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A Case Report

Life threatening anemia (hemoglobin of 1.4g/dl) secondary to severe renal failure: management in a resource-constrained setting.

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Abstract-

Anemia is a common finding in patients with chronic kidney disease and its prevalence varies with the degree of renal dysfunction, with a higher prevalence as renal function worsens. It has been associated with increased morbidity, cardiovascular and all-cause mortality. We present a 33-year-old man who presented to the emergency department for the first time with bilateral leg swelling and shortness of breath and was found to have life-threatening anemia with hemoglobin of 1.4g/dl, metabolic acidosis, hyperkalemia and severe renal impairment (blood urea nitrogen of 401.4mg/dl and creatinine of 47.6mg/dl). He was admitted; had emergent hemodialysis with transfusion of packed red blood cells and was eventually discharged home to continue follow up on an outpatient basis.

Keywords: anemia, chronic kidney disease, hyperkalemia, late presentation

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Introduction

The National Kidney Foundation defines anemia as a hemoglobin level less than 13.5 g/dl in men and 12.0 g/dl in women and life-threatening anemia as hemoglobin level < 6.5g/dl(1). Anemia occurs early in the development of kidney disease and worsens with declining kidney function and is almost invariably present in patients with end-stage kidney disease(2), however, a hemoglobin value less than 2g/dl in the setting of severe renal dysfunction is a rare finding.

Unfortunately, there are still many barriers to the management of patients in resource- constrained environments including late presentation, limited health care infrastructure and insurance(3). We highlight a young patient with delayed presentation of chronic kidney disease

with the lowest hemoglobin and highest creatinine level recorded so far in our practice.

Case Presentation

A 33-year-old man presented to the emergency department with complaints of recurrent bilateral leg swelling of five months, generalized weakness and worsening breathlessness of two months' duration. Bilateral leg swelling was insidious in onset, initially recurrent, however became persistent in the two months preceding his presentation, and progressively worsened to involve the thighs. He endorsed a reduction in urine output and frothiness of urine, two-pillow orthopnea, paroxysmal nocturnal dyspnea, dry cough, palpitations, intermittent upper abdominal pain and hiccups. He had no facial or abdominal swelling, vomiting, change in bowel habits, melena, hematochezia, weight loss, arthralgia, joint swelling, or skin changes as well as no preceding history of sore throat or skin rash. There was no history of polyuria, polyphagia, polydipsia or lower urinary tract symptoms. He had no history of chronic use of non-steroidal anti-inflammatory medications or other over-the-counter medications.

He had a history of Guillain-Barre syndrome 16years earlier and made a full recovery, however, his blood pressure was noted to have been persistently elevated at that time but he never followed up on an outpatient basis for this for further evaluation or treatment. He had no prior history of sickle cell disease, blood transfusions or a hematopoietic disorder.

Clinical examination revealed a conscious but lethargic young man in obvious respiratory distress, who was markedly pale and had bilateral pitting pedal edema up to the knees with asterixis. He also had tachycardia of 124bpm, tachypnea of 32cpm with an oxygen saturation of 89% on room air, and bibasilar fine crackles. His blood pressure was elevated and his apex beat was located at the 6^{th} left intercostal space, lateral to the mid clavicular line and the 1^{st}, 2^{nd} and 3^{rd} heart sounds with a hemic murmur were heard. He had epigastric tenderness and digital rectal examination was negative for melena.

Investigations revealed severe renal impairment (blood urea and nitrogen of 401.4mg/dl and creatinine of 47.6mg/dl) with associated severe anemia (hemoglobin concentration of 1.4g/dl with mean corpuscular volume of 78fL), metabolic acidosis (serum bicarbonate < 10mmol/L) and hyperkalemia (serum potassium of 7.1mmol/l). Abdominopelvic ultrasound revealed bilateral small kidneys with the right kidney measuring 8.1 x 4.9 cm and the left measuring 8.8 x 5.9 cm; they had increased parenchymal echogenicity equal to that of the liver with loss of corticomedullary differentiation. A conclusion of bilaterally shrunken kidneys with renal parenchymal disease grade II was made. Chest radiograph revealed cardiomegaly. Urinalysis showed 2+ protein. Serology for Human immunodeficiency virus, Hepatitis B surface antigen and Hepatitis C Virus were negative. Spot urine for albumin-creatinine ratio, electrocardiogram, echocardiogram, fasting lipid profile, reticulocyte count, peripheral blood film, iron studies (serum ferritin and transferrin saturation) and stool for ova and parasite as well as occult blood and several other investigations were requested but could not be done as the patient had financial constraints.

A diagnosis of acute on chronic kidney disease of unclear etiology complicated by severe anemia, uremia, severe metabolic acidosis, hyperkalemia and volume overload was made. He was admitted, started on oxygen supplementation, received temporizing measures for hyperkalemia; and was planned for emergent hemodialysis. He subsequently had 3 sessions of hemodialysis, was transfused with 7 units of packed red blood cells, started on anti-hypertensive medications, intravenous iron and erythropoietin, and was discharged home after eight days to continue follow up on an outpatient basis. *Table 1* shows the trend of his laboratory results while hospitalized. He attended follow up visits for a short while but was later unfortunately lost to follow-up due to inability to afford the cost of further evaluation and hemodialysis.

Table 1: Serial Complete blood count and Basic metabolic panel done during admission

Complete blood count						
Date	PCV (%)	Hb (g/dl)	PLT ($x10^9$/L)	WBC ($x10^9$/L)	Neutrophils (%)	Lymphocytes (%)
DOA	4.6	1.4	228	7.89	86.1	7.7
2DPA	15.3	5.3	196	5.27	61.7	33.2
4DPA	20.4	N/A	N/A	N/A	N/A	N/A
7DPA	22.8	N/A	N/A	N/A	N/A	N/A

Electrolytes, Urea and Creatinine						
Date	Na (mmol/L)	K (mmol/L)	HCO_3 (mmol/L)	Cl (mmol/L)	Urea (mg/dL)	Cr (mg/dL)
DOA	128	7.07	<10	100	401.4	47.6
2DPA	126	4.94	11	107	214.8	31.9
4DPA	130	5.66	16	100	150.6	21.4
7DPA	139	5.38	20	103	114	11.9

PCV=Packed cell volume, Hb=Hemoglobin, PLT=Platelet, WBC=White blood cell count, Na=Sodium, K=Potassium, HCO_3=Bicarbonate, Cl=Chloride, Cr=Creatinine, DOA = Day of admission, DPA = Days post admission.

Discussion

To our knowledge, this is the lowest reported hemoglobin level in a patient with concomitant renal failure and one of a few cases worldwide. Most cases that reported hemoglobin levels <2g/dl have been in the setting of menorrhagia and malignancies. A case series described three females with uterine fibroids and menorrhagia who had hemoglobin levels <2g/dl, the lowest of which was 1.1g/dl(4). Crawford et al discussed a female with hemoglobin of 1.9g/dl with severe iron deficiency and endometrial cancer(5). Three different studies reported hemoglobin values of 1.7g/dl, 1.6g/dl and 1.2g/dl in young females with menorrhagia, two of whom were found to have uterine leiomyoma(6–8). Schmitt et al reported a young male with hemoglobin of 1.8g/dl who was found to have colon cancer(9), while another study reported a young female who was eventually diagnosed with coeliac disease who presented with a hemoglobin of 1.7g/dl(10). Kyvetos et al discussed a 97-year old patient with a hemoglobin of 1.7g/dl presumed to be secondary to chronic gastrointestinal bleeding(11).

Many studies have demonstrated an association between the hemoglobin concentration and kidney function. The Third National Health and Nutrition Examination Survey (NHANES III), assessed more than 15,000 people in the general U.S. population between 1988 and 1994 and found an inverse relationship between GFR < 60 ml/min/1.73 m2 and prevalence of anemia. Using estimated GFR, the prevalence of anemia, defined as a hemoglobin concentration < 12 g/dl in men and < 11 g/dl in women, increased from 1% in patients with a GFR of 60 ml/min per 1.73 m^2 to 9% at a GFR rate of 30 ml/min/1.73 m^2 and to 33% for men and 67% for women at a GFR of 15 ml/ min/1.73 m^2.(2,12)

In a study that assessed the longitudinal relationship between hematocrit and estimated glomerular filtration rate (eGFR) in African-Americans, the relationship differed based on eGFR and was steeper when baseline eGFR was < 45ml/min/1.73m^2. The absolute reduction in hematocrit for every 10ml/min/1.73m^2 decrease in eGFR was -0.5%, -1.3% and -3.7% respectively for baseline eGFR of 60, 40 and 20ml/min/1.73m^2. Other factors that were associated with higher hematocrit reduction per unit decrease in longitudinal eGFR were male sex, younger age (< 65years) and higher baseline proteinuria (protein creatinine ratio > 0.22)(13). Our patient was a young black male with proteinuria although we were unable to quantify his proteinuria.

Our patient's baseline creatinine and hemoglobin values were unknown so it was difficult to determine the rate of decline of his hemoglobin compared to his eGFR, however his symptoms had been ongoing for 5 months, and he had a history of history of long-standing hypertension which was untreated as well as proteinuria and bilateral shrunken kidneys on ultrasound all of which supported a diagnosis of underlying chronic kidney disease (CKD) which could be related to hypertensive CKD but would definitely have benefited from further evaluation of other causes of CKD especially considering his presentation with life-threatening anemia. We were however unable to do tests for further evaluation as the patient was an unemployed graduate with poor social support, without health insurance and was unable to afford the cost of a comprehensive evaluation. Fortunately, his hemoglobin responded appropriately to blood transfusion, erythropoiesis-stimulating agents and IV iron sucrose so we presume it was largely in part secondary to chronic kidney disease. Late presentation in patients with CKD appears to be a global problem although it generally appears to occur more commonly in resource constrained settings than in higher-income regions(14–16). In addition, while in western countries, late presentation appears to be mainly as a result of delayed referral to the nephrologist, in resource-constrained environments, factors such as lack of insurance, lower socioeconomic status and educational level, limited

healthcare infrastructure, poor health seeking behavior as well as scarcity of trained physicians play a major role(3).

The major mechanism for the development of anemia in CKD is the reduced production of erythropoietin from the kidney(1). Iron deficiency or decreased availability, caused mainly by increased levels of hepcidin, due to inflammation accompanying chronic uremia, is another important mechanism(17). Additionally, folate and vitamin B12 deficiency, due to malnutrition and chronic inflammation result in increased red blood cells and immature erythroblasts apoptosis(1). Other factors include platelet dysfunction leading to an increased risk of bleeding, shortened red cell survival time, and hemolysis, as well as bone marrow suppression due to the accumulation of uremic toxins. In patients receiving dialysis and especially those on hemodialysis, chronic blood loss resulting from frequent phlebotomy for laboratory studies and loss of blood in the dialysis tubing and dialyzer after each hemodialysis treatment may also play a role in decreasing hemoglobin values(18).

Anemia in CKD patients is associated with poor quality of life, increased hospital admissions, progression of kidney disease, and increased mortality. It leads to poor quality of life by reducing energy levels, physical capacity and well-being as well as reducing neurocognitive function(19,20). Anemia induces adaptive cardiovascular mechanisms to maintain tissue oxygen supply and this leads to development of left ventricular hypertrophy, left ventricular dilation, and myocardial ischemia, which are risk factors for cardiovascular disease and death(20). Our patient did have cardiomegaly on physical examination as well as on the chest radiograph although he was unable to afford an echocardiogram to further evaluate his cardiac function. The early identification and treatment of anemia is therefore of utmost importance as it has been shown to attenuate the loss of kidney function and thus progression to end stage renal disease(21).

Conclusion

This case highlights the lowest hemoglobin level reported in the setting of severe renal dysfunction. Patients with life-threatening anemia in this setting would also benefit from extensive evaluation to exclude other ominous causes of anemia including malignancy, however this could not be done in our patient due to resource-constraints.

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ITS, LCC and BTB drafted, edited and revised the manuscript. The authors participated in the care of the patient. All authors approved the submitted manuscript

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