A Case of Refractory Anemia in Patient of Chronic Kidney Disease and the Challenges in its Management

Komal Gade1*, Charulata Londhe2, Sangeeta Pednekar3, Dharmendra Pandey4, Namita Padwal5, Ashish Agrwal6

Received: 17 April 2023; Accepted: 08 May 2023

Abstract

Anemia is a common complication of chronic kidney disease (CKD) that has been classically attributed to inadequate production of endogenous erythropoietin.1 Though there are many other common causes of refractory anemia in CKD like iron deficiency, vitamin B12, and folic acid deficiency, noncompliance to dialysis and erythropoietin therapy rare causes like blood loss, bone marrow failure, infections causing aplastic crisis like CMV, parvovirus B19 should be ruled out. Parvovirus has an extreme tropism for erythroid cells and is an uncommon cause of anemia in patients with CKD on maintenance dialysis (MHD) and on erythropoietin.7 Here we are reporting a rare case of refractory anemia in a patient of CKD on MHD secondary to parvovirus-related aplastic crisis.

Introduction

In immunocompetent hosts acute parvovirus B19 infection is mild and associated with transient anemia, arthritis, and rash.3 Patients with renal failure on dialysis have disruptions in their immune system due to the immunosuppressive effect of uremia. Therefore dialysis patients have increased susceptibility to acute and chronic anemia after B19 infection. Moreover, B19 infection can induce aplastic crisis in these patients.4

Case Report

A 45-year-old female with hypertension and chronic kidney disease (CKD) on regular maintenance hemodialysis for the last 10 years was admitted with complaints of generalized weakness, easy fatigability, and dyspnea on exertion. On examination, there was pallor without icterus and pedal edema. All other systemic examinations were within normal limits.

Laboratory tests revealed hemoglobin 4.9 gm/dL with total leucocytes of 3600 and platelets 35000 with mean corpuscular volume 92.2 fL, mean corpuscular hemoglobin concentration 28.2 pg. Peripheral smear showed anisocytosis with normochromic normocytic anemia. The reticulocyte count was 2.6 with a reticulocyte production index of 0.4. Iron studies were within normal limits. Biochemical analysis revealed creatinine of 5.5 with normal liver function tests. Serum B12, folic acid were within normal range.

Viral markers like human immunodeficiency virus, hepatitis B surface antigen, and hepatitis C virus were negative. Tests for dengue, hepatitis C virus were negative. Tests for f, hepatitis A, hepatitis E, and leptospirosis were negative.

Hematological parameters of the patient:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Admission</th>
<th>2 Weeks</th>
<th>1 Month</th>
<th>2 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>4.9</td>
<td>8.8</td>
<td>5.9</td>
<td>8</td>
</tr>
<tr>
<td>TLC</td>
<td>3600</td>
<td>4200</td>
<td>3400</td>
<td>4600</td>
</tr>
<tr>
<td>Platelets</td>
<td>35000</td>
<td>1.1 lac</td>
<td>1 lac</td>
<td>1.23 lac</td>
</tr>
</tbody>
</table>

The patient has been compliant with dialysis and erythropoietin treatment for the last 10 years and never received a blood transfusion in the past. During this admission, the patient received four units of packed red cell transfusions and was discharged on persistent request with hemoglobin of 8.8 gm/dL. She was advised for optimum compliance with dialysis and erythropoietin therapy. Around 1 month after discharge she was again readmitted with similar complaints with hemoglobin of 5.9 total leucocytes of 3400 and platelets of 1 lakh in spite of being on regular dialysis and proper erythropoietin therapy. Again she has transfused two units of packed red cells to buildup hemoglobin to 8 gm/dL. We did her bone marrow biopsy in view of pancytopenia which was suggestive of hypocellular bone marrow with suppressed erythroid lineage. In background knowledge of CKD being an immunocompromized state, we suspected aplastic crisis secondary to parvovirus B19 as a cause of refractory anemia in our patient. Her parvovirus polymerase chain reaction (PCR) was done which came positive.

The patient started on intravenous immunoglobulin therapy (IVIg) which was administered on alternate days after dialysis at a minimum infusion rate of 0.5 mL/kg/hour with frequent monitoring of pulse, blood pressure, oxygen saturation, and signs of fluid overload. However, after three doses of IVIg patient had dyspnea on exertion. On examination, there was pallor without icterus and pedal edema. CT brain venography was normal. The patient improved after control of BP. We terminated IVIg therapy after three doses.

Subsequently, her hemoglobin level was stabilized and no further drop was noted. After two months her hemoglobin was stable at 8 gm/dL.

Discussion

Parvovirus B19 is a small nonenveloped single-stranded DNA virus belonging to the Paroviridae family.2 This virus has severe manifestations in immunocompromised patients. Anemia is present in around 99% of patients of parvovirus B19 with immunocompromised state and is often associated with erythropoietin resistance. Parvovirus B19 (PVB19) infection should be suspected early in cases of anemia in immunocompromised patients, including transplant patients, and prompt evaluation should be initiated. Viral detection in clinical specimens is important for the diagnosis of PVB19 infection.

Causes of poor response to erythropoietin therapy in CKD patients:

<table>
<thead>
<tr>
<th>Common causes</th>
<th>Uncommon causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Iron deficiency</td>
<td>1. Blood loss</td>
</tr>
<tr>
<td>2. Infection</td>
<td>2. Bone marrow failure due to myelofibrosis</td>
</tr>
<tr>
<td>3. Inadequate dialysis</td>
<td>3. Aplastic crisis due to hyperparathyroidism</td>
</tr>
<tr>
<td>4. Vitamin B12 and folic acid deficiency</td>
<td></td>
</tr>
<tr>
<td>5. Poor compliance to erythropoietin therapy</td>
<td>6. Parvovirus B19, and HIV</td>
</tr>
</tbody>
</table>

1.6 Senior Resident; 2,4,5 Associate Professor; 3Professor, Department of General Medicine, Lokmanyaa Tilak Municipal Medical College and General Hospital Sion, Mumbai, Maharashtra, India; *Corresponding Author

Our patient presented with anemia inspite of erythropoietin therapy and regular dialysis. We suspected parvovirus B19 associated aplastic crisis as no other cause of anemia was found on laboratory work and her parvovirus B19 PCR came positive.

The IVIg is the mainstay therapy for PVB19-associated pure red cell aplasia, and it is a widely used regimen, with a total dose of 2 gm/kg over 2–5 days, although the daily dose and duration of therapy may vary according to centers.

Unfortunately, our patient could only receive three doses as she had IVIg-induced PRES which is a rare side effect of IVIg therapy but she responded IVIg well to treatment and currently not requiring any blood transfusion. IVIg also can cause anaphylaxis, volume overload, thromboembolism, and acute kidney injury. Hence IVIg should be administered cautiously specially in renal failure patients.

**Conclusion**

Anemia in CKD patients requires a thorough workup to ensure a correct diagnosis and therapeutic approach. Although anemia secondary to parvovirus B19 infection is uncommon it must be considered in the differential diagnosis of refractory anemia with resistance to erythropoietin therapy in CKD patients as they are immunocompromized hosts and prone to such infections. It responds to IVIg treatment very well.

**References**