Case Report

Heterotopic bone formation in renal cell carcinoma: A diagnostic challenge

Singh V, Sinha RJ, Sankhwar SN, Dalela D
Department of Urology, CSMMU (formerly KGMC), Lucknow, Uttar Pradesh, India.

Correspondence to: Dr. Vishwajeet Singh, E-mail: vishwajeeturo@sify.com

Abstract

Formation of bone in cases of renal cell carcinoma is a rare finding and only a couple of case reports from Japan and one from India are mentioned in the literature. Calcification inside renal mass has been reported earlier but the prognostic implications have not been clearly elucidated. We report a case which showed heterotopic bone formation (ossification) inside the renal mass and was managed by radical nephrectomy. The histopathology showed clear cell renal carcinoma with multiple centers of ossification in the region of calcification suggesting bone formation. In this case report we discuss bone morphogenetic proteins which have been implicated as a prognostic and causative factor, highlight the difficulties in distinguishing between calcification and bone formation on the basis of radiological investigations and mention the geographic implications of this rare phenomenon which has not been described earlier.

Key words: Bone morphogenetic proteins, carcinoma, environmental, ossification, renal cell

Introduction

Renal cell carcinoma (RCC) may have calcifications within them.[1] Heterotopic bone formation by ossification inside the renal tumor gives an appearance similar to that of calcification. It is difficult to distinguish between bone formation and calcification on the basis of radiological imaging alone. Demonstration of ossification centers on histopathological examination[2] and expression of bone morphogenetic protein (BMP) in RCC may help in clinching a definite diagnosis.[3-6]

Case Report

A 45-year-old male presented with gross painless total hematuria of one-week duration. There were no other urinary symptoms. General examination of the patient was normal. Physical examination of abdomen revealed a hard lump in the left flank. Ultrasonography (USG) of abdomen showed a heterogeneous mass in the left kidney with a middle calyceal stone casting a distal acoustic shadow. The computerized tomography (CT) scan of the abdomen confirmed a left renal mass with dense calcification concentrated over a 2 cm spherical area near the center of the mass [Figure 1]. The renal mass showed enhancement after administration of intravenous contrast. No lymph node enlargement was seen on CT scan.

The patient underwent left radical nephrectomy through the transperitoneal route.

Gross pathology of the kidney revealed a tumor involving the mid-portion and the lower pole measuring 10 cm x 9 cm x 7 cm. While incising the specimen, there was a grating sensation and cut section of the specimen gave a bony hard feel. The cut surface showed a well circumscribed variegated mass having a grayish white bony area measuring 3 cm x 2 cm. Histopathological examination confirmed this as renal cell carcinoma - clear cell type (pT2). The calcified portion was bone with centers of ossification clearly visible [Figure 2].

Currently the patient is on a regular follow-up for the last three years and is free of tumor recurrence or metastasis.

Discussion

Though calcification has been reported in literature in renal cell carcinoma but bone formation in this type of tumor is a rare phenomenon.[3] Few cases have been reported in Japanese literature,[5] and only one case has previously been reported from India.[7] So is there a geographical or environmental association or an Asian link? This question appears difficult to answer at this point but

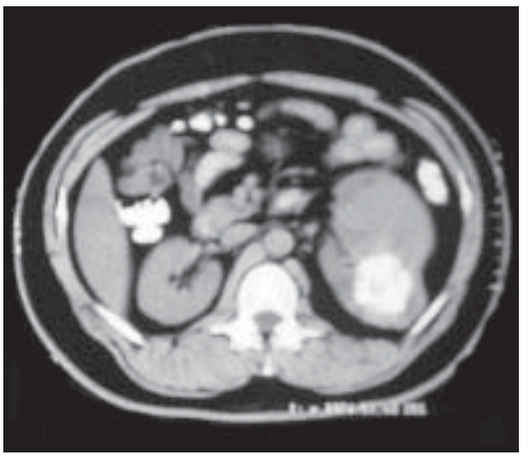

Figure 1: CT scan of abdomen showing left renal mass with areas of bone formation and calcification

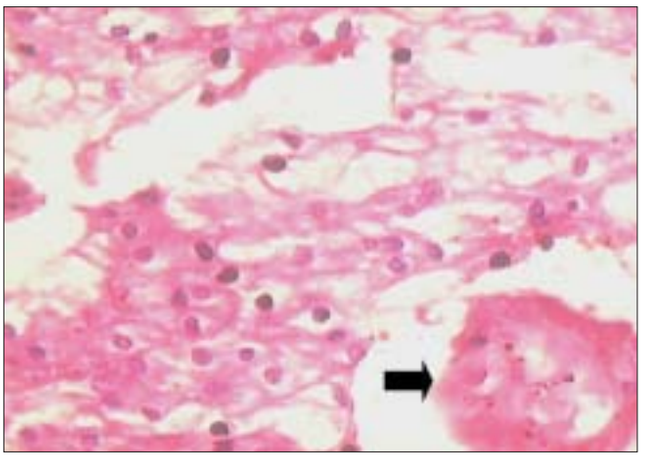

Figure 2: Photomicrograph showing clear cells of renal cell carcinoma with foci of ossification (arrow)

may be an observation which is worth exploring. Though, it should always be kept in mind that a single case report cannot be the basis of any definitive conclusion; until and unless more studies of a similar kind or a study comprising a large number of patients is reported.

As mentioned previously, it may be difficult to distinguish between bone formation and calcification despite the use of sophisticated radiological imaging like CT scan. In the above mentioned case, USG report was that of calyceal stones. CT scan reported it as calcification inside the renal mass. We hypothesize that in a patient with renal mass, if ultrasound shows calyceal stone casting with distal acoustic shadow and plain CT scan shows calcification over the same area, one should strongly suspect bone formation.

The exact mechanism of bone formation in renal cell carcinoma is not known. According to Chalmers and associates, ossification requires three conditions: osteogenic precursor cells, ossification-inducing agents and an environment permitting osteogenesis.

BMP has been suggested as a possible cause of heterotopic bone formation in RCC and tumors of other organs. Various subtypes of BMP are being investigated for their role in prognostication of renal cell carcinoma.[8]

The prognostic implications of calcification per se are not very clearly mentioned in the literature.[9] It is even harder to comment on the survival impact of heterotopic bone formation but case reports[3-5] have depicted good survival. Though case reports represent the lowest level of evidence and no definitive conclusion may be made based on case reports. Role of BMP as a marker for prognosis is still investigational.

The above mentioned patient is doing well and has not exhibited any recurrence on three year follow-up. So we can only presume that ossification does not have adverse prognostic implication but definite answer can only be given once the patient has a longer follow-up period or we come across similar case studies or case reports in near future with survival analysis from Asia or other parts of the world.

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