Case Report

Erythrocytosis in patients taking long-term hemodialysis: A case series

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ABSTRACT

Anemia is one of the common findings and complications in patients with end-stage kidney disease (ESRD). Most patients need to take the therapies to control target hemoglobin level and these treatments can add to the high cost and adverse events in these patients. In our hemodialysis center, regular monitoring of hemoglobin was done for all regular hemodialysis patients and we found that two patients who have different etiologies of ESRD had high hemoglobin levels without the help of erythropoietin stimulating agents and blood transfusion. They had the duration of hemodialysis for more than 10 years and they were found to have acquired cystic kidney disease at the time of assessing the etiologies of erythrocytosis. There are few case reports and research about erythrocytosis due to acquired cystic kidney disease. Acquired cystic kidney disease is frequently found in patients with longer duration of dialysis and erythrocytosis is one of the beneficial consequences for chronic kidney disease patients. It can avoid the high cost of erythropoietin-stimulating agent and iron therapy, and their adverse events. Phlebotomy is an easy way to maintain the level of hemoglobin in such patients.

Key words: End-stage kidney disease, Erythrocytosis, Hemodialysis

Patients with chronic kidney disease (CKD) suffer from anemia due to impaired erythropoietin production. Therefore, erythrocytosis is an uncommon presentation in CKD and it is necessary to proceed with further investigation and management for etiologies [1]. Erythrocytosis is classified as primary and secondary. Etiologies of secondary erythrocytosis include tissue hypoxia or erythropoietin overproduction due to renal cysts, malignancy with ectopic erythropoietin production, and renal artery stenosis [2].

In this case series, we discuss the cases of patients with end-stage kidney disease (ESKD or ESRD) who presented with erythrocytosis after initiating hemodialysis.

CASE SERIES

In our hemodialysis center, we found a surprising and amazing finding in two out of 50 patients with ESRD on regular hemodialysis biweekly when we check hemoglobin level monthly in every hemodialysis patient. In these patients, hemoglobin level was maintained at above 11 g/dL without the help of the erythropoietin stimulating agent and iron therapy or blood transfusion. Hence, we proceeded with the required investigations to find out the etiologies of erythrocytosis in these patients. Informed consent was taken from these patients before proceeding with further investigations, treatment, and publishing this case series.

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Case 1

A 40-year-old female with ESRD secondary to djenkolism toxicity started to take hemodialysis therapy in 2008. She had hypertension and mineral bone disease due to CKD. Her hemoglobin level is shown in Fig. 1. She took erythropoietin-stimulating agent (ESA) injections till 2018. The other regular medications were nifedipine, carvedilol, and sevelamer. From 2018, ESA therapy was necessary to withhold due to increasing levels of hemoglobin above 11 g/dL. Due to the gradually rising hemoglobin level, investigations were done to find out the underlying cause of erythrocytosis. In CP auto, only polycythemia was found and white blood cell (WBC) (total and differential count) and platelet count were normal. Polycythemia vera was excluded after consultation with a hematologist. Iron study showed transferrin saturation (TSAT) (78%) and serum ferritin (>2000 ng/mL) in case 1. Chest X-ray did not reveal any pulmonary parenchymal abnormalities. Kidney ultrasound (USG) showed multiple cysts in both small-sized kidneys (>10 in number with multiple variable sizes) and the impression was acquired cystic kidney disease due to dialysis. There were no features of renal cell carcinoma in USG. After excluding primary erythrocytosis and

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causes of secondary erythrocytosis, a diagnosis of acquired cystic kidney disease was made due to small-sized kidneys with multiple variable-sized cysts. Therefore, regular monitoring of hemoglobin was done monthly and 1 time phlebotomy was done in 2023 because of the hemoglobin level was at 18 g/dL. Regular cardiac assessment and kidney USG were done for 3 months. There was no cerebrovascular accident apart from cardiomegaly due to hypertension and CKD. Although her hemoglobin level was above 11 g/dL, there were no vascular complications. At follow-up, she was feeling better than before and took regular hemodialysis and outpatient visits.

Case 2

The second one is a 56-year-old male with ESRD due to hypertension. The man started to take hemodialysis therapy in 2008. He took a blood transfusion of about 10 units for upper gastrointestinal bleeding due to duodenal ulcer bleeding in 2019 and took ESA injections from 2012 to 2018. The patient's regular medications were nifedipine, methyldopa, allopurinol, aspilet, atorvastatin, and sevelamer. From 2019, hemoglobin levels started to rise gradually without receiving the erythropoietin-stimulating agents or blood transfusion (Fig. 2). Investigations to find out the underlying cause of erythrocytosis showed only polycythemia with normal WBC (total and differential count) and platelet count was found. Polycythemia vera was excluded after consultation with a hematologist. Iron study showed TSAT (13%) and serum ferritin (208 ng/mL). Chest X-ray did not reveal any pulmonary parenchymal abnormalities. Kidney USG showed multiple cysts in both small-sized kidneys (>10 in number with multiple variable sizes) and the impression was acquired cystic kidney disease due to dialysis. There were no features of renal cell carcinoma in USG. After excluding primary erythrocytosis and causes of secondary erythrocytosis, a diagnosis of acquired cystic kidney disease was made due to small-sized kidneys with multiple variable-sized cysts. His hemoglobin level is between 11 g/dL and 15 g/dL. During follow-up from 2008 to 2024, the patients did not develop any vascular complications. He is still on scheduled dialysis sessions with regular cardiac assessment and hemoglobin monitoring.

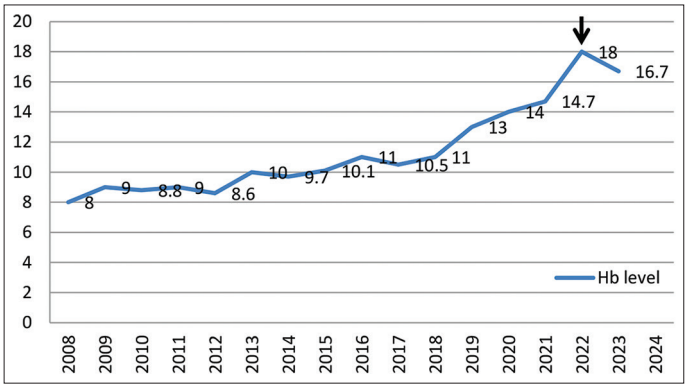

Figure 1: Hemoglobin level of 40-year-old lady (case 1)

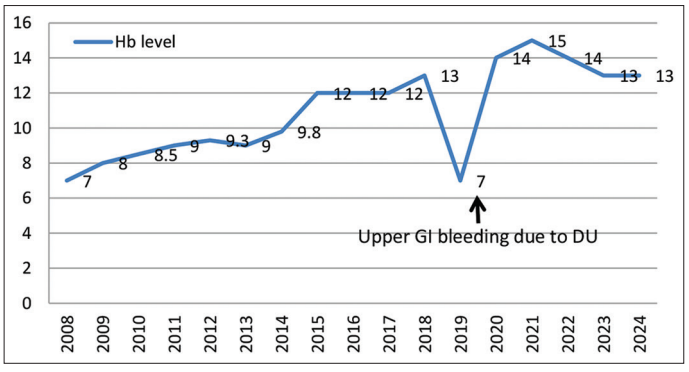

Figure 2: Hemoglobin level of 56-year-old man (case 2)

DISCUSSION

Erythrocytosis is uncommon in chronic renal failure on hemodialysis because almost all patients require high-cost treatments for anemia in ESRD. In contrast, this uncommon condition helps these two patients to spend less on treatment costs in comparison with other patients on regular hemodialysis. When we review the etiologies of erythrocytosis in patients on hemodialysis, there are many causes of it (Table 1) [3].

Multiple and bilateral renal cysts are frequently found in CKD (especially in patients on dialysis) [4]. In dialysis patients, the longer duration of dialysis increases the incidence of acquired cystic disease. Narasimhan *et al*. studied 130 patients with ESRD and they found that the incidence of multiple cysts was increased in those on dialysis than in those with chronic renal failure (22% vs. 7%). The number of renal cysts increased progressively with the longer duration of dialysis (no cysts in 15 months, one to three cysts in 28 months, and more than 10 cysts in 49 months) [5].

Table 1: Mechanisms of erythrocytosis [3]

Mechanism	Example
Excess erythropoietin production	• Exogenous erythropoietin production by tumors • Hepatocellular carcinoma • Renal cell carcinoma • Hemangioblastoma Gastric cancer • Exogenous erythropoietin production from the liver • Primary erythrocytosis in polycythemia vera • Erythropoietin production by the lining epithelium of renal cysts
Chronic hypoxia through hypoxia-inducible factor 1	• Right-to-left cardiac shunts • Obstructive sleep apnea • Chronic pulmonary disease • High altitudes • Chronic carbon monoxide poisoning • Hemoglobinopathies
Activation of the renin-angiotensin system	• Following renal transplant • Renal artery stenosis • Chronic severe hypotension
Hematopoietic growth factors (IGF-1, sSCF)	• Following renal transplant
Endogenous androgens	• Following renal transplant

IGF-1: Insulin-like growth factor-1, sSCF: Serum-soluble stem cell factor

When the duration of dialysis is more than 10 years, renal cysts are detected in 50–80% of patients [6]. The risk of acquired cystic kidney disease is high in men than women and in African Americans than women or Caucasians [4]. In patients on hemodialysis, acquired cystic disease of the kidney (ACDK) has been described as a complication since 1977. The underlying pathogenesis is unclear and there are no associated cysts in other organs. Like in the cysts in autosomal dominant polycystic kidney disease, most of the cysts in ACDK are the origin in the proximal tubules [7]. Despite polycythemia being reported in patients with ACDK, the association of the development of cysts with the hemoglobin concentration is unclear. However, there is a significant correlation between the number of cysts and plasm Epoetin level [8].

Although there are many options for treatment in post-transplant erythrocytosis, it is poorly studied for treatment for erythrocytosis in dialysis patients. In post-transplant erythrocytosis, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are preferred and their action on the erythrocytosis is unclear. However, the inhibition of the renin-angiotensin system which reduces kidney hypoxia, might be the answer [9]. Other options in the treatment of post-transplant erythrocytosis are theophylline, antiproliferative agents, and intermittent phlebotomies. There is a report on controlling erythrocytosis in a dialysis patient with theophylline, an adenosine antagonist. The underlying mechanism might be the role of adenosine in the release of erythropoietin and the response of bone marrow to erythropoietin [10]. However, theophylline can give a high toxicity profile because of the narrow therapeutic index. Therefore, intermittent phlebotomy will be an effective treatment in dialysis patients but the patients need to monitor the features of iron deficiency [11]. It is unknown the target hemoglobin level in these patients. Many practitioners maintain the hemoglobin level at 11–13 mg/dL which is the same target in patients taking the erythropoietin stimulating agents [12].

Although erythrocytosis is one of the beneficial effects of acquired cystic kidney disease, there are vascular events as the consequences of erythrocytosis. Vascular complications are reported in Bender and Piraino's study. In this study, a patient presented with stroke and another patient with multiple vascular complications including splenic infarction, left popliteal artery occlusion, and stroke [13]. Since vascular complications are common in ESRD, erythrocytosis might make ESRD patients prone to develop vascular complications. Therefore, it needs to control aggressively the level of hemoglobin and hematocrit at a beneficial level.

Our country, Myanmar, is a developing country and we have limitations in diagnosing the definitive etiologies of erythrocytosis in these patients. It is necessary to measure the erythropoietin level in patients with erythrocytosis to find out the association between the erythropoietin level and cystic kidney disease. Since the erythropoietin level is not available in our country and it is expensive, we cannot assess the association between the erythropoietin level and cystic kidney disease in these patients. In patients on dialysis, phlebotomy is a safe and easy treatment to control the hemoglobin level but it is necessary to do much prospective research for the beneficial target of hemoglobin level in such patients.

CONCLUSION

Erythrocytosis in ESRD patients is a rare presentation. Acquired cystic kidney disease has been found to improve in anemia of patients on dialysis. It can have a beneficial effect on the patients on dialysis with the freedom from high cost due to erythropoietin stimulating agent and iron. Acquired cystic kidney disease is frequently found in patients on longer duration of dialysis and can effectively raise the levels of erythropoietin and hemoglobin.

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