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Original Research Article

Myriad causes of hemolysis: A case series

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Abstract

Hemolysis is said to occur if there is excessive destruction of red blood cells. The etiology of hemolysis can be myriad. It can be due to acquired or hereditary causes. The destruction of red cells can be intravascular or extravascular, resulting in a broad spectrum of symptoms. Certain hereditary disorders like hereditary spherocytosis may remain asymptomatic for long periods, however disorders like sickle cell anemia may present with life threatening hemolysis.Hemolysis can also be precipitated by drugs, toxins, infectious agents or autoimmune disorders. It is very important to recognize the etiology of hemolysis to institute prompt management measures.We hereby describe five patients who presented to us with clinical features suggestive of hemolysis. One of these patients was diagnosed to have hemolysis due to a hereditary spherocytosis and the rest were diagnosed to have acquired hemolysis due to varied etiologies like Evans syndrome, thrombotic thrombocytopenic purpura, vitamin B12 deficiency and adelayed hemolytic transfusion reaction.

Keywords: Hemolysis, spherocytosis, Evans syndrome, thrombotic thrombocytopenic purpura,vitamin B12 deficiency ,delayed hemolytic transfusion reaction.

Introduction

Hemolysis refers to increased destruction of the red blood cells. It may be inherited or acquired and the site of hemolysis may be predominantly intravascular or extravascular. With respect to mechanism, it may be due to intracorpuscular or extracorpuscular causes. We hereby describe five patients who presented to us with clinical features suggestive of hemolysis. One of these patients was diagnosed to have hemolysis due to a hereditary cause and the rest were diagnosed to have acquired hemolysis due to varied etiologies.

Case series

Hemolysis associated with Evans syndrome

A 62 year old female with history of systemic hypertension and type 2 diabetes mellitus presented to us with complaints of fatigue and loss of appetite of 2 months duration and yellowish discolouration of eyes of 2 weeks duration. Clinical examination revealed severe pallor and

icterus. There was no edema or significant lymph node enlargement. Liver was palpable 3 centimetres below the right costal margin, with a span of 16 centimetres and spleen was palpable 2 centimetres below the left costal margin. Other systems were within normal limits.
Labs revealed a hemoglobin of 6.4 gm, ESR of 132 mm/hour, platelet count of 90,000/ cubic mm. Reticulocyte count was 25%, and corrected reticulocyte count was 13.2%. LDH was 1073 U/L. Serum bilirubin values were 3.5 mg with indirect fraction of 3.3 mg. Liver enzymes were within normal limits. Peripheral smear showed an isopoikilocytosis, spherocytosis and numerous polychromatophilic RBC's, normal WBC's, and reduced platelet count (Figure :1). As the investigations were suggestive of hemolysis, we proceeded with workup for autoimmune hemolysis, a direct Coomb's test was done and it was positive. In view of autoimmune hemolysis and thrombocytopenia, a diagnosis of Evans syndrome was made.

As Evans syndrome can be primary or secondary, further work up was done. A bone marrow study was done and it was normal (Figure: 2). ANA was positive- 70 (Normal value being less than 20). Anti-ds DNA was also positive- 40(normal value being less than 20). She also gave history of recurrent oral ulcers in the past. As she satisfied > 4 SLICC criteria for systemic lupus erythematosus, a diagnosis of systemic lupus erythematosus was made. Hence hemolysis in this patient was due to Evans syndrome secondary to systemic lupus erythematosus. She was started on prednisolone and she improved.

Hemolysis associated with vitamin b 12 deficiency

A 17 year old girl presented to us with complaints of fatigue and yellowish discolouration of eyes of 1 week duration. No history of fever/ abdominal pain. There was no history of intake of any drugs. On examination she was pale, had icterus, all systems were within normal limits.
The following investigations were noted- hemoglobin of 6.3 gm, ESR of 65 mm/hour, platelet count of 3.1 lakhs/ cubic mm. Reticulocyte count was 22%, LDH was 1073 U/L. Serum bilirubin values were 5.6 mg with indirect fraction of 5.0 mg. Liver enzymes were within normal limits. Peripheral smear showed anisopoikilocytosis, normocytes , macrocytes and numerous nucleated RBC's, normal WBC's, and normal platelet count(Figure :3), suggestive of hemolysis. A direct Coomb's test was done and it was negative. ANA was also done was found to be negative.
We proceeded with a bone marrow study it showed hypercellular marrow with erythroid hyperplasia with megaloblastoid maturation and nuclear budding and nuclear bridging. There was an increase in the myeloid series also with large myelocytes, megakaryocytes were normal (Figure: 4).
In view of the bone marrow findings, the possibility of megaloblastic anemia with dyserythropoesis and hemolysis was considered. Vitamin B12 and folate levels were assayed. Vitamin B12 levels were reduced. She was started on parenter alcobalamin and she improved.

Hemolysis associated with thrombotic thrombocytopenic purpura

A 30 year old female with complaints of fever and myalgia of 6 days duration, was referred to us as she was detected to have thrombocytopenia from a hospital elsewhere. On the first day of admission, she was conscious, oriented, and was noticed to have pallor and mild icterus. On the next day, she remained conscious, but was confused and had irrelevant talk. System examination was normal.

Figure 1: Peripheral Smear

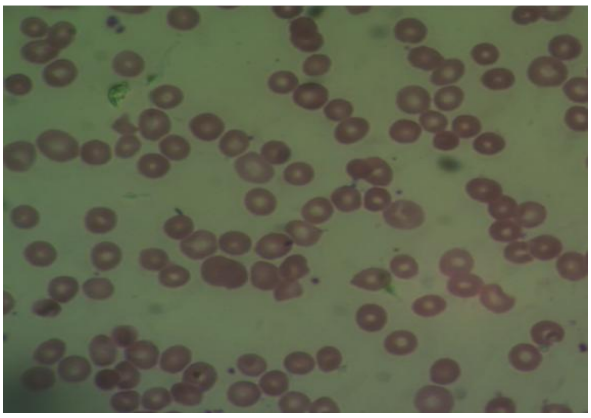


Figure 2: Bone Marrow Study

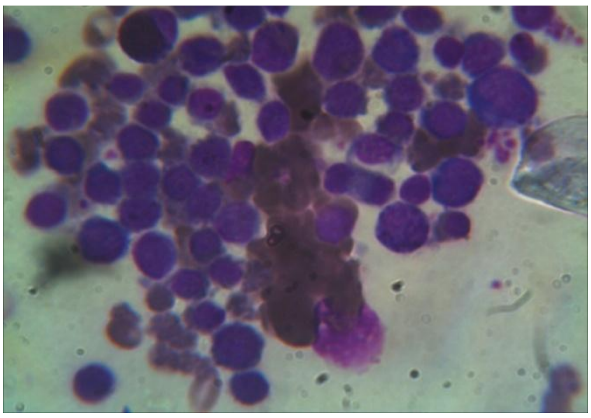


Figure 3: Peripheral Smear Showing

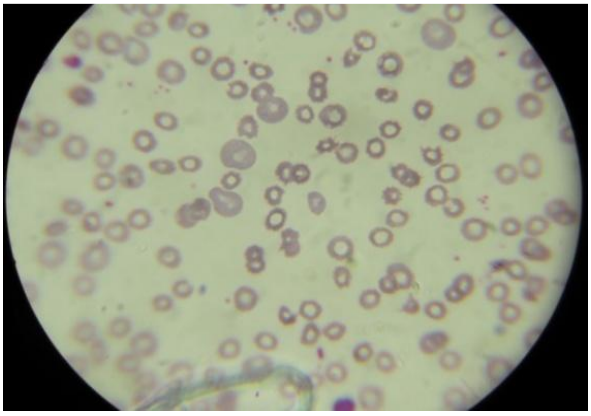


Figure 4: Bone Marrow Showing

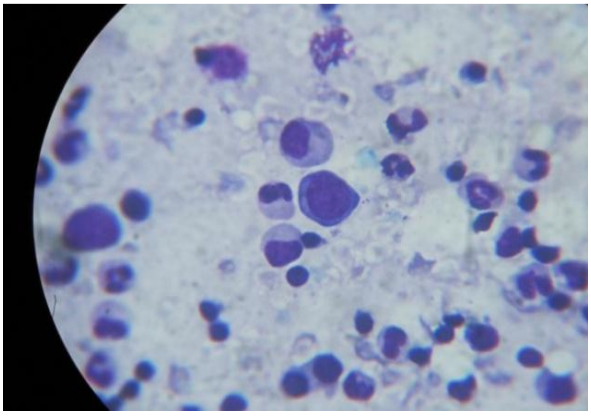


Figure 5: Peripheral Smear Showing

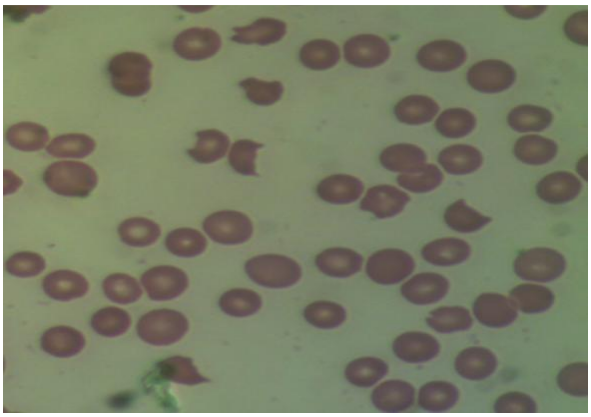
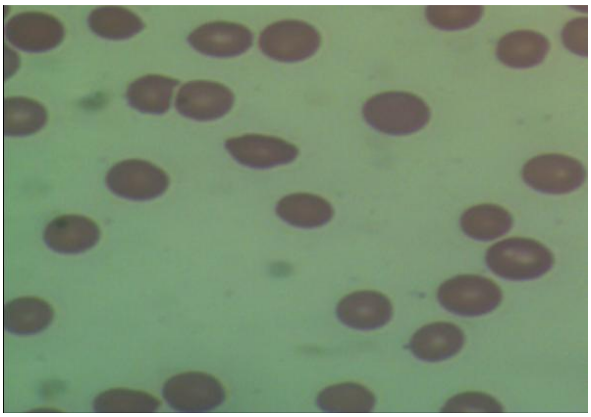


Figure 6: Peripheral Smear Showing



Her lab reports were- a hemoglobin of 7.7gm, ESR of 135 mm/hour, platelet count of 18,000/ cubic mm. Reticulocyte count was 5.2%, and corrected reticulocyte count was 3.3 %. LDH was 1797 U/L. Serum bilirubin values were 3.4 mg with indirect fraction of 3.2 mg. Liver enzymes were within normal limits. Peripheral smear showed anisopoikilocytosis, schistiocytes, spherocytosis and numerous polychromatophilic RBC's, normal WBC's, and reduced platelet count(Figure :5), suggestive of microangiopathic hemolytic anemia.

In view of fever, delirium, thrombocytopenia and micro angiopathic hemolytic anemia, the diagnosis of thrombotic thrombocytopenic purpura was made. She was started on plasmapheresis and she improved.

Hemolysis associated with a delayed hemolytic transfusion reaction

A 72 year old lady, with long standing type 2 diabetes mellitus, systemic hypertension and coronary artery disease presented to us with complaints of exertion aldyspnoea, palpitation of 2 months duration and melena of 1 week duration. She was on aspirin. On examination, she was pale and had bilateral pitting pedal edema, system examination was within normal limits.

Investigations showed hemoglobin of 5.5 gm, ESR of 50mm/ hour, MCV of 76 fl, stool occult blood was positive, serum ferritin was 5. Liver function and renal function tests were normal. Peripheral smear showed microcytic hypochromic anemia. Hence, the diagnosis of iron deficiency anemia was made and she was transfused with one unit of packed red cells. Two days later, she developed icterus and her serum bilirubin was 10.1 mg with indirect fraction of 9.8 mg. Reticulocyte count was 11.2%, LDH was 747. Repeat peripheral smear showed spherocytes, polychromatophilic RBC's suggestive of hemolysis. In view of icterus, indirect hyperbilirubinemia and reticulocytes is developing 48 hours after blood transfusion, the diagnosis of delayed hemolytic transfusion reaction was made.

Hemoysis due to hereditary spherocytosis

A 35 year old male visited our outpatient department with complaints of yellowish disccolouration of eyes of 1 week duration. On examination, no abnormality was found, except for mild icterus. His hemoglobin was 13g, ESR was 5mm/hour. Reticulocyte count was 3%. Serum bilirubin was 4 mg, with indirect fraction 3.6 mg, LDH WAS 582. Direct Coomb's test was negative. Peripheral smear showed numerous spherocytes, WBC's and platelets were normal (Figure :7). Hence the diagnosis of hereditary spherocytosis was made.

Table 1: Causes of Hemolysis

	Intra corpuscular	Extra corpuscular
Hereditary	Hemoglobinopathies	Familial hemolytic uremic syndrome
	Membrane cytoskeleton defects	
	Enzymopathies	
Acquired	Paroxysmal nocturnal hemoglobinuria	Microangiopathic
		Infectious
		Autoimmune
		Drugs/toxins

Discussion

Hemolysis is said to occur if there is excessive destruction of red blood cells. It can occur due to myriad causes. The causes of hemolysis are summarized in Table 1.

One of our patients had hereditary spherocytosis as cause for hemolysis. 4 of our patients had acquired causes of hemolysis- autoimmune, microangiopathic and dyserythropoesis.

Hereditary spherocytosisis an abnormality of the red cell membrane cytoskeleton.

The spectrum of clinical severity of hereditary spherocytosis is broad, it may range from asymptomatic to severe hemolysis. Severe cases may present in infancy with severe anemia, whereas mild cases may present in young adults or even later in life.

Evans syndrome is an autoimmune disorder characterized by simultaneous or sequential development of autoimmune haemolyticanaemia (AIHA) and idiopathic thrombocytopenic purpura (ITP) (Dhingra and Jain, 2008). It can be primary or secondary (Evans et al., 1951). Secondary Evans syndrome may be associated with autoimmune disorders like systemic lupus erythematosus, hematological malignancies, immune deficiencies, and lymph proliferative disorders (Michel et al., 2004; Savasan, 1997)

Concurrent hemolysis in patients with cobalamin deficiency is a well-recognized phenomenon and it is due to intramedullary destruction of erythrocytes (in effective erythropoesis) (Acharya and Gau, 2008; Prueksarit et al., 2013)

Thrombotic thrombocytopenic purpura is a syndrome of Coomb's negative micro angiopathichemolysis and thrombocytopenia in the absence of an alternative explanation for these manifestations (Neame et al., 1973). Presence of fever, neurological and renal abnormalities along with it characterizes the classic pentad (Anselmi et al., 2005)

Delayed hemolytic transfusion reaction occurs after 24 hours, usually within 2 weeks after transfusion of RBC products that appeared compatible , usually in patients with previous alloimmunization to minor antigens from previous transfusions, pregnancy or transplants (anamnestic response) (Syed et al., 1996; Nguyen et al., 2010). Hemolysis can occur due to various reasons. It is very important to recognize hemolysis, identify the etiology and institute treatment promptly.

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