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Case Report

Ineffective red blood cell transfusion in a case of macrocytic normochromic anemia: what is the cause?

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ABSTRACT

Blood transfusion is an essential medical procedure used to replace blood loss due to bleeding or to increase red blood cell count in patients with certain conditions such as anemia. The effectiveness of a transfusion is generally assessed by an increase in hemoglobin levels 1 g/dl each packed of red blood cell and clinical improvement following transfusion. Transfusions are typically administered when hemoglobin levels fall below 7 g/dl in stable patients, or below 8 g/dl in those with cardiovascular disease. Ineffectivenes of tranfusion may be caused by many factors, the common cause that the anemia may be associated with hemolysis. However, not all such cases are attributable to hemolytic anemia hemolytic. That can be caused by active bleeding, poor blood component quality, massive transfusion, underlying clinical conditions such as hypersplenism and chronic kidney disease can also cause transfusion failure. We explore the possible causes that may affect the effectiveness of blood transfusion.

Keywords: Ineffective transfusion, Anemia management, Gastrointestinal bleeding

INTRODUCTION

Anemia is a condition characterized by a decrease in the number of red blood cells or the hemoglobin concentration below the normal reference range, leading to reduced oxygen-carrying capacity of the blood. It is a common clinical finding with a wide range of etiologies and varying degrees of severity.

The etiology of anemia is multifactorial, leading to its classification based on the underlying cause. Broadly, anemia can be divided into the following categories such as deficiency of essential substrates, blood loss, or hemolytic anemia.[1]

Blood transfusion is a life-saving medical procedure that involves the transfer of blood or blood components from a healthy donor to a patient in need.[9] Red blood cell transfusion aims to increase oxygen-carrying capacity, improve tissue perfusion, and stabilize the patient's condition.[2] In clinical practice, transfusions are typically administered when hemoglobin levels fall below 7 g/dl in stable patients, or below 8 g/dl in those with cardiovascular disease.[4] However, not all transfusions yield the expected clinical benefits.

In certain situations where blood transfusion proves ineffective, we consider the possibility that the anemia may be associated with hemolysis. However, not all such cases are attributable to hemolytic anemia. To raise awareness of this issue, this case report will discuss how post-transfusion anemia can also be caused by other conditions.

Here we present a case report of a 60-year-old female with macrocytic normochromic anemia and melena who received red blood cell transfusion therapy and did not achieve a significant increase in hemoglobin.

CASE REPORT

A 60-year-old Balinese female presented to the hospital for planned cephalomedullary nailing due to a right intertrochanteric femur fracture. The patient reported a fall with trauma to the right leg and complained of pain around the wound. She had not had a bowel movement for two days prior to the incident. Laboratory results showed hemoglobin at 6.9 g/dl. After receiving 5 units of packed red cells (PRC), hemoglobin only increased to 7.3 g/dl. Upon further questioning, the patient reported having episodes of black, tarry stools (melena) a few days prior, which resolved spontaneously. The stools were dark, passed 1–2 times a day in small amounts, and had occurred several times before. She admitted to occasional use of pain medications. She denied alcohol or tobacco use. However, she had a history of hypertension, left ventricular hypertrophy, and suspected coronary artery disease under treatment.

On examination, she was alert (GCS E4V5M6), blood pressure was 140/90 mmHg, pulse 90 bpm, respiratory rate 20 breaths/min, temperature 36°C, and oxygen saturation 99% on room air. She appeared anemic with pale conjunctiva. Pupils were 3 mm bilaterally and reactive. No generalized lymphadenopathy was found. Cardiac, pulmonary, and abdominal exams within normal limits. Capillary refill time was under 2 seconds.

A complete blood examination found WBC 4.77/µl, hemoglobin 6.8 g/dl, hematocrit 21%, and thrombocyte 318,000/µl. MCV 112 fl, MCH 29.0 pg, MCHC 31.0 g/l. Reticulocyte count is 9.20%, peripheral blood smear showed macrocytic normochromic red cells with no abnormal inclusions. Electrolyte examination found sodium 139 mmol/l, potassium 3.6 mmol/l, chloride 100 mmol/l. Blood glucose examination 125 mg/dl, triglycerides 118 mg/dl, total cholesterol 160 mg/dl, HDL direct 57 mg/dl, and LDL 90 mg/dl.

Figure 1: Clinical appearance of melena.

The patient had received 5 units of red blood cells, which resulted hemoglobin increase from 6.9 to 7.3 g/dl post-tranfusion. For the gastrointestinal bleeding, she was treated with omeprazole 40 mg BID, tranexamic acid 500 mg TID, and sucralfate 15 ml TID.

DISCUSSION

Anemia is described as a reduction in the proportion of the red blood cells. Anemia is not a diagnosis, but a presentation of an underlying condition.[1] Whether or not a patient becomes symptomatic depends on the etiology of anemia, the acuity of onset, and the presence of other comorbidities, especially the presence of cardiovascular disease. Most patients experience some symptoms related to anemia when the hemoglobin drops below 7.0 g/dl.[13] Anemia may be broken down into several forms and categories. Anemia can be caused by a number of red cell defects, including those that affect red cell production (aplastic anemia), maturation (megaloblastic anemia), haemoglobin synthesis (iron deficiency anemia), genetic maturation defects (thalassaemia), or physical loss of red cells (haemolytic anemias).[1]

Not all cases of anemia warrant an indication for blood transfusion. In critically ill normovolaemic patients' transfusion is considered at a haemoglobin level of ≤7 mg/dl with a target of 7-9 g/dl, unless specific co-morbidities or acute illness-related factors modify clinical decision-making. In haemodynamically stable patients with cardiovascular disease transfusion is considered for Hb ≤8 g/dl, or the presence of symptoms of inadequate oxygen delivery.[13] Complications of blood transfusion may be divided into 2 categories corresponding to the time of the appearance of the first symptoms, acute reactions that occur during or within 24 hours after blood transfusion, and delayed complications that occur later than 1 day after administration of the blood product. Possible causes of ineffective transfusion include hemolytic transfusion reaction, non-immune causes and underlying clinical conditions.

Hemolytic transfusion reactions are a common possible complication of blood transfusions. Hemolysis is the rupture of red blood cells which can occur intravascularly or extravascularly. They include naturally occurring antibodies in the blood recipient as well as antibodies made in response to foreign antigens (alloantibodies). This allergic reaction commonly arises from antigen-antibody interactions between the patient and the transfused product.[12]

Aside from hemolytic anemia, other factors may also contribute to ineffective blood transfusion, including the non-immune causes. Blood stored >21 days may undergo biochemical and structural changes (storage lesion), reduce oxygen-carrying capacity and increase transfusion risks.[7] Data from observational clinical studies reporting transfusion of 'older' red blood cells describe a wide range from 14 days to 24 days. During storage, red blood cells lose potassium, diphosphoglycerate, adenosine 5′-triphosphate (ATP), lipids and membranes, while becoming more rigid and demonstrating reduced oxygen off-loading. Stored units become more acidotic and the suspending fluid has higher concentrations of free haemoglobin and biologically-active lipids, and contains

greater quantities of negatively-charged microvesicles with pro-inflammatory and pro-coagulant activity. Transfusion of red blood cells after prolonged storage may produce harmful effects such us reduction in the efficacy of transfused blood components by reducing their flow, functional capacity, and survival.[6]

Massive transfusion associated complication can also cause transfusion failure. Persistent transfusion requirement of >4 packed red cells (approximately 1000 ml) within 1 h or the transfusion of 10 units of packed red blood cells within a 24-hour period is a commonly accepted definition in clinical settings. Indications to start the massive transfusion protocol are as follows: blood lactate level ≥5 mmol/l; arterial base excess (BE) < −6 mmol/l; blood hemoglobin (Hb) concentration ≤9 g/dl; systolic blood pressure (SBP) ≤90 mmHg. In addition to the general adverse transfusion reactions described in this review, patients receiving massive transfusion are especially prone to developing coagulation abnormalities, hypothermia and acidosis.[10] It is important to remember that over resuscitation leading to high arterial and venous pressures may be deleterious as it may dislodge haemostatic clots and cause more bleeding.[3]

Underlying clinical conditions such as active bleeding, hypersplenism and chronic kidney disease can also cause transfusion failure. Transfusion may also be indicated in patients with active or acute bleeding and patients with symptoms related to anemia and hemoglobin less than 8 g/dl. Anemia may occur due to external loss, inadequate production, internal destruction, or a combination of these factors. While many patients experiencing active bleeding become anemic, anemia in itself does not become an indication for transfusion. Unless the patient is actively bleeding, it is recommended to transfuse 1 unit of packed red cells at a time, which will typically increase the hemoglobin value by 1 g/dl and hematocrit by 3%. Follow up by checking post-transfusion hemoglobin. In trauma, surgery, or gastrointestinal bleeding, transfused blood may be lost before having therapeutic impact. This explains why transfusion may fail to raise hemoglobin effectively.[13] Any situation resulting in acute blood loss and hemodynamic instability is a potential indication of a massive transfusion.[8] Hypersplenism is a common disorder characterized by an enlarged spleen which causes rapid and premature destruction of blood cells. The spleen is the largest lymphoid organ, and is an important site for the production of antibodies. Antigens unprocessed by the liver may enter the periphery of splenic lymphoid follicles (splenic nodules), where reactions of immature lymphocytes and plasma cells occur after antigen stimulation, thus producing antibodies, which may destroy blood cells and it can cause hemoglobin not to rise as expected after a blood transfusion.[13] In chronic kidney disease, the primary mechanisms behind anemia of CKD, including end-stage renal disease (ESRD), involve decreased erythropoietin production (the hormone responsible for stimulating RBC production), decreased gastrointestinal iron absorption due to chronic inflammation, and a decreased lifespan of red blood cells (RBCs). Before the therapeutic options currently available, the mainstay of treatment was blood transfusion, which came with numerous complications, including infections, hemosiderosis, fluid overload, and transfusion reactions. Blood transfusions can temporarily increase hemoglobin, but without erythropoietin the production of new blood cells remains low, which can cause blood transfusions to be ineffective.[4]

In this case, the patient had normochromic macrocytic anemia and received a blood transfusion, but there was no significant increase in hemoglobin due to active bleeding. After treating the cause of the bleeding, another blood transfusion was administered, resulting in an increase in hemoglobin to 10 g/dl.

CONCLUSION

In this case, ineffective blood transfusion was not caused by a hemolytic process but rather by upper gastrointestinal bleeding. Transfuse 1 unit of packed red cells will typically increase the hemoglobin value by 1 g/dl and hematocrit by 3%. Follow up by checking post-transfusion hemoglobin. Therefore, before administering transfusion, it is essential to evaluate and address underlying causes such as active bleeding that may render transfusion ineffective also administer therapy to the source of bleeding.

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