Case Report

Polycythemia, increased erythropoietin levels in a patient with renal lymphoma

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Abstract

A young male presented to our clinic with 3 months history of shortness of breathness and progressive distension of abdomen. On investigations, patient had renal failure, polycythemia and nephromegaly. A diagnosis of non-Hodgkin's lymphoma was made on renal and lymph node biopsy. Serum erythropoietin concentrations were physiologically inappropriate. – Erythropoietin immunohistochemistry on renal tissue samples demonstrated positive staining for tumor cells. This patient was managed as a case of infiltrative lymphoproliferative disorder with kidney involvement having polycythemia owing to paraneoplastic Erythropoietin production and possibly local hypoxia produced by tumor cells. With maximum efforts, we could not find such an association in the literature.

Key Words: Lymphoma, polycythemia, renal failure

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Received: 13.12.2012, **Accepted:** 15.05.2013

INTRODUCTION

Involvement of kidneys with primary renal lymphoma is very rare, because this organ is normally free of lymphoid tissue.[1] Renal involvement with bilateral infiltration is often secondary to rapidly growing hematological malignancies such as systemic lymphoma or acute leukemia.[2,3] Widespread infiltration of the kidney is present in almost one-third of patients with lymphoma at autopsy.[4] Acute renal failure (ARF) is an unusual manifestation of lymphoma and a rare presenting sign of a hematological malignancy.[4,5] In this case report, we describe a rare presentation of symptomatic polycythemia with bilateral enlarged kidneys in a young male patient that on evaluation was found to have lymphoproliferative disorder involving kidneys.

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.135417

CASE REPORT

A 14-year-male presented with a 3 months history of shortness of breath, burning sensation in the skin and decreased appetite. For 2 weeks, his predominant complaints were progressive distension of abdomen, swelling over face and feet and decreased appetite. Patient denied any complaint of fever, night sweats, history of dysuria, hematuria or oliguria or any history of renal disease in the past. He was initially seen by a primary care physician who noticed facial plethora and bilateral abdominal lumps in loin with which he was referred to our institute. The patient was

How to cite this article: Bhat RA, Khan I, Khan I, Mir MA. Polycythemia, increased erythropoietin levels in a patient with renal lymphoma. Adv Biomed Res 2014;3:147.

admitted in our hospital. He was conscious and had facial plethora. Blood pressure was 122/72 mmHg. Pedal edema was present along with mild facial puffiness. There were multiple small (<1 cm) palpable lymph-nodes in cervical (submandibular) region, left axilla (posterior group). Examination did not reveal any abnormality in respiratory, cardiovascular and central nervous system. On abdominal examination, there was no ascites and liver and spleen were not enlarged. Bilateral kidneys were palpable, ballotable with a smooth surface and were non-tender.

Baseline investigations revealed: Hemoglobin – 18.8 g/dl (normal value, 13-17.5), hematocrit – 58.4% (normal value, 40-50), red blood cell count – 9.5 million/mm^3 (normal value, 4.2-6.5), total leukocyte count – 5,600/mm^3, platelet count – 2.2 lakhs/mm^3, creatinine – 3.2 mg/dl, urea – 100 mg/dl, uric acid – 4.4 mg/dl, serum bilirubin – 0.3 mg/dl. Routine urine examination revealed protein of two plus (++) with 5-10 white blood cells/high power field with a spot albumin creatinine ratio of 0.8. The 24 h urinary protein was 7.2 g. X-ray chest was normal. Abdominal ultrasonography showed bilaterally grossly enlarged kidneys. There was no evidence of cysts or hydronephrosis. Erythropoietin (EPO) levels were ordered and the levels were 150 mU/ml (normal value, 30-110 mU/ml). Computed tomographic scan of the abdomen [Figure 1] was carried out, which revealed bilaterally enlarged kidneys homogeneous in appearance. Patient was subjected to renal biopsy. The sections were stained with H and E stain, periodic acid-Schiff stain, silver methenamine, masson's trichrome and congo red. Microscopic examination revealed diffusely infiltrated by a monotonous population of atypical lymphoid cells with intermediate sized nuclei, scant cytoplasm, scattered mitoses and few tangible body macrophages [Figure 2]. The immunostaning pattern was globally negative. Features were suggestive of renal involvement in a lymphoproliferative disorder. EPO — immunohistochemistry on tissue samples demonstrated positive staining in tumor cells and occasional normal renal cells. A diagnosis of mixed diffuse lymphocytic lymphoma was suggested on subsequent lymph node biopsy. A diagnosis of lymphoma (non-Hodgkin's) with kidney infiltration was made. Polycythemia was evidenced by increased red cell mass in combination with increased hematocrit and high EPO levels. Patient subsequently received chemotherapy and is presently doing well and is under close follow-up. Post-chemo urinary protein showed a decreasing trend with improvement in renal parameters.

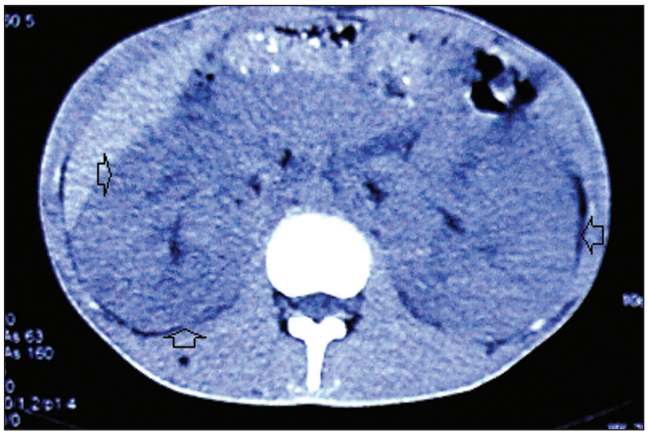

Figure 1: Non-contrast computed tomography abdomen showing bilateral enlarged kidneys (black arrows)

DISCUSSION

Renal involvement in lymphoma is uncommon and it can manifest as Nephrotic syndrome secondary to minimal change disease or membranoproliferative glomerulonephritis.[6,7] Rarely, it may cause nephromegaly and ARF secondary to a disseminated lymphoma and it is still rare for lymphoma to present in such a manner. So far, various reports of lymphoma and polycythemia have been reported[8-10] although, the association of renal lymphoma with polycythemia and documented raised EPO levels has not been reported so far. We could only find one animal study of such an association.[11] Polycythemia can present as Nephrotic syndrome.[12] However, mechanism is not fully elucidated. Various malignancies can give rise to increased EPO levels such as: Renal cell carcinoma, hepatoma, cerebellar hemangioblastoma, adrenal cortical tumors, pheochromocytomas, virilising ovarian tumors, Wilm's tumor.[9] Since there is no lymphoid

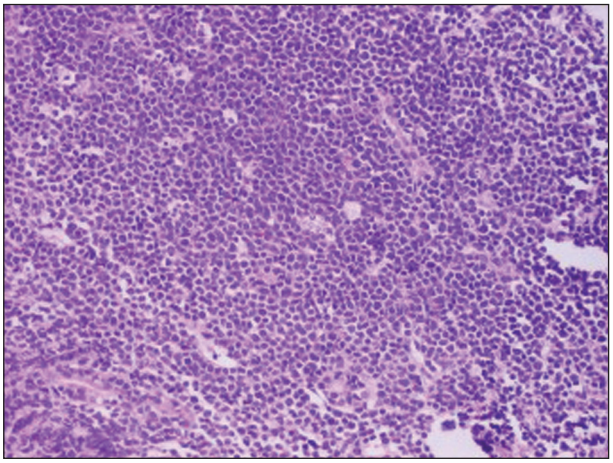

Figure 2: Histopathological examination of the renal biopsy tissue stained with H and E, periodic acid-Schiff, silver methenamine, masson's trichrome and congo red showing diffuse infiltration by a monotonous population of atypical lymphoid cells with intermediate sized nuclei, scant cytoplasm, scattered mitoses and few tangible body macrophages. Three unremarkable appearing glomeruli are seen

tissue in kidneys, a primary renal lymphoma is unlikely, although primary renal lymphoma does occur and the criteria for diagnosis of this entity have also been mentioned.[1] Polycythemia and elevated EPO levels in this patient may be explained by paraneoplastic EPO production and local hypoxia-induced EPO production from compression of normal renal cells and vasculature.

In our case, other causes of enlarged kidneys were promptly ruled out. Obstructive nephropathy was excluded by ultrasonography. Polycystic kidney disease was similarly excluded by imaging. The absence of extensive hyperuricemia (serum uric acid > 20 mg/dl) and uric acid crystals argues against a diagnosis of uric acid nephropathy. The presence of massively enlarged kidneys and histopathologic evidence of diffuse lymphocytic infiltration points to lymphoma-proliferative disorder as the cause of renal failure, which was supported by lymph node biopsy. Tissue diagnosis can usually be made by lymph node or bone marrow biopsy in most patients with widespread lymphoma and renal involvement. It is believed that kidney biopsy is the most expeditious and direct way to establish the diagnosis of renal masses besides providing clues to etiology of ARF.[1]

A rare presentation of lymphproliferative should be suspected in a patient who presents with bilateral nephromegaly and renal failure and where the radiological imaging excludes other known causes of enlarged kidneys.

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Source of Support: Nil, **Conflict of Interest:** None declared.