Case Report:

Renal Medullary Carcinoma in Sickle Cell Disease: Radiological and Pathological Findings

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Abstract

We report two cases of renal medullary carcinoma collected from Almana General Hospital in KSA. The incidence of sickle cell trait in KSA is high; however, this tumor is rare and only case reports were described in literature. Both patients were males with the ages of 32 and 25 years. The most frequent presenting symptoms were gross hematuria and flank pain. The duration of symptoms ranged from 3 weeks to 2 months. The tumors were poorly circumscribed arising centrally in the renal medulla. Sizes in both patients were 6 and 8 cm and hemorrhage and necrosis were common findings. Both cases described showed sickle red blood cells in the tissue and one patient was confirmed to have sickle cell disease and the other was sickle cell trait. Both cases showed the characteristic reticular pattern, reminiscent of yolk sac testicular tumors of reticular type with areas of microcystic, tubular, trabecular, solid and adenoid-cystic patterns, and stromal desmoplasia. The characteristic collections of neutrophiles with foci of necrosis and microabscesses were seen. One patient died within 6 months after diagnosis.

Key Words: Sickle cell trait – Hematuria – Renal medullary carcinoma – Renal tumors.

Introduction

RENAL medullary carcinoma is a rare collecting duct neoplasm affecting teenagers and young adults with sickle cell trait or hemoglobin sickle cell disease. Presumably an unidentified genetic component is a factor in its pathogenesis. The tumor has a distinctive microscopic appearance consisting of a diffuse and glandular growth pattern, an inflammatory infiltrate, and the presence of rhabdoid/plasmacytoid cells or even sarcomatoid cells. This entity should be considered in a young patient with sickle cell trait or hemoglobin SC disease that develops hematuria. Distant metastasis at the initial presentation is not uncommon. These tumors are centrally located and infiltrate the renal parenchyma and renal sinus; occasionally a necrotic tumor communicates with the collecting system. They show heterogeneous contrast enhancement, presumably due to necrosis. Venous invasion and nodal metastases are common. This is an aggressive malignant neoplasm having a poor prognosis. The interval from diagnosis to death averages only several months; no objective response is seen to chemo and immunotherapy [1].

Case 1:

A 32-year-old man presented to our general hospital with frank hematuria. The patient had history of sickle cell trait which is pandemic at that area in Middle East (certain group of Arab population having strict positive consanguinity).

Intravenous urography (IVU) was done (Fig. 1) and showed normal appearance of kidneys, ureters and urinary bladder with apparent distortion of the left renal lower calyx. So, cystoscopy was done and showed normal appearance of urinary bladder and ureteric orifices with evident blood-urine jet from left ureteric orifice.

Ultrasonographic examination (Fig. 2) showed well defined lesion 6.2×4.6 cm seen at the lower renal zone with peripheral aspect distorting the echogenic renal sinus, color flow mapping showed increased vascularity around the lesion.

Multislice CT study using Seimens 128 machine (soma tom definition AS+) pre and post dynamic contrast study (Fig. 3) including axial and coronal MIP images which showed left renal lower zonal hypodense mass with no evident contrast uptake.
The lesion showed well defined outline, overlying capsule seen intact, and subtle stranding of perirenal fat planes was seen. The renal vein and artery were looking unremarkable.

The main radiologic diagnostic concern was either benign renal neoplasm (onchocytoma), but due to possibility of stranding we put the differential diagnosis of malignant renal growth. The patient subjected to true cut renal biopsy under sonographic guidance, 18 gauge needle was used. Follow up CT study showed pulmonary nodules.

Case 2:

A 25 year-old man presented to our general hospital with left flank pain and frank hematuria. The patient had history of sickle cell disease. Intravenous pyelography showed normal appearance of kidneys, ureters and urinary bladder.

Multislice CT study using Seimens 128 machine pre and post dynamic contrast study including axial and coronal MIP images which showed left renal midzonal hypodense well defined mass with overlying capsule intact, and perirenal fat, the renal vein and artery showed unremarkable changes.

Ultrasongraphic examination showed well defined lesion 8.5x5 cm seen at the midzone with increased vascularity around the lesion. The main radiological diagnostic concern was suspicious mass. Nephrectomy was decided.

Gross characteristics of both cases were more or less the same affecting the left kidney which showed poorly circumscribed tumor mass, firm to rubbery with whitish to gray color and both of them occupied a central location. Their sizes were 6.5 to 8.5 cm and their cut sections showed areas of necrosis, and hemorrhagic areas.

Histopathological analysis showed both tumors had very similar microscopic characteristics. A reticular pattern of growth and a prominent stromal desmoplasia were the most constant features. The reticular pattern consisted of tumor cell aggregates forming spaces of varied size, reminiscent of yolk sac testicular tumors of reticular type (Fig. A & B). The stromal desmoplasia showed several appearances among the tumors and within the same tumor: densely collagenous, edematous, mucoid or myxoid. Microcystic, tubular, trabecular, solid and adenoid-cystic (Fig. C & D) patterns were also identified in some of the tumors.

**Fig. (1):** IVU in a male patient, 32 years old showed apparent indentation seen at the left renal lower calyx when images reviewed retrograde.

**Fig. (2):** Ultrasound of the same patient showed evident left renal rather well defined solid homogenous isoechoic lesion, overlying capsule is seen intact mass.

**Fig. (3):** Multislice CT post contrast CT study and coronal MIP images showed left sided non enhanced hypodense lower zone renal mass distorting lower calyx. Renal artery and vein are seen intact with very subtle strandy perirenal fat.
Case (1): Reticular pattern of growth reminiscent of the yolk sac testicular tumor (A & B) Tubular pattern with prominent dense collagenous stromal desmoplasia and Adenoid-cystic appearance (C & D) with Sickle RBCs.

Gross pathology showed poorly circumscribed tumor mass, firm to rubbery with whitish to gray color

Axial CT chest lung window with evident right sided lung nodule.

Discussion

Renal medullary carcinoma is a rare, rapidly growing tumor that affects young individuals with sickle cell trait. This tumor was described in 1995 by Davis, et al. [2] which considered it the seventh sickle cell nephropathy.

Hematuria is the most common symptom. Since this variant seems to originate in the medulla and has a predominately tubular configuration, a collecting duct dedifferentiation is suggested.

The mass is usually localized to the renal medulla, with distortion of the pelvicalyceal system and often with infiltration into the adjacent renal cortex. The shape of the kidney is usually more or less preserved [3]. The tumors are generally firm and white or grayish (not yellow) because of an accompanying desmoplastic reaction (usually no necrosis or hemorrhage).
Extension into the renal vein does not occur.

Medullary carcinoma, has been identified in patients suffering from sickle cell trait. With imaging: in ultrasound (US) the tumor is slightly hypoechoic or almost isoechoic, as in the cases reviewed in our study, poorly margined, and typically centrally located on US. In computed tomography (CT) the tumor appears homogeneous and isodense compared to the renal parenchyma on unenhanced CT. After intravenous contrast administration, the tumor is hypovascular [4]. There may be central low attenuation areas, due to the extensive reactive fibrotic reaction (not necrosis), which accompanies the infiltrative growth of this neoplasm, rather than necrosis or hemorrhage.

In reviewing the literature, Davis, et al. [2] at the Armed Forces Institute of Pathology reviewed 55 cases of renal pelvic carcinoma diagnosed over a 22-year period. Two distinct tumor types emerged. Twenty-one of the fifty-five cases were typical transitional cell carcinoma. The remaining thirty-four cases were highly aggressive, infiltrating, poorly circumscribed, renal tumors occurring primarily in young black patients with sickle trait. These tumors occurred in patients ranging in age from 11 to 39 years. Macroscopically, the tumors occupied primarily the renal medulla and invaded the calyces; satellite lesions were often present on the renal cortex. Most (23 of 31) involved the right kidney and all demonstrated lymphatic and/or vascular invasion.

Histologically, the tumors demonstrated a distinctive reticular growth pattern with some transitions to a more adenoid cystic appearance. Acute inflammation and stromal proliferation was present. Nine patients had known sickle trait; one patient had SC disease. The sickle cell disease status of the remaining patients was unknown, but all patients had sickled cells identified microscopically within the tumor or adjacent renal parenchyma. The relationship of renal medullary carcinoma to sickle cell trait is unclear. It is not uncommon for patients with sickle cell trait to develop renal insufficiency in the second to fourth decades of life, [5] but sickle cell nephropathy in a patient with hematuria should be a diagnosis of exclusion. In such cases (in sickle cell patients) the differential diagnosis includes papillary necrosis, renal infarction and renal medullary carcinoma.

Radiographically, renal medullary carcinomas are generally centrally located, infiltrative, and associated with pelvic encasement [6]. These findings are not specific for renal medullary carcinoma but suggest the diagnosis in patients with sickle cell trait. Renal infarction can deform the renal calyx and cause scarring, but this does not usually manifest itself as a mass [7]. Papillary necrosis can cause overlying scarring of the renal parenchyma with depression of the capsular surface over the injured lobe [8].

References