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Ossification of renal cell carcinoma: a favorable marker

Case Report

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Abstract: Although foci of calcification in renal cell carcinoma is frequently observed, ossification is extremely rare and may be a marker for favorable prognosis. We report a case of renal cell carcinoma with a focus of ossification; this case was not detected with imaging techniques prior to surgery and diagnosed initially on pathologic examination, unlike other cases. If the radiographic evaluation for ossification is inconclusive but the mass is extremely hard to palpate or difficult to cut, the surgeon should remember the favorable prognosis of such lesions and might consider a limited procedure such as partial nephrectomy while waiting for pathological analysis.

Keywords: *Calcification • Ossification • Partial nephrectomy • Renal cell carcinoma*

1. Introduction

Although foci of calcification in renal cell carcinoma (RCC) is frequently observed, ossification is extremely rare and it has been suggested to be a marker for favorable prognosis, since there is typically no tumor invasion beyond the gross margin of the ossified RCC [1,2]. If ossification is detected before or during surgery, then a less radical surgery, such as partial nephrectomy, might be considered [2].

To our knowledge, we report the tenth case of a RCC with a focus of ossification that was not detected with any imaging techniques prior to surgery and diagnosed initially on pathologic examination unlike other cases.

2. Case Report

A 56-year-old diabetic man with a left incidental renal mass diagnosed at routine urinary ultrasonographic examination was presented. Physical examination and blood biochemistry (serum multiple analysis) were all within normal limits except an elevated blood glucose level which was 207 mg/dl. An ultrasonographically detected renal mass was confirmed on subsequent magnetic resonance imaging (MRI) which showed a 18x20 mm, slightly hypointense intraparenchymal mass at the lower pole of the left kidney on both T1 and T2 weighted images (Figure 1). A left partial nephrectomy was performed and the patient was discharged at the fourth postoperative day without any complications. He remains free of recurrent or metastatic disease at 8 months, postoperatively.

The removed renal mass was 28 gr in weight and 5x3x2.5 cm in dimensions. Its color was yellowish orange. A 4x2.5 cm tumor nodule with focal hemorrhage was observed. There were no signs of necrosis on the cut surface and no evidence of capsular penetration where the distance between the tumor and the capsule was less than 1 mm. Representative tissue sections were cut at 4 μm intervals and stained with both hematoxylin-eosin and periodic acid-Schiff (PAS). Immunohistochemical staining was performed using citrate buffer and antibodies against epithelial membrane antigen (EMA) (clone GP1,4, incubation time 30 minutes, Neomarker®), vimentin (clone V9 incubation time 30 minutes, Sitogen®), cytokeratin (cocktail AE1 and AE3, incubation time 60 minutes, Cell marque®). The tumor

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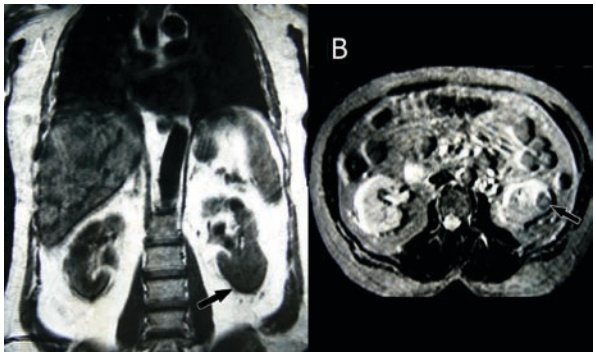

Figure 1. The tumor was detected on T1 (B) and T2 (A) weighted magnetic resonance images revealing a well-defined solid tumor arising from the lower pole of the left kidney without any signs of ossification.

was composed of solid tubular sheets of polygonal epithelial cells with abundant clear cytoplasm and prominent cell borders in the stroma containing vascular structures. The cells were with small, round and dense nuclei, but without any nucleolus at 100X magnification (Fuhrman grade 1). At the periphery, a 2x1 mm focus of metaplastic ossification with no bone marrow elements surrounded by areas of hyalinization was observed. Immunohistochemical staining was positive for EMA, cytokeratin and vimentin in the tumor cells (Figure 2).

3. Discussion

Calcification of RCC can be observed frequently as 10% to 20% of all renal cell carcinomas, but ossification is extremely rare [1,3]. Although the first case was reported in 1938, its mechanism is still unclear [2-4]. However, in their case report Yamasaki et al. suggested that ossification in RCC may result from the metaplasia of pluripotent stem cells into osteoblastic cells by the mechanism of paracrine secretion of bone morphogenetic protein 2 (BMP-2) from the tumor cells, like gastrointestinal tract glandular tumors with ossification [5].

As demonstrated in previous case reports, the presence of extensive osseous metaplasia introduces several difficulties in the clinical and pathological diagnoses [1]. Mature cystic teratomas, adrenal neoplasms, soft tissue sarcomas, extraskeletal osteosarcomas, angiomyolipomas and metastatic carcinomas should be considered besides RCC [1]. Unlike other cases in the literature, neither ossification nor calcification of RCC was observed in any preoperative imaging studies such as plain X-ray , CT scan, or MRI. To our knowledge, it is the first ossifying RCC case published in the English literature that was diagnosed initially on pathologic examination [1-5]. In contrast to

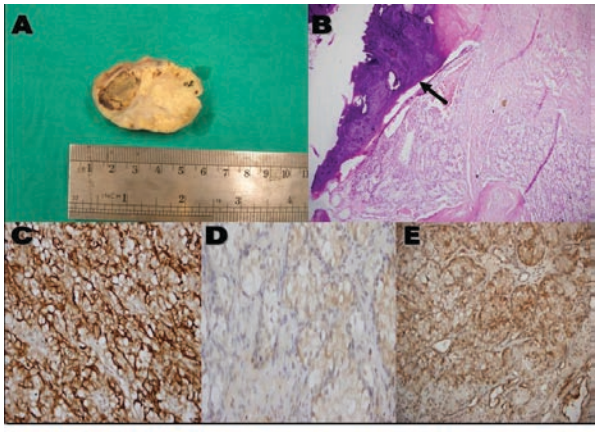

Figure 2. Gross appearance of renal cell carcinoma (A). The tumor is variegated with a combination of solid hemorrhagic and necrotic areas. No osseous metaplastic area is obviously seen within the tumor with bare eye. Microscopic appearances of renal cell carcinoma, clear cell type (B). The tumor cells are optically clear cytoplasm and sharply outlined cell membrane. Osseous metaplasia (arrow) is apperantly seen within the tumor (hematoxylin-eosin, 100X). Immunohistochemically membranous and cytoplasmic staining with EMA (Neomarker®) at 400X (C), cytokeratin (Cell marque®), at 400X (D) and vimentin (Sitogen®) at 200X (E) magnification in renal cell carcinoma.

the previously reported cases, the tumor in our case was not relatively large and did not contain any bone marrow elements [1-5]. Positive immunohistochemical staining with both cytokeratin, vimentin, EMA together with the hematoxylin-eosin staining findings support the diagnosis of RCC with osseous metaplasia.

Ossification of RCC has been suggested to be a rare but significant marker for favorable prognosis just like calcified RCCs [2,3]. Unlike osseous metaplasia demonstrated in other tumors, such as colorectal carcinomas, which have been shown to be not associated with a significant difference in prognosis, patients with ossified RCC usually have an early stage tumor and there is typically no tumor invasion beyond the gross margin of ossified RCC [1]. Besides that, as mentioned in previously reported cases of ossified RCC, the tumor in our case has low nuclear grade (Fuhrman grade 1) which again suggests a favorable prognosis [1]. However, we believe that additional cases with longer clinical follow up are necessary to confirm this expression.

As a conclusion, if ossification is detected prior to or during surgery, less radical surgery such as partial nephrectomy might be considered. If the radiographic evaluation for ossification is inconclusive but the mass is extremely hard to palpation or difficult to cut, the surgeon should remember the favorable prognosis of such lesions and might consider a limited procedure while waiting for pathological analysis.

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