usually classified as mild to moderate in terms of severity [2].

Several medications have been linked to the onset of acute pancreatitis, including but not limited to acetaminophen, corticosteroids, metronidazole, azathioprine (AZA), mercaptopurine, and diuretics like thiazides.

In gastroenterology practice, azathioprine (AZA) along with its derivative 6-mercaptopurine (6-MP) are recognized for their effectiveness in managing Crohn's disease (CD), especially when corticosteroids are deemed unsuitable for long-term maintenance due to their potential side effects [3]. Azathioprine has received approval for treating various inflammatory disorders affecting the skin.
The drug azathioprine is sanctioned for use in conditions such as pemphigus vulgaris, systemic lupus erythematosus, and dermatomyositis. Additionally, it is frequently employed in an off-label capacity to address a range of conditions including atopic eczema, bullous pemphigoid, pyoderma gangrenosum, chronic actinic dermatitis, cutaneous vasculitis, among other skin-related issues.

Case Report

Case History/Examination

A 55year old female presented to our gastroenterology department with complaints of acute onset epigastric and umbilical, deep boring continuous abdominal pain, which was associated with nausea and vomiting and pain aggravated with food intake with radiation to back and decreased on sitting and leaning forward position.

Patient did not give any history of trauma, breathing difficulties, previous surgeries, similar complaints in past, no comorbidities, no significant family history with normal bowel, bladder habits prior to the onset of symptoms and no addictions.

Three months prior to onset of symptoms, patient consulted a dermatologist for complaints of gradual onset generalised itching and darkening of skin and was clinically diagnose as having lichenoid dermatitis for which patient was treated initially with topical emollients and anti- histamines with poor response. For this patient was started on oral steroids which were gradually tapered over 4 weeks along with other supportive treatment. Patient improved symptomatically. So on further follow up, patient was started on azathioprine 50mg OD (as steroid sparing agent) after doing baseline investigations and patient was continued on topical applications. 15 days after starting this patient presented to us with abdominal pain.

Status of skin lesion at presentation in Figures 1 and 2.

On examination: PR- 90/min, BP-110/70mm Hg, Temp-98.6 F

Spo2- 98% in room air, RR-16/min

Per abdomen- soft, no localised tenderness with no organomegaly with bowel sounds present

Other system examinations was found to be within normal limits.

Based on the above patient was clinically diagnosed to be having acute pancreatitis.

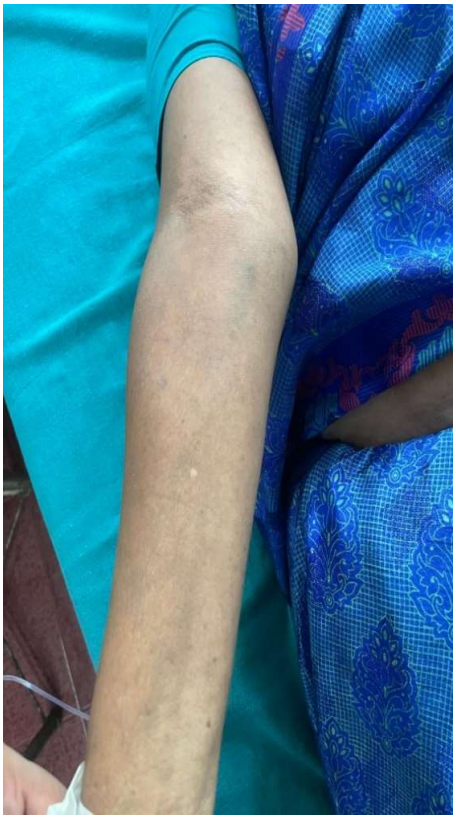

Figure 1. Lesions on limbs.

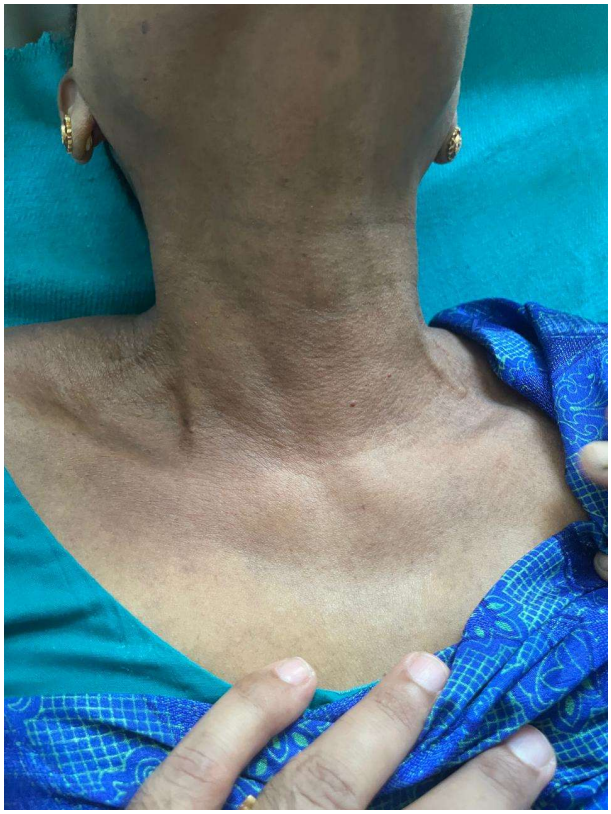

Figure 2. Lesions on neck and upper chest.

Methods

Investigations

Hb-12.4 g/dl

Total wbc count- 16310 cells/mm3

PCV -40.1%

ESR- 52/ 1st hour

Total bilirubin-0.5mg/dl

SGOT/SGPT- 20/19

ALP-95 IU/ml

Blood urea/S.creatinine- 44/ 0.7

Na+/K+- 136/3.6

Serum amylase- 550.1 IU/L

Serum lipase -3293.2 IU/L

S. ca2+: 8.4 mg/dl

Fasting lipid profile: total cholesterol: 190mg/dl, LDL- 117 mg/dl, HDL -52 mg/dl

IGG4 – 1.1.g/L

CT abdomen

Impression

Bulky pancreas is seen. Significant peripancreatic fluid and inflammation is seen. Oedematous second and third part of duodenum seen.

Features are suggestive of acute pancreatitis. No evident located collections.

The diagnosis was confirmed as Acute pancreatitis – mild severity Probable aetiology- Drug induced (Azathoprine)

Patient was admitted and was treated with iv fluids, analgesics and other supportive treatment. Azathioprine was discontinued. Patient was discharged when patient became asymptomatic and was taking oral feeds. Patient was asked to follow up in OPD. In subsequent follow ups patient remained asymptomatic.

Conclusion and Results

Our case highlights the importance of having a good clinical history to diagnose uncommon causes of acute pancreatitis.. AZA should be held at the time of admission in patients with high clinical suspicion of DIAP while waiting for a workup to rule out other common causes of pancreatitis. Our patient had an uncomplicated hospital course with discontinuation of AZA and conservative management. Our patient did not develop any further episodes acute pancreatitis and is under regular follow up. Whether AZT was definitely indicated for our patient's dermatologic condition is unsure. Till now no flare up of patient's skin lesions and the patient is comfortable with the current condition of her skin.

Discussion

The condition known as acute pancreatitis presents a serious health challenge, with its mortality rates ranging widely from 1% to 30% [4], depending on various factors. A multitude of drugs have been identified as potential triggers for pancreatitis, acting through different mechanisms. These include immune system-mediated hypersensitivity, direct damage to cells, accumulation of harmful metabolites, reduced blood supply (ischemia), formation of blood clots within vessels (intravascular thrombosis), increased thickness of pancreatic fluids, and unpredictable reactions unique to the individual [5]. This has been presented in Figure 3.

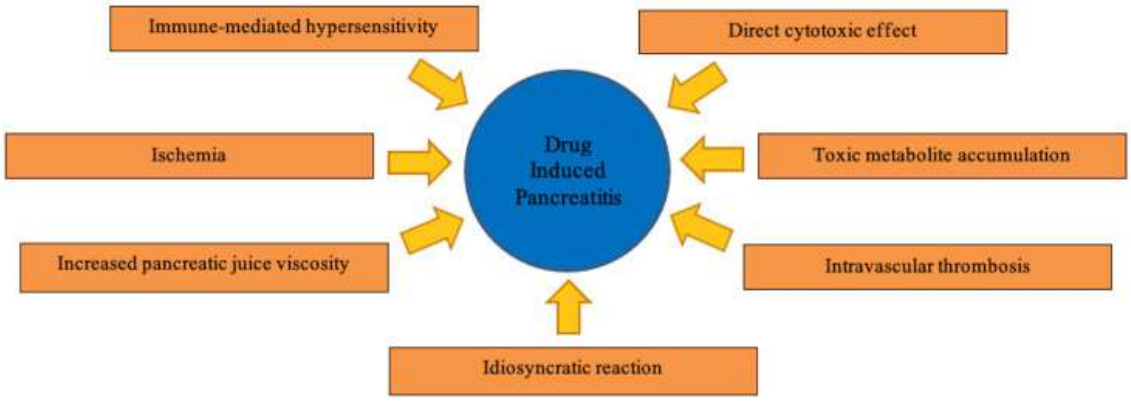

Figure 3. Possible mechanisms for drug induced acute pancreatitis

AZA is a known medication that can cause idiosyncratic DIP [6]. Studies of inflammatory bowel disease patients on AZA revealed an incidence of AZA-induced pancreatitis of 7.5%, with a mean time of 25 days until developing pancreatitis from drug initiation, and a mean dose of 88 mg.

Risk factors for developing AZA-induced pancreatitis are shown in Table 1.

Smoking
Concomitant budesonide use
Single daily dose of azathioprine
Genetic variants in the HLA gene region
Crohn's Disease

Risk factors for azathioprine-induced pancreatitis [7]

Identifying drug-induced acute pancreatitis (DIAP) poses a diagnostic challenge. A definitive diagnosis of DIAP necessitates the exclusion of other potential causes, onset of pancreatitis following drug exposure, resolution after stopping the drug, and recurrence upon re-administration of the drug [8]. However, most documented instances lack rechallenge data, which is pivotal in establishing causation. Moreover, the prevalence of other illnesses that can lead to acute pancreatitis often complicates the determination of a drug's role.

It's crucial for medical professionals to recognize the array of medications that may lead to DIAP and to consider this diagnosis when faced with cases of acute pancreatitis that have no apparent cause. Typically, patients with DIAP experience a relatively mild and non-threatening progression of the condition, with a generally positive outlook for recovery [9]As AZT pose a risk for pancreatitis, the indications for its use in clinical practice should be ver well defined.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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Ethical Disclosure

Informed consent obtained from patient before publication.

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