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Case report

Renal cell carcinoma as a cause of iron deficiency anemia

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KEYWORDS
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Abstract
A case of a 66-years-old male with iron deficiency anemia for more than 16 years, refractory to management with iron therapy is reported. Fecal occult blood test done several times was found to be negative. Upper and lower endoscopy revealed no source of bleeding. Capsule enterscopy showed no vascular malformations in the jejunum and ileum. The patient was managed with repeated blood transfusions. Abdominal ultrasound followed by CT scan abdomen revealed right renal soft tissue lesion. A CT-guided biopsy was then taken; the histopathology revealed a clear cell renal cell carcinoma. Right radical nephrectomy was done; the patient's hemoglobin showed a dramatic increase to 14 g/dL within one month. The dramatic response of the anemia to surgery mandates considering renal cell carcinoma in the workup of the possible causes of iron deficiency anemia. Only one similar case has been previously reported.

Introduction

Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults and represents approximately 80% of renal neoplasms [1]. It is described as being among the most lethal of all the urological cancers [2]. It is a collection of different types of neoplasms, each derived from the various parts of the nephron (epithelium or renal tubules) and possessing distinct genetic characteristics, histological features, and to some extent, clinical phenotypes [9]. Historically, medical practitioners expected a person to present with classic triad [3] is hematuria, flank pain, and an abdominal mass, similar to bloating but larger. It is now known that this classic triad of symptoms only occurs in 10–15% of cases, and is usually indicative that RCC is in an advanced stage [3]. Other signs and symptom may include [4]; malaise, weight loss and/or loss of appetite, erythrocytosis due to increased erythropoietin secretion [4], varicocele, which is seen in males as an enlargement of the tissue at the testicle (more often the left testicle) [4] hypertension resulting from secretion of renin by the tumor [5]; hypercalcemia, which is [6]; sleep disturbance or night sweats [7]; recurrent fevers [7]; and chronic fatigue [8], anemia resulting from depression of erythropoietin [4]. Today, RCC is often asymptomatic (meaning little to no symptoms) and is generally detected incidentally when a person is being examined for other

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ailments [4]. Although association with anemia is reported in one third of patients with renal cell carcinoma. Initial treatment is most commonly a radical or partial nephrectomy and remains the mainstay of curative treatment [10]. Considering the paucity of data in the literature concerning the rare presentation with iron deficiency anemia, we reported our experience with a patient diagnosed as renal cell carcinoma, incidentally after long journey of iron therapy.

Case report

A 66 years old male who is a known case of type-II diabetes diagnosed in 1999 as reported. He is on regular treatment with metformin 850 mg twice daily and Gliz 2 mg per day. The patient gave history of recurrent anemia since 1962, which was diagnosed as iron deficiency anemia based on complete blood count, serum iron and ferritin plus TIBC. The patient did not bleed from any site and was in good nutritional status. Different diagnostic tools were included: Stool for occult blood was negative. Upper and lower GIT endoscopy revealed normal findings. The patient developed dyspnea on mild excretion in addition to signs of impeding heart failure, mild hepatomegally with raised JVP and hemic murmur. Therefore, he had to have packed red blood cells transfused.

In 2012, 10th of March the patient presented to the outpatient clinic with fatigability and dyspnea during exertion associated with palpitation. There was no history of cough, but there were syncopal attacks that developed three times before he sought medical advice. CBC was done; results showed Hb 6.9 g/dL, RBC 2.82, HCT 23.6%, MCV 83.7 fL, MCH 24.5 pg, MCHC 29.2 g/dL, platelets 363 × 109/L with TWBC 7.8 × $10^{9/}$L and RDW (CV) 19.5. Serum iron and ferritin were extremely low (3.1 and 2, respectively). TIBC was 674 g/dL. Stool for occult blood was initially positive. Repeated analysis after withdrawal of ferrous supplement for 3 days yielded negative results. Abdominal scan was requested and a gastroenterology physician was consulted. He did upper and lower GIT endoscopy, a well defined ovoid shaped soft tissue mass in the right kidney implicating its anterior aspect, measuring 62 × 48 mm with faint arterial enhancement. No calcification was detected and excretory function was adequate. The left kidney was unremarkable. Renal function tests were normal and there was no microscopic hematuria. A CT guided biopsy of the mass was requested. Biopsy result showed a renal cell carcinoma consisting of polygonal cells with clear cytoplasm and centrally located nuclei interspersed by blood vessels with hemosiderin laden macrophages (Fig. 1), which indicate that this tumor is a classic (clear cell) renal cell carcinoma with abundant iron within the tumor, which could be explained by the tumor eating the iron. The patient was referred to the urology department, after correction of the anemia with 4 units of packed red blood cells. Nephrectomy done and his Hb monitored on monthly basis.

Discussion

The usual clinical presentation of renal cell carcinoma is triad of symptoms of hematuria, flank pain, and an abdominal mass 10–15% of cases [3]. Although anemia was described in one third of patients with renal cell carcinoma, the majority of cases are anemia of chronic disorder due to depression of erythropoietin production. Interesting in this case is that the patient has been treated in hematology department for more than 16 years as a case of iron deficiency anemia refractory to management. Since the only symptoms and

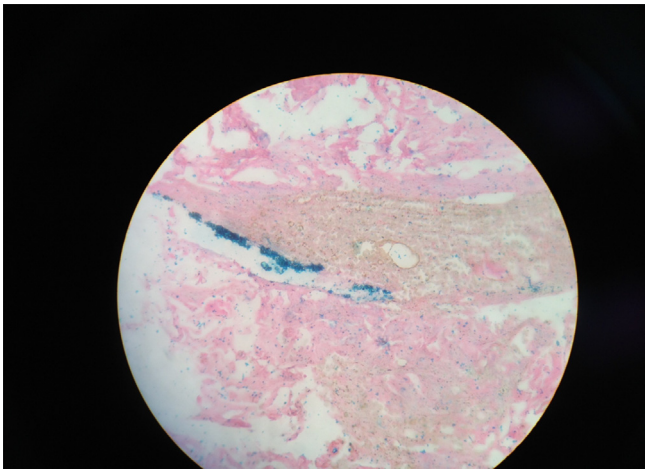

Figure 1 Tumor with Perl's stain showing hemosiderin laden macrophages with abundant iron deposition.

signs is related to anemia, which was confirmed by low Hb with the combination of low MCV, MCH and high RDW with peripheral blood picture of microcytic hypochromic anemia, that is commonly seen in the differential diagnosis of iron deficiency anemia, thalassaemia, sideroblastic anemia, and anemia of chronic disorder. Our patient is an elderly patient and the condition started 1962 with features of anemia, worsening when he stopped using iron supplement. This feature excludes thalassemia as a cause. On the contrary, there was no history of repeated transfusions or exposure to toxin and no basophilic stippling noted in the peripheral blood film, findings which exclude thalasaemia and sideroblastic anemia. The diagnosis of iron deficiency anemia was confirmed by increased TIB, low serum iron and ferritin. Searching for an underlying cause in this type of anemia is the core for appropriate management, because ongoing losses or failure to alleviate the underlying cause will lead to refractory iron deficiency anemia and will worsen the situation. The commonest cause for iron deficiency anemia among this age group is chronic blood loss, followed by nutritional causes, and ingestion of drugs such as ibuprofen, aspirin or anti-acids. The screening for a source of bleeding showed stools to be negative for occult blood with normal OGD. Capsule enterscopy was normal. CEA and CA19-9 were negative. There was no evidence of colonic or gastric carcinoma or hemorrhoids. The patient was nutritionally supported and there was no history ingestion of aspirin, ibuprofen or anti acid. It is unusual for iron deficiency anemia to be the presenting feature of renal cell carcinoma as it is the case in our patient for whom abdominal ultrasound revealed a renal mass for histopathological correlation. Computed tomography guided biopsy was done showed a clear renal cell carcinoma. To the best of our knowledge, only one similar case has been previously reported in 1984 by Kroll et al. [11].

Conclusion

There is a variant of clear renal cell carcinoma which is associated with consumption of iron. Whether this finding is accidental or related to the pathophysiology of the renal cell carcinoma, it needs to be elucidated. Hence iron stain (Perl's stain) should be done for clear renal cell carcinoma. Investigating causes of iron deficiency anemia are not complete without imaging of internal organs

(kidneys). Nephrectomy might be the sole answer for the management of iron deficiency anemia due to renal cell carcinoma.

Conflict of interest

No conflict of interest in this case report.

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