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Case Report

Hydroxyurea-induced hemolytic anemia in myeloproliferative disorder: A case report

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ABSTRACT

This case study addresses the side effects of hydroxyurea medication in a male patient, age 62, who has had myeloproliferative disease for two years. The patient presented with symptoms of giddiness, chillness, and loss of appetite, prompting admission to the general medicine department. As a result of hemolytic anemia and thrombocytopenia, hematological and biochemical analyses showed a marked decrease in the number of red blood cells (RBCs), hemoglobin (Hb), hematocrit (PCV), and platelets. Additionally, abnormal values in liver function tests and electrolyte levels were observed, suggesting multi-system involvement. A one-year treatment of hydroxyurea, thalidomide, and folic acid was part of the patient's medical history. A concerning rise in mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW) was seen in the hematological report, which further demonstrated the seriousness of the hemolytic process. The detailed analysis underscores the adverse effects of hydroxyurea, leading to hemolytic anemia, and exacerbating the existing myeloproliferative disorder. This case emphasizes the critical need for close monitoring of patients undergoing hydroxyurea therapy. Healthcare providers should remain vigilant for potential adverse reactions, especially hemolytic anemia, to ensure timely intervention and optimization of patient care. Adjustments to the treatment plan, along with comprehensive management strategies, are essential to mitigate risks and enhance the overall well-being of individuals with myeloproliferative disorders undergoing hydroxyurea therapy.

1. Introduction

Hemolytic anemia is the condition when red blood cells (RBCs) break down before they should live for 120 days.[1] Hemolytic anemias include different disorders with varied clinical and molecular features, marked by a decrease in red blood cells in the bloodstream. This often leads to severe anemia or compensated hemolysis, with higher levels of young red blood cells called reticulocytes.[2] The reasons why anemia occurs are Either intravascularly or extravascularly, erythrocytes are prematurely destroyed. Hemolysis aetiologies are commonly classified as acquired or hereditary. Hemolytic anemia can be acquired via autoimmune, microangiopathy, and infection. Acute anemia, weariness, tachycardia, hematuria, jaundice, dyspnea, and potentially hypotension are the signs and symptoms. The breakdown of red blood cells, which normally have a 120-day lifespan, is the pathophysiology of hemolytic anemia. This could be a potentially fatal procedure that is either acute or chronic. Hemolysis can occur intravascularly or extravascularly. Owing to their incapacity to reshape, red blood cells with illnesses such as sickle cell disease may become stuck in the spleen and undergo phagocytosis.

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Decreased energy production (enteropathies like G6PD deficiency), fragmentation (microangiopathic hemolytic anaemias like thrombotic thrombocytopenic purpura (TTP), disseminated intravascular coagulation (DIC), HELLP syndrome), increased oxidative stress, immune-mediated mechanisms where antibodies bind to red blood cells causing phagocytosis, drug-induced hemolysis, infections, or direct trauma can also cause destruction. Treatment for anemia is based on the severity of the illness; depending on the underlying cause of hemolytic anemia, quick measures like plasmapheresis, diuresis, or blood transfusions may be required. The mainstay of care for severe anemia is usually blood transfusions, especially when there is ongoing bleeding. More specialized therapy options that are catered to the particular cause of anemia may be sought once hemolysis is found to be the cause, or if immediate intervention is not necessary. An immunological and non-immune cause of hemolysis can be distinguished with a direct antiglobulin (Coombs) test if the initial cause is unknown. Treatment options that have been demonstrated to be effective for patients with sickle cell disease (SCD) include bone marrow transplants, hydroxyurea, erythropoiesis-stimulating medications, and blood transfusions.A diverse range of conditions known as myeloproliferative neoplasms are caused by the aberrant growth of one or more terminal myeloid cell lines in the peripheral circulation[3]For patients with essential thrombocythemia (ET) and polycythemia vera (PV), the goal of treatment is to return blood counts to normal to reduce the risk of thrombotic episodes. The two most widely utilized cytoreductive alternatives for patients with ET and PV who are at high risk of vascular issues are interferon-α (IFN-α) and hydroxyurea (HU).[4]

2. Case Presentation

Mr.T, a 62-year-old male patient, was admitted to the general medicine department (Hospital name - Vivekananda medical care Hospital, Elayampalayam, Tiruchengode, Namakkal- 637205) (Year of Evaluation – 2000) due to his complaints of giddiness for 4 days, chillness for 3 days, and loss of appetite. He also had a past medical history of myeloproliferative disorder for 2 years, and his past medication history was capsule hydroxyurea 500 mg, tablet thalidomide 50 mg, and folic acid 5mg for a 1-year history. Vitals show elevated pulse rate and decreased blood pressure(Table 1), and his hematological report shows increased RDW, MCH, and decreased RBC, HB, PCV, eosinophils, basophils, and platelets(Table 2). His liver function test report shows increased total bilirubin, direct bilirubin, indirect bilirubin, decreased albumin, and protein.

The electrolyte report shows decreased sodium, and finally, the patient was diagnosed with Haemolytic anemia, hyponatremia, myeloproliferative disorder, and thrombocytopenia. Treatment involves infusion of normal saline, Cap. Hydroxyurea (500 mg OD), T. Folic Acid (5 mg OD), T. Thalidomide (50 mg OD), T. Prednisolone (30 mg OD), One unit of Blood transfusion was done on day 2 and day 3 of admission.

3. Discussion

In this case, the patient was prescribed the following treatment which involves a multidisciplinary approach, including infusion of normal saline to correct dehydration and medications like Cap. Hydroxyurea (500 mg OD)-Prescribed to suppress bone marrow activity and reduce cell proliferation, which is crucial in the management of myeloproliferative disorders. T. Folic Acid (5 mg OD)-Given to support erythropoiesis and prevent potential folic acid deficiency induced by hydroxyurea therapy. T. Thalidomide (50 mg OD)-Likely prescribed to manage symptoms related to myeloproliferative disorder. T. Prednisolone (30 mg OD)- Administered for its anti-inflammatory and immunosuppressive properties, which may help alleviate symptoms associated with hematological disorders and modulate immune responses.Necessary to rapidly improve oxygen-carrying capacity and alleviate symptoms associated with severe anemia, One unit of Blood transfusion was done on day 2 and day 3 of admission. Hydroxyurea is a medication commonly used in treating myeloproliferative disorders, conditions where the bone marrow overproduces blood cells. Its mechanism involves reducing cell production to control the disease. However, like any medication, Hydroxyurea can have serious side effects. One such example mentioned in this case is hemolytic anemia. Hydroxyurea induces bone marrow depression leading to anemia with megaloblastosis and decreased platelet and leukocyte counts.[6,7] This added stress from hemolytic anemia can worsen the underlying myeloproliferative disorder. The causality assessment using the WHO Naranjo adverse reaction probability scale scored 7 indicating a probable adverse reaction in terms of severity (Table 3).

4. Conclusion

In this case, the patient was prescribed hydroxyurea for myeloproliferative disorder treatment. However, it led to adverse effects, including hemolytic anemia, exacerbating the existing condition. This highlights the importance of closely monitoring patients on hydroxyurea therapy for potential adverse reactions, such as hemolytic anemia, to ensure effective management of their condition and minimize harm. Adjustments to the treatment plan may be necessary to mitigate these risks and optimize patient care.

5. Ethical Approval

EC/NEW/INST/2024/TN/0529.

Table 1: Baseline data

Parameters	D1	D2	D3	D4	D5	D6	Reference range
Blood pressure	110/60↓	120/80	110/60↓	100/60↓	110/80	110/60↓	120/80mmHg
Pulse rate	116↑	106↑	80	96	94	88	60-100 beats/min
Temperature	98.2	98	95.4	98.2	98.6	97.8	97-99
Respiratory rate	20	23	21	21	22	20	12-20 breaths/min

Table 2: Hematological report

CBC Parameters	D1	D2	D3	D4	D5	D6	Reference range
RBC	2.36 ↓	2.36 ↓	1.84 ↓	2.24 ↓	1.87 ↓	1.99 ↓	4.7-6.1million cells/microliter
Hb	7.5 ↓	7.5 ↓	6.2 ↓	7.4 ↓	6.3 ↓	6.6 ↓	13.5-17.5g/dl
PCV	21.5 ↓	22.3 ↓	19.0 ↓	20.2 ↓	18.2 ↓	19.5 ↓	38.32-48.6%
Eosinophils	0.3 ↓	0.3 ↓	0.3 ↓	0.1 ↓	0.4 ↓	0.2 ↓	1-4%
Basophils	0.4 ↓	0.6 ↓	1.9	1.8	1.2	1.3	0-1%
Platelets	0.56 ↓	0.31 ↓	0.33 ↓	0.16 ↓	0.29 ↓	0.28 ↓	1.5-4.5lakhs
RDW	6.4↓	19.1 ↑	23.5 ↑	20.5 ↑	20.0 ↑	19.7 ↑	11-14.5%
MCH	31.6	31.7	33.7 ↑	33.1 ↑	33.7 ↑	33.6 ↑	27-31 pg/dl

Table 3: Naranjo scale (adverse drug reaction probability scale).[5] Definite: ≥9; probable: 5-8; possible: 1-4; Doubtful: ≤0.

Naranjo Adverse Drug Reaction Probability Scale				
Question	**Yes**	**No**	**Do Not Know**	**Score in our case**
1. Are there previous conclusive reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	0
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	0
Total Score				7

6. Conflicts of Interest

The authors declare no conflicts of interest.

7. Source of Funding

None.

References

1. Phillips J, Henderson AC. Hemolytic anemia: evaluation and differential diagnosis. *Am Fam Physician*. 2018;98(6):354–61.
2. Guillaud C, Loustau V, Michel M. Hemolytic anemia in adults: main causes and diagnostic procedures. *Expert Rev Hematol*. 2012;5(2):229–70.
3. Thapa B, Fazal S, Parsi M, Rogers HJ, Neoplasms M. Myeloproliferative Neoplasms. StatPearls Publishing; 2023.
4. Mascarenhas J, Kosiorek HE, Prchal JT, Rambaldi A, Berenzon D, Yacoub A, et al. A randomized phase 3 trial of interferon-α vs hydroxyurea in polycythemia vera and essential thrombocythemia. *Blood J*. 2019;139(19):2931–72.
5. 2019.
6. Jabr FI, Shamseddine A, Taher A. Hydroxyurea-induced hemolytic anemia in a patient with essential thrombocythemia. *Am J Hematol*. 2004;77(4):374–6.
7. Dhaliwal G, Cornett PA, Tierney LM. Hemolytic anemia. *Am Fam Physician*. 2004;69(11):2599–606.

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