CASE REPORT

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Renal Cell Carcinoma with Polycythemia

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ABSTRACT

Renal cell carcinoma (RCC) is the most common renal tumor and participates in about 80-85% of primary renal tumors. It is usually diagnosed incidentally during the evaluation for other medical problems; or it may be presented with gross hematuria, loin mass or pain. However, it infrequently presents as a paraneoplastic syndrome (PNS) which includes, hypertension, hypercalcemia, and abnormal liver function. A 75-year-old gentleman presented with an incidental left renal mass following the evaluation of the left loin pain with headache and dizziness. The patient had a history of hypertension for 10 years on control medical therapy and no history of smoking or chronic obstructive airway disease. The complete blood picture was showed a marked elevation in hemoglobin 21.7 g/dl and hematocrit level 65%. Ultrasound was showed left renal mass and a computerized tomography scan was showed the enhancement in the left renal mass picture suggestive of RCC. After phlebotomy of 2 units of blood, the patient underwent radical nephrectomy, then the histopathology was reported clear cell type RCC Fuhrman nuclear grading system II. At 2 months following surgery, the patient's hemoglobin level and hematocrit were returned to normal. The pathogenesis of PNS may be due to an abnormal immune system response to a cancerous cell. There is a wide range of the PNS concerning RCC including non-specific constitutional features for example; cachexia, weight loss, and fever, and specific metabolic and biochemical disorders (i.e. hypercalcemia, non-metastatic hepatic dysfunction, amyloidosis, etc.). PNS is often unrecognized but polycythemia should be considered important biomarkers in RCC, therefore, it can be used as a tumor marker in the diagnosis and follow-up of the patient after surgery.

Keywords: Renal cell carcinoma; polycythemia; kidney; Hematocrit.

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INTRODUCTION

Renal cell carcinoma (RCC) represents 80-85% of primary malignant kidney tumors. It could possess approximately 5% in men and 3% in women of adult malignancies [1]. Polycythemia is one of rare 1-5% paraneoplastic syndromes (PNS) associated with RCC (due to hormones or peptides released from tumor cells or cross reactivity of tumor antigens and patient antigens), which has been associated with the production of erythropoietin (EPO) from RCC [2, 3]. The level of serum EPO is reported to be elevated in 33-38% of patients with RCC. Patients with RCC manifesting polycythemia have been rarely seen and the EPO level could be used as a tumor marker in these groups of patients. It has been founded that EPO level is correlated with grade and stage of RCC that equip prognostic information [4, 5]. The production of EPO in normal kidneys occurs in the peritubular cells and it is controlled by oxygen sensor in epithelial cells in the proximal tubules [6]. The pathogenesis of polycythemia in RCC is related to Von Hippel gene mutation and increases hypoxia-inducible factor (HIF) production which promotes erythropoietin gene transcription [7]. The presented case had left renal mass associated with elevated hemoglobin and hematocrit level which could be helpful as a tumor marker.

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CASE PRESENTATION

A 75-year-old man was presented to Al-Jumhory Teaching Hospital, Mosul city, Iraq with left loin pain and had a history of headache, dizziness, fatigue, and weakness for the last 4 months. The patient denied any features or history of deep venous thrombosis. He has no history of smoking. He had a history of hypertension for 10 years on controlled treatment. There was no history of cardiopulmonary diseases.

Physical examination was showed erythema of the face and hands. Vital signs were revealed a pulse rate of 80 beats/minute, blood pressure 140/90 mmHg, and temperature 37.4°C. The abdominal examination was normal with no palpable abdominal mass. The complete blood picture was showing a high hemoglobin level 21.7 g/dl, and hematocrit 65%. While blood urea nitrogen and serum creatinine were within the normal range. The EPO was not measured owing to the unavailability of the EPO test in our locality and blocked of transportation due to COVID-19 disease. Chest X-ray and echocardiography were normal. Ultrasound of abdomen was showed a left renal mass, cross-sectional imaging with contrast-enhanced computerized tomography (CT) of abdomen and pelvis was showed heterogenous enhancing left renal mass 10 × 6 cm in the lower pole as shown in Figure 1.

After venesection of 2 units of blood at a one-week interval, the hemoglobin was dropped to 17.5 g/dl, and hematocrit was dropped to 52%. An open radical nephrectomy was performed with prophylactic administration of enoxaparin to prevent thromboembolic complications. The excised specimen was showed a mass in the lower pole of the left kidney with a golden yellow color as shown in Figure 2.

Histopathological examination was showed a conventional clear cell RCC. The cell had prominent nucleoli with abundant, clear cytoplasm as shown in Figure 3 with Fuhrman grade II and pathological stage T2 N0 M0.

At the 2 weeks postoperative follow-up, the hemoglobin and hematocrit were decreased to 16.5 g/dl and 49.5% respectively. At 2 months after surgery, the level of hemoglobin was decreased to 12.5 and hematocrit 37.5%. The general condition of the patient was stable and the symptoms of headache and dizziness were disappeared. Informed consent was taken from the patient to publish the case in a scientific journal.

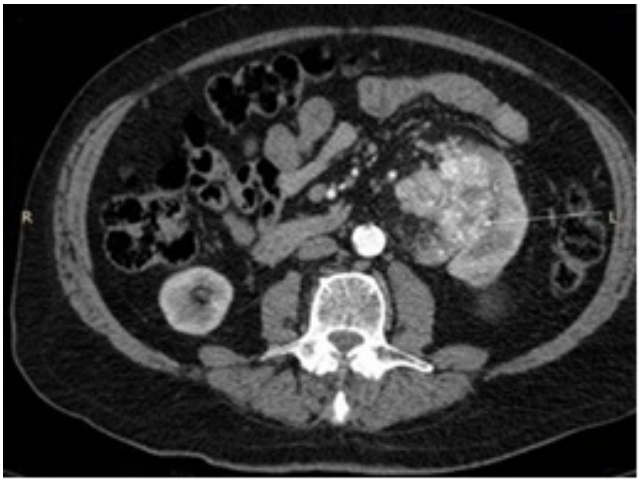

Figure 1. Contrast CT-scan axial section showing heterogenous enhancing left renal mass 10 × 6 cm in lower pole (white arrow).

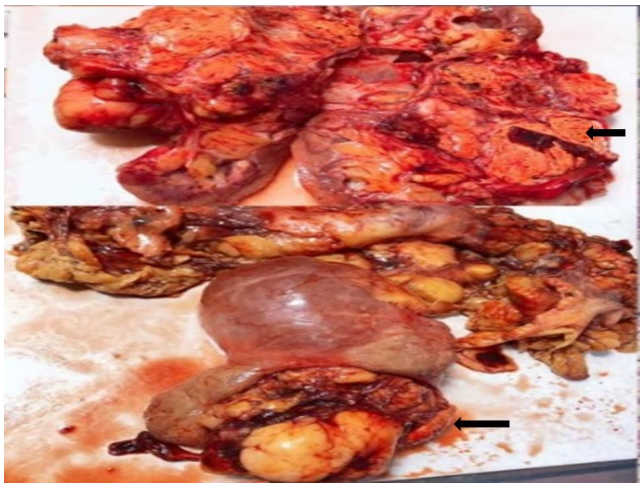

Figure 2. Left renal specimen after radical nephrectomy showing left lower pole renal mass with golden yellow color (black arrows).

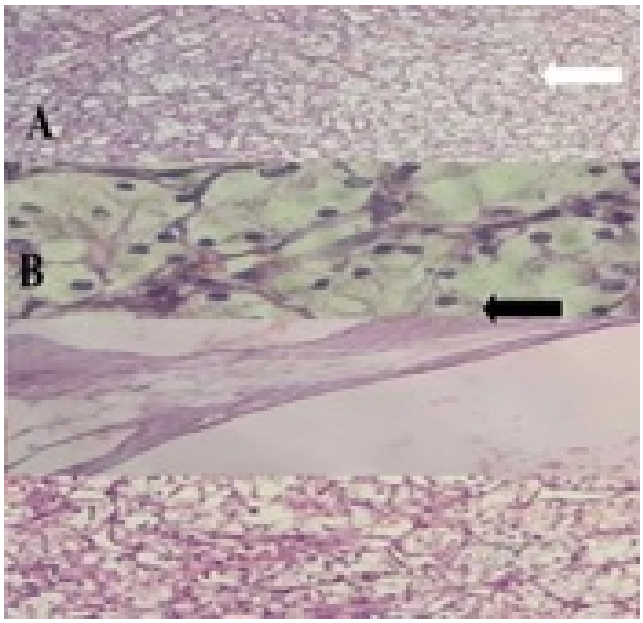

Figure 3. Microscopic appearance of tissue sliding of left renal tumor specimen showed clear cell RCC. A: Histopathological (hematoxylin and eosin × 40) examination shows delicate vascular network interspersed within a homogeneous nest of a cell (white arrow). B: The cell had prominent nucleoli with abundant, clear cytoplasm (black arrow) feature of RCC, Fuhrman nuclear grade 2 (hematoxylin and eosin × 100).

DISCUSSION

Clear RCC is the most common histological type of RCC of about 75-85%. It is associated with PNS [8] in some patients. One of these syndromes is polycythemia, which explained by an overproduction of EPO [9].

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The kidney manufacturers as a glycoprotein substance which is called EPO that plays an important role in the control of erythropoiesis. Increased production of EPO from kidney results in secondary erythrocytosis, which has been represented as an indicator in a variety of tumors such as RCC [2]. RCC might be associated with polycythemia in which these carcinomal cells of the kidney will produce high levels of EPO leading to polycythemia and this was assumed in general [3].

The pathogenesis of polycythemia in RCC is related to Von Hippel gene mutation and increases HIF production which promotes EPO gene transcription [7]. In a patient with clear cell RCC with polycythemia and an increase in serum EPO level, the hemoglobin and hematocrit are usually high, after removal of the tumor, these levels returned to normal. The presence of PNSs with RCC does not indicate a tumor of unknown primary, nor is it a contraindication for surgical removal; however, it might carry a worse prognosis [8]. RCC malignant cells have up-regulated HIF which had a downstream product of the EPO gene. In certain patients, EPO levels were elevated with RCC and this elevation has associated with polycythemia and the advanced stage of the tumour that provides enough information to prognosis [4, 10]. Despite the EPO was not measured in the presenting case, the large tumor size and no obvious cause of the polycythemia might be indicated that the level of the EPO was high.

However, surgical excision of the RCC and dealing with the surrounding vasculature were successfully resolved the majority of unwanted complications [11]. Further investigation is required to elucidate the mechanism underlying polycythemia EPO production.

CONCLUSION

PNS are important because they could be the first symptom that the patient present with and be a pointer to the presence of an occult malignancy. However, being familiar with their symptomatology is important to minimize patient morbidity and for surgical planning. Moreover, early detection of the PNS features could lead to the diagnosis of a biologically aggressive tumor.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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