In the Shadows of Pancytopenia: A Tale of Iron and Myelodysplasia in End-Stage Renal Strife

Meher Nigar Alam[1], Md. Abdul Wahab Khan[2], Ahmmad Shamir Shawrov[3]

[1.] Senior Medical Officer, Nephrology, Bangladesh Specialized Hospital.
[2.] Consultant, Nephrology, Bangladesh Specialized Hospital.
[3.] Registrar, Nephrology, Bangladesh Specialized Hospital.

Case Report

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*Corresponding Author:

Dr. Meher Nigar Alam
Senior Medical Officer
Department of Nephrology
Bangladesh Specialized Hospital. 21, Mirpur Road, Dhaka 1207, Bangladesh.
E-mail: mehernigar83@gmail.com

ABSTRACT:

Anemia is a prevalent complication in patients with end-stage renal failure undergoing maintenance hemodialysis, typically managed with recombinant erythropoietin therapy. However, when accompanied by Hemoglobin E (Hb E) trait, these patients often require regular blood transfusions to maintain hemoglobin levels within an acceptable range. This repeated exposure to iron-rich blood products can lead to iron overload, increasing the risk of organ damage and complications, including bone marrow suppression and the development of pancytopenia. In patients with Hb E trait receiving hemodialysis, the potential for iron accumulation is further amplified, complicating their clinical management.

The interplay between iron overload, renal function, and the underlying hematologic condition presents a diagnostic challenge. Excess iron can exert toxic effects on the bone marrow, disrupting effective hematopoiesis and contributing to the development of Myelodysplastic syndrome. Accurate diagnosis in resource-limited settings frequently requires invasive procedures, while effective monitoring of iron overload remains crucial for patient management in underserved regions of the developing world.

By integrating the expertise of various specialists-such as hematologists, gastroenterologists, and dietitians-healthcare teams can provide comprehensive care tailored to each patient's unique needs.

Key words: Heamoglobin E trait, Secondary Haemochromatosis, Pancytopenia, Haemodialysis, Myelodysplastic Syndrome.

INTRODUCTION:

Hemoglobin E (HbE) is a prevalent structural hemoglobin variant predominantly found among populations in Southeast Asia, India, Sri Lanka, and Bangladesh. As a β-hemoglobin variant, HbE is produced at a reduced rate, resulting in a phenotype similar to mild β-thalassemia. Individuals with HbE disease typically do not produce hemoglobin A and may exhibit mild anemia, with only a small percentage requiring blood transfusions.[1]

In patients with concomitant kidney disease, the situation can be exacerbated, leading to significant renal anemia that necessitates regular treatment with iron supplementation and/or blood transfusions, often in conjunction with recombinant human erythropoietin. However, excessive blood transfusions and inappropriate intravenous iron therapy can precipitate secondary hemochromatosis, which poses a risk of multi-organ damage due to iron overload.[3] Notably, iron deposition in the bone marrow can potentially contribute to the development of myelodysplastic syndromes (MDS).[4,5]

In this case report, we present a patient with multiple comorbidities, highlighting the intricate relationship between renal anemia, iron overload, pancytopenia and myelodysplastic changes in the bone marrow. This case illustrates the complexity of these conditions and their associated complications, emphasizing the importance of a comprehensive and multidisciplinary approach strategies in affected individuals.

CASE REPORT:

Patient Profile:

A 31-year-old female with a history of systemic hypertension, Hemoglobin E trait, and end-stage renal disease, currently on dialysis for five years, was admitted to a tertiary care hospital in Bangladesh.

Presenting Complaints:

The patient was admitted to the hospital with complaints of significantly elevated blood pressure and increasing abdominal distension over the past two days. The abdominal distension has been associated with mild discomfort but no significant pain. She denied nausea, vomiting, or changes in bowel habits.

Initial Physical Findings:

On admission, the patient was alert but distressed due to headache; appeared slightly pale. She had Blood Pressure: 200/110 mmHg; Heart Rate: 92 beats per minute; Respiratory Rate:18 breaths per minute; Temperature: 98.6° F; Oxygen Saturation: 98% on room air; Weight: 70 kg (previous weight not documented).

Her abdomen was distended but soft to palpation; mild hepatomegaly and splenomegaly were noted on palpation in conjunction with moderate ascites. Bowel sounds were present; no guarding or rebound tenderness were observed. However, auscultation of her chest revealed clear breath sounds with bilateral basal crackles. There was also mild bilateral pedal edema. All other systemic examinations were normal.

Past Medical History:

- Systemic hypertension diagnosed at age 25, poorly controlled.
- End-stage renal disease secondary to hypertension, on regular hemodialysis (thrice weekly) – for last 5 years.
- Hemoglobin E trait – requires blood transfusion once or twice every month for last 2 years.
- No history of diabetes or other significant medical conditions.

On further exploration of her medical history, it was revealed that the patient had a childhood history of severe lower limb purpura and acute kidney injury, and was suspected as a case of Henoch-Schonlein purpura based on clinical features and deteriorated renal function in a remote area of Bangladesh. During that course of illness an ultrasonogram also revealed her congenital renal deformities, with one kidney being smaller than the other. While she recovered from the acute conditions, the combination of her congenital kidney anomalies and Henoch-Schonlein purpura are likely to have contributed to her subsequent renal failure. In 2019, she was admitted in a local hospital with sepsis and was discovered to have severe renal impairment, leading to her ongoing maintenance dialysis.

Medications:

- Antihypertensives (specific medications not specified)
- Erythropoiesis-stimulating agents for anemia management
- Phosphate binders and vitamin D analogs

Laboratory Findings:

On admission, her laboratory reports revealed significant pancytopenia: hemoglobin level at 5.1 g/dL (RBC 1.85 million/μL), white blood cell count at 2.84 K/μL, and platelet count at 60 K/μL. She had hyperkalaemia (K – 6.1 mmol/L) and with raised urea and creatinine.

Her liver function tests indicated a slight elevation in serum bilirubin 1.4 mg/dL, gamma-glutamyl transferase (GGT) 78 U/L, and serum glutamate-pyruvate transaminase (SGPT) 40 U/L.

An abdominal ultrasound showed mild hepatomegaly with a non-homogeneous echotexture, grade 2 splenomegaly, and gross ascites.

However, she was found to be Hepatitis C virus positive.

An echocardiogram indicated dilated cardiomyopathy with valvular dysfunction.

Additionally, her serum ferritin level was markedly elevated at 23,214 ng/mL (6.24-137), with slightly raised serum iron 180.3 μg/dl (37-170) and normal total iron-binding capacity (TIBC) of 309.3 μg/dl (265-497).

Further Evaluations:

To investigate her pancytopenia, a peripheral blood film study was conducted, which demonstrated red blood cells with anisochromia and anisocytosis, including normocytes, microcytes, teardrop cells, and target cells. The white blood cells and platelets appeared mature with normal morphology but were reduced in number.

Given the combination of splenomegaly, hyperbilirubinemia, and pancytopenia, additional workup was performed. This revealed a negative Coombs test, a reticulocyte counts of ≤ 1.0%, and a negative HIV screen. Lactate dehydrogenase (LDH) was measured at 290 U/L, while folate and vitamin B12 levels were normal.

Diagnosis:

After excluding all possible causes, the findings strongly suggested that her pancytopenia was due to progressive marrow failure likely a consequence of repeated blood transfusions.

A subsequent bone marrow study revealed scanty marrow particles; however, many cellular elements were present, predominantly myelocytes, with occasional myeloblasts. The report suggested the possibility of myelodysplasia (MDS).

Treatment Plan:

A multidisciplinary approach was initiated, involving nephrologists, hematologists, and gastroenterologists. The patient was treated with intravenous iron chelating agents (deferoxamine) after each session of hemodialysis, intravenous synthetic filgrastim (a colony-stimulating factor) for pancytopenia, and an antiviral regimen consisting of a combination tablet containing sofosbuvir and velpatasvir for hepatitis C.

Outcome:

Following these treatments, her serum ferritin levels decreased, and her blood cell counts improved.

Discharge Instructions:

Upon discharge, the patient was advised to continue her iron chelation therapy, maintain regular blood workup to monitor for any recurrence of pancytopenia, and seek guidance of the multidisciplinary team regarding further bone marrow stimulating agents as needed.

DISCUSSION:

Pancytopenia, characterized by the simultaneous reduction of red blood cells, white blood cells, and platelets, presents a multifactorial challenge in patients with end-stage renal failure (ESRF).[2] This case underscores the complexities that arise in patients with multiple comorbidities, particularly when the treatment for one condition inadvertently leads to the development of another. The patient's history, beginning with childhood Henoch-Schonlein purpura and culminating in chronic renal failure requiring maintenance hemodialysis, illustrates how interconnected health issues can evolve.

In ESRF, several factors contribute to the development of pancytopenia. Uremic toxins accumulate, leading to bone marrow suppression and ineffective hematopoiesis.[2] Additionally, chronic renal failure affects the production of erythropoietin, resulting in anemia. The presence of myelodysplastic changes in the bone marrow further complicates the clinical picture, as these changes indicate a potential progression towards acute myeloid leukemia (AML).[5] This case exemplifies how ESRF can precipitate not only hematological complications but also a more complex hematological disorder.

Iron overload is prevalent among patients receiving regular blood transfusions, a common practice in managing anemia associated with ESRF.[3] In the developing world with limited health facilities, patients may have limited access to iron chelation therapies and the risk of iron accumulation is heightened.[6] The deposition of excess iron in vital organs, such as the heart and liver, not only contributed to dilated cardiomyopathy and hepatic impairment but also complicated her clinical picture with the acquisition of hepatitis C virus infection.[7] This highlights a concerning interaction, as iron overload can exacerbate HCV replication, further aggravating liver damage. The challenge lies in balancing the management of anemia and iron overload, particularly when resources for comprehensive care are scarce.

The myelodysplastic features observed in this patient raise concerns regarding the potential for progression to more severe hematological conditions.[4,5] Myelodysplastic syndromes (MDS) are known to be associated with increased morbidity and mortality, and in resource-limited settings, the ability to monitor for such changes may be restricted. This highlights the need for enhanced awareness and training among healthcare providers in these areas to identify early signs of MDS and implement appropriate management strategies.

Furthermore, strategies such as providing low-cost or generic medications and advocating for policies that improve access to essential treatments can significantly impact patient outcomes in these economically constrained settings.

CONCLUSION:

The interplay of chronic kidney disease, repeated blood transfusions, and iron overload presents a multifaceted challenge in the management of pancytopenia. The findings of this case emphasize the critical need for healthcare professionals to implement routine monitoring for iron overload in patients undergoing frequent blood transfusions. Addressing the underlying causes of iron accumulation is critical for improving patient outcomes.

Iron chelation therapy is crucial in preventing further complications from iron overload; however, access to these treatments can be a significant barrier. Therefore, community health initiatives that focus on education about the importance of monitoring iron levels and promoting adherence to transfusion guidelines are vital.

Early detection through appropriate testing can prevent the serious complications associated with iron accumulation, thereby safeguarding organ function and improving overall patient outcomes. Timely interventions, including the potential use of iron chelation therapy, are essential in mitigating the adverse effects of excess iron retention in the body. This case serves as a call to action for enhanced vigilance and a multidisciplinary approach in the management of patients with complex medical histories.

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