

AZATHIOPRINE INDUCED MYELOSUPPRESSION IN CROHN'S DISEASE PATIENT- A CASE REPORT

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INTRODUCTION:

Azathioprine is a cytotoxic drug. Co-administration of azathioprine along with corticosteroids causes adverse effects such as myelosuppression.⁽¹⁾ 5-25% of patients may experience side effects such as myelosuppression due to azathioprine drug. Thiopurine methyltransferase inactivates the toxic products of azathiopurine metabolism, and its activity varies greatly between individuals. Individuals with Thiopurine methyltransferase defect are at risk of suffering from the toxic effect of azathioprine.⁽²⁾ There are two types of side effects for azathioprine drug, one is allergic non- dose related such as fever, rash and others are non- allergic and dose related side effects such as leucopenia.⁽³⁾

CASE REORT:

A 22 year old male presented with dyspnoea since 1 month and palpitations. He was clinically diagnosed to have Crohn's disease and was treated with azathioprine, mesalamine and prednisolone 5 months back. His vital signs were as follows: blood pressure- 130/70 mm Hg; pulse rate- 86/min. On physical examination, patient was gross pallor, abdomen was flat. Complete blood count reports showed pancytopenia in view of which azathioprine was withheld. The haemogram showed a haemoglobin drop to 2.5 g%, packed cell volume to 25.6 vol % total leukocyte count to 3200 /cubic mm, platelets to 1.10 L/cubic mm, white blood cells to 17.73/ mL. Peripheral blood smear report showed anisopoikilocytes, macrocytes, microcytes, tear drop cells, ovalocytes with severe hypochromia, leucopenia, thrombocytopenia.

The suspected cause of myelosuppression was found to be co-administration of azathioprine(100 mg/day) and prednisolone(60 mg) which belongs to category corticosteroid. Suspecting a diagnosis of azathioprine induced myelosuppression, azathioprine was discontinued. Pancytopenia was managed with packed red blood cells transfusion. Haemoglobin level raised from 2.5 g/dl to 8.5 g/dl after 5 pint transfusion.

DISCUSSION:

The thiopurine drug azathioprine is used in the treatment of moderate to severe inflammatory bowel disease for maintenance of remission in both Crohn's disease and ulcerative colitis and for induction of remission in Crohn's disease.⁽⁴⁾

If patients with inflammatory bowel disease are treated with azathioprine in range 1-2 mg/kg/day there are chances of presenting with pancytopenia within weeks to months.⁽⁵⁾

The effect of Azathioprine is largely dose dependent. If dose is less than 2.5 mg/kg/day, it causes mild leukopenia. Low to moderate doses of Azathioprine (<2 mg/kg/day) causes sudden, severe and unexpected myelosuppression.⁽⁶⁾

In this patient, the main cause of myelosuppression is co-administration of azathioprine and prednisolone to treat inflammatory bowel disease 5 months back which is in accordance with Li- Kai Lo et al.

The three important enzymes responsible for metabolism of azathioprine are xanthine oxidase, thiopurine S-methyl transferase, and hypo- xanthine phosphoribosyl transferase. Azathioprine is converted to 6- mercaptopurine via non- enzymatic reaction. It gets oxidized by enzymes and forms 6- thioguanine nucleotide (6-TGN). Patients with low thiopurine S-methyl transferase activity have elevated 6-TGN when treated with standard doses (2-2.5 mg/kg/day) of azathioprine and are at greatly increased risk of myelosuppression.^(5,7,8)

Adverse events of azathioprine may be either dose- dependent, pharmacologically explainable events which can occur at any time of treatment and are well known such as myelosuppression or which occurs within 2-4 weeks after start of treatment such as rashes, vomitings. The most common adverse event such as myelosuppression can be managed by either reducing the dose of the drug or discontinue the drug.⁽⁸⁾

In this patient, the main reason for stopping azathioprine drug was myelosuppression. The management of azathioprine induced myelosuppression includes hospitalization of patients with febrile neutropenia and early commencement of empirical broad-spectrum antibiotics, prophylactic or therapeutic blood and platelet transfusion to meet physiological demand.

Blood testing throughout the duration of azathioprine treatment is recommended for every 2 weeks in first three months of therapy.⁽⁹⁾

CONCLUSION:

The patient represents a possible case of azathioprine induced myelosuppression with a Naranjo probability score of 4. Immunosuppressant drug azathioprine has a significant potential for adverse reactions such as bone marrow suppression. Frequent blood count monitoring is recommended for patients with azathioprine therapy.

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