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Renal cell carcinoma containing abundant non-calcified fat

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Abstract

Renal masses found to contain macroscopic fatty elements on CT or MRI imaging can generally be classified as benign angiomyolipomas. Rarely, renal cell carcinomas may also contain evidence of macroscopic fat. When true adipocytic elements are present, this is generally due to a process of osseous metaplasia in which both fat cells and calcification are co-localized within the mass. We present a patient with a large papillary renal cell carcinoma containing abundant fat with sparse, punctate calcification remote from the fatty elements on imaging. This report highlights the need for radiologists to maintain caution when diagnosing renal angiomyolipomas on the basis of macroscopic fat and reviews the current literature on fat-containing renal masses.

Key words: Renal cell carcinoma—Macroscopic fat—Osseous metaplasia—CT

Renal masses which contain CT or MRI evidence of intralesional fat cells, so-called macroscopic fat, can be diagnosed with confidence as benign angiomyolipomas in almost all patients using imaging alone [1]. Relatively, recently it was discovered that in extremely rare instances, renal cell carcinoma may contain CT or MRI evidence of fat cells and thus may be misdiagnosed as an angiomyolipoma [2–10]. As a result, the confident diagnosis of an angiomyolipoma now requires that a fat-containing renal mass not be calcified [11]. An important aspect of these initial case reports is the fact that the described renal masses generally contained small, subtle amounts of fat, and that the calcifications were located immediately adjacent to regions of fat. Isolated reports of renal cell carcinoma containing fat without calcification have since emerged, but like the others, the quantity of fat has generally been sparse [2, 6, 8]. We report an example of renal cell carcinoma that contains multiple foci of abundant fat, and in regions that are not calcified. This report emphasizes the importance of recognizing that renal cell carcinoma may contain abundant, non-calcified fat, and allows us to understand better the genesis of fat cells in renal cell carcinoma.

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Case description

A 65-year-old asymptomatic male with a past medical history of controlled hypertension and hypercholesterolemia was evaluated at an outside institution for abnormal liver function tests. The work-up included an abdominal sonogram that revealed only an incidental 14-cm mass in the left kidney. This mass demonstrated markedly heterogeneous internal echogenicity as well as evidence of internal vascular flow on color Doppler evaluation (Fig. 1).

The patient was subsequently referred to urology. Physical examination revealed a palpable mass in the left flank. Serum chemistries, liver function tests and creatinine were rechecked and found to be normal. A renal mass protocol CT scan was performed using a multidetector row scanner (Aquilion 64, Toshiba America Medical Systems, Tustin, CA) both before (kidneys only) and after 80-cc iopromide injection (Ultravist 370, Bayer Healthcare, Leverkusen, Germany). The unenhanced, enhanced nephrographic phase (100-s delay, kidneys only) and excretory phase (8-min delay, abdomen only) scans were all performed using a kVP of 120, and a modulated mA (reference mAs of 200). The CT scan revealed a $13.0 \times 12.0 \times 9.1$ cm partially exophytic

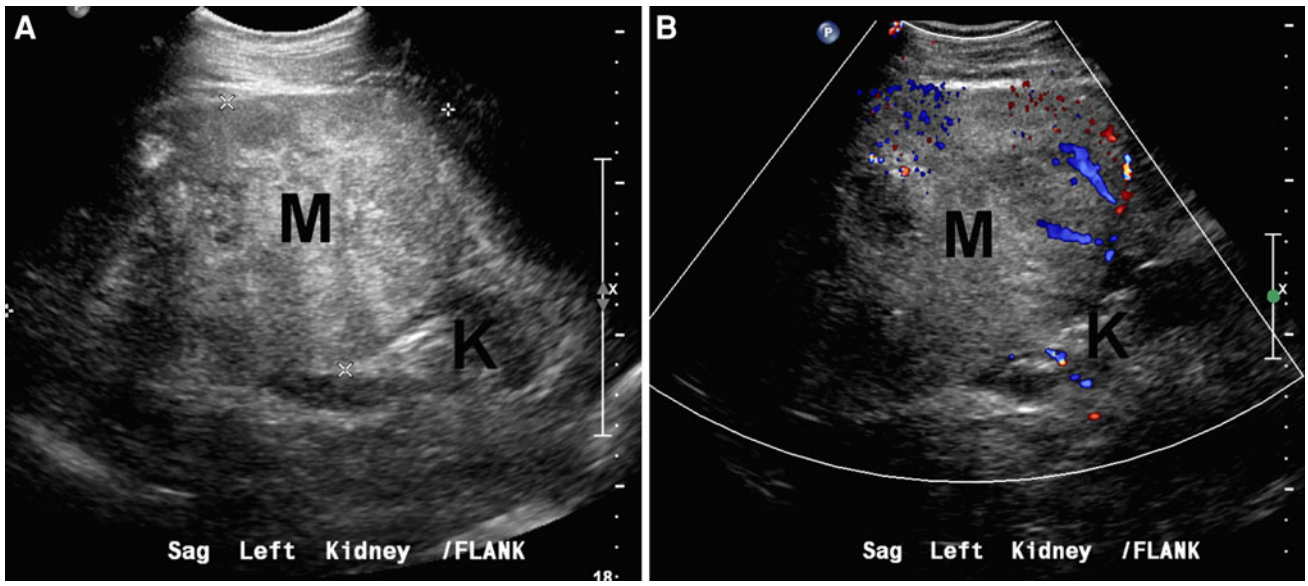

Fig. 1. Abdominal ultrasound performed for abnormal liver function tests shows an incidental 13-cm solid mass (*M*) arising from the upper pole of the left kidney (*K*). The mass demonstrates markedly heterogeneous internal echogenicity (**A**). Color Doppler evaluation reveals internal vascularity (**B**).

mass arising from the posterior upper pole of the left kidney, resulting in anterior renal displacement (Fig. 2). Numerous intralesional low-attenuation 4–14 mm round-to-oval foci were visualized, demonstrating region-of-interest mean attenuation values ranging from −71 to −42 HU, diagnostic of macroscopic fat. Distant from these regions were scattered, sparse, punctate foci of calcification predominantly localized to the periphery of the mass. There was moderate, relatively homogeneous enhancement of the non-fatty, non-calcified components of the mass, with an unenhanced attenuation of 35 HU, and an enhanced nephrographic phase attenuation of 57 HU, for an enhancement difference of 22 HU. There were no findings of cystic change or necrosis. The renal veins, inferior vena cava, and adrenal glands were normal. There was no evidence of perirenal or retroperitoneal lymphadenopathy.

A differential diagnosis of angiomyolipoma and renal cell carcinoma was offered and percutaneous CT-guided needle biopsy of the mass was performed. The biopsy procedure was performed via a left posterolateral intercostal approach with the patient in the prone position (Fig. 3). A 20-gage biopsy needle (Chiba, Cook Medical, Bloomington, IN) was placed into the non-fatty elements of the mass and four, 25-gage samples obtained. An intra-procedural preliminary cytopathology impression of papillary renal cell carcinoma was subsequently confirmed. There was no evidence of smooth muscle to suggest an angiomyolipoma.

On the basis of these findings, the patient underwent a left radical nephrectomy with regional lymphadenectomy. Surgical pathology demonstrated a 13.0 cm well-circumscribed renal cell carcinoma of the papillary type, with prominent papillary architecture, that was confined to the kidney (AJCC stage pT2). Tumor cell nuclei were enlarged and demonstrated prominent nucleoli, consistent with Fuhrman nuclear grade III (of IV). Numerous lipid-laden histiocytes were present in the majority of tumor papillae; however, these did not correspond to the discrete islands of fat detected on CT. Instead, the fat-attenuation areas on CT correlated at pathology with discrete round aggregates of adipose tissue (fat cells), measuring up to 8 mm in diameter, and scattered throughout the mass (Fig. 4). Rare microscopic foci of osseous metaplasia were present, some of which were associated with adipose tissue; however, no hematopoietic elements were identified. The patient had an unremarkable post-operative recovery, and has had no signs or symptoms of recurrence at 12 months.

Discussion

Despite the fact that angiomyolipomas may be diagnosed in renal masses that contain macroscopic fat by CT or MRI, this case exhibited features of renal cell carcinoma in the differential diagnosis. The considerations included: (1) renal cell carcinomas that contain macroscopic regions of fat usually demonstrate calcifications in close approximation to fatty elements, (2) angiomyolipomas containing minimal fat are almost always small (≤3 cm), (3) angiomyolipomas are hypervascular neoplasms that usually enhance intensely, and (4) calcification within an angiomyolipoma is exceedingly rare. To our knowledge, only four cases of angiomyolipomas containing calcification have been reported in the literature to date [12–15].

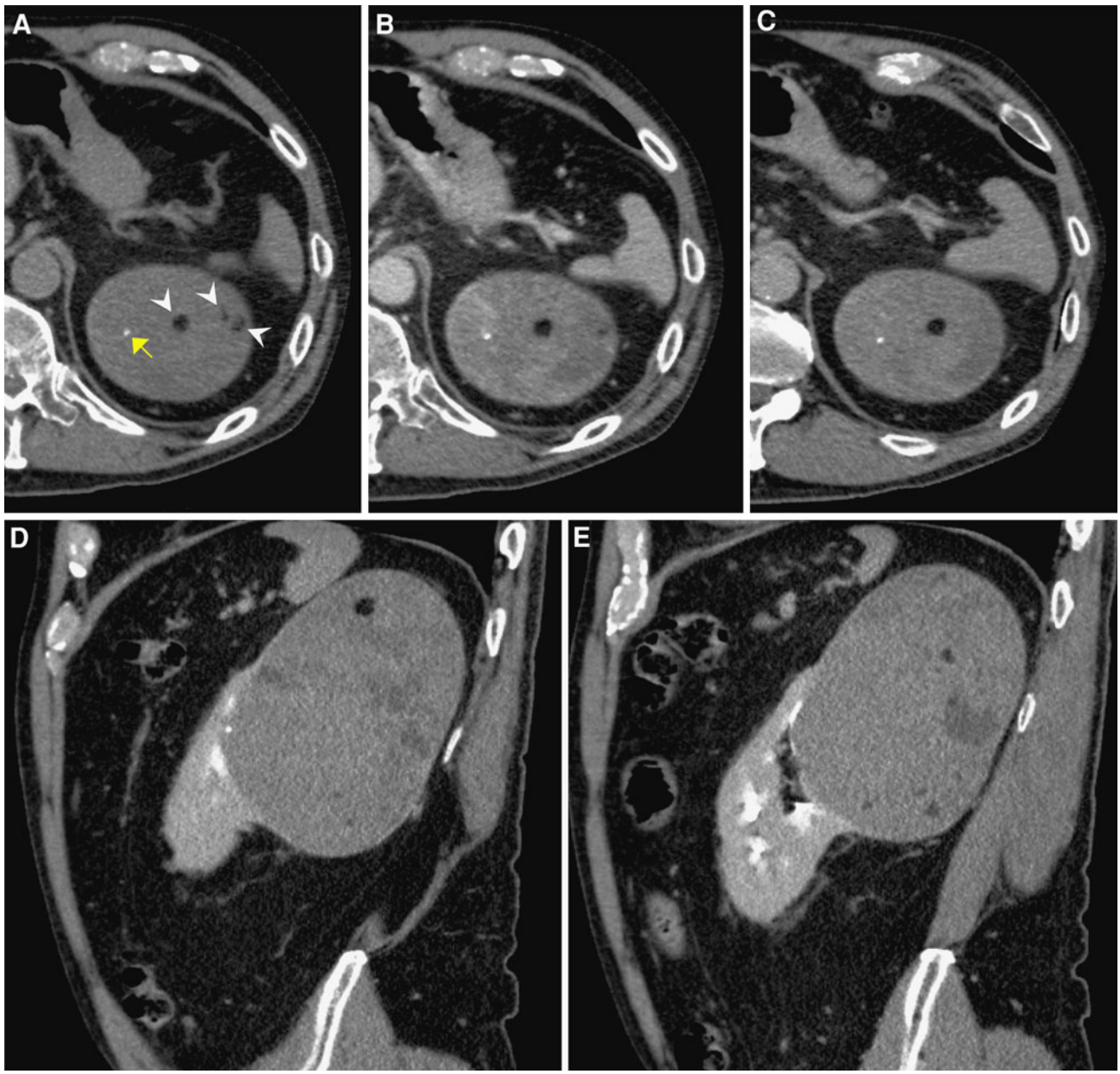

Fig. 2. Axial CT images in pre-contrast (**A**), post-contrast nephrographic (**B**) and excretory (**C**) phases demonstrate well-defined regions of fat density (*arrowhead*) within an enhancing exophytic renal mass. Sparse, punctuate foci of calcification are also noted separate from the regions of fat (*yellow arrow*). Numerous fatty elements are noted scattered throughout the mass, best appreciated on sagittal excretory phase images (**D** and **E**).

Our patient's renal mass showed evidence of macroscopic fat, was large, only moderately vascular, and contained only a few visible calcifications which were remote from the fat deposits. Percutaneous biopsy can be used to diagnose both angiomyolipoma and renal cell carcinoma, and was critical to appropriate patient management in this case [11, 16].

In order to understand the significance of fat within angiomyolipomas and renal cell carcinomas, it is helpful to recognize that renal cell carcinoma, particularly of the clear cell type, may contain intracytoplasmic lipid within the neoplastic cells. Angiomyolipomas contain fat cells that, by their very nature, also contain intracytoplasmic lipid. In both cases, water molecules and lipid molecules coexist within MRI voxels. As a result, the finding of intracytoplasmic lipid (sometimes referred to as microscopic fat) using chemical shift MR imaging cannot be used alone to differentiate angiomyolipoma from renal cell carcinoma. On the other hand, frequency-selective, fat-suppression techniques enable detection of fat cell aggregates that result in MRI voxels containing abundant lipid but almost no water molecules. Fat-suppres-

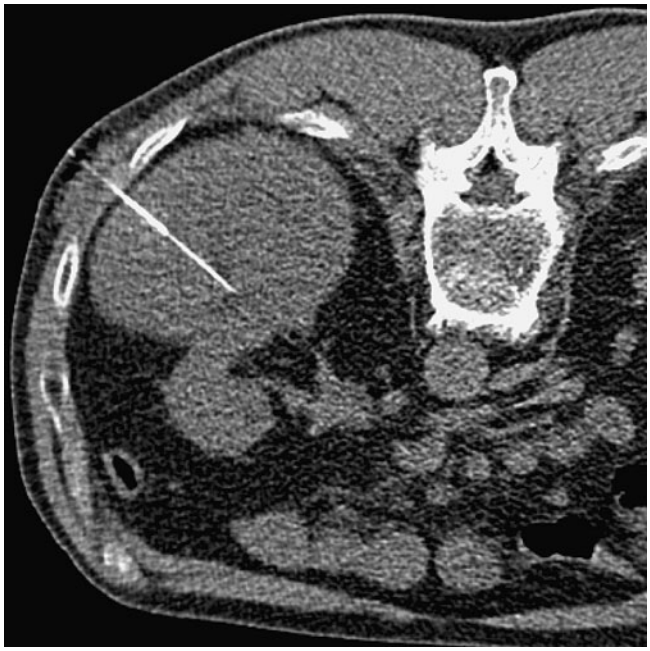

Fig. 3. Intraprocedural CT fluoroscopic image obtained with the patient in prone position reveals a 25-gage biopsy needle inserted through an introducer, sampling soft tissue elements contained within the left renal mass.

sion techniques are more reliable in identifying fat cell aggregates in a renal mass and thus facilitate the differentiation of angiomyolipoma from renal cell carcinoma.

Nevertheless, the finding of macroscopic fat, using CT attenuation values of −10 HU or less, or frequency-selective fat suppression, is also not fully diagnostic of an angiomyolipoma since renal cell carcinoma may rarely contain fat cell aggregates also. There are several currently accepted mechanisms by which renal cell carcinomas may appear to contain macroscopic foci of lipid attenuation (−20 to −120 HU), or evidence of fat cells. First, renal cell carcinomas may grow to engulf and thereby incorporate perirenal or renal sinus fat into the mass [17]. Although the images may suggest that the lesion contains fat, it intrinsically does not, and hence when considering only those pathophysiologic mechanisms that result in the tumor containing foci of internal lipid density, there are only three heretofore described explanations [3, 5, 18]. Tumor necrosis may lead to the formation of cholesterol clefts and lipid vacuoles from precipitated cellular debris [5, 17]. Some of these areas may become confluent and sufficiently large to be detected radiologically. Fat cells in most renal cell carcinomas are thought to be secondary to cholesterol necrosis [5]. Second, as suggested by Davidson in the first report of a patient with a fat cell-containing renal cell carcinoma, necrotic elements within a rapidly growing carcinoma can result in scar formation with associated dystrophic calcification. In turn, this process may lead to the development of osseous metasplasia and eventually bone-forming elements, including marrow fat [18]. The third and least commonly reported mechanism is the development of well-defined nodules of mature adipose tissue (clusters of fat cells) in the absence of closely associated calcifications or other findings to indicate osseous metaplasia. This mechanism could explain the findings in our patient but is indeed rare. To our knowledge, only two other such patients have been previously reported. In the first described case, multiple small regions of fat attenuation were noted within a renal mass without imaging evidence of calcification; however, microscopic calcifications were ultimately present on

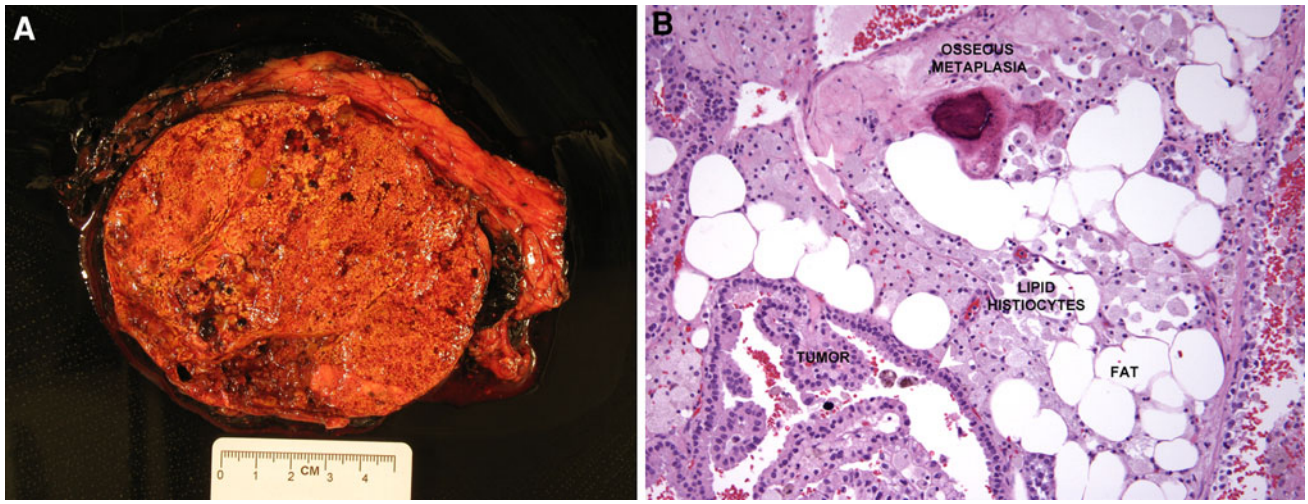

Fig. 4. Cut section through the tumor specimen (**A**) reveals a 13.0-cm encapsulated mass with multifocal regions of hemorrhage as well as visible islands of well-defined fat (*arrowheads*). Photomicrograph through a representative portion of the mass (**B**) demonstrates mature adipocytes (*FAT*) intermixed with foci of osseous metaplasia, lipid-laden histiocytes and papillary tumor. Original magnification ×20.

histology. As in our patient, the carcinoma was of the papillary subtype [2]. A more recent report of a fat-containing clear cell renal cell carcinoma showed subtle, sparse areas of fat attenuation without radiographic evidence of calcification. Histology demonstrated regions of osseous metaplasia associated with the fatty elements [8]. In our patient, osseous metaplasia was found to be present, but most of the fat cells in the mass were not located in regions of metaplasia.

Our patient's tumor contained lipid-laden macrophages, both at cytology and confirmed with histologic evaluation at nephrectomy; this is a common histologic feature and is seen in approximately two-thirds of patients with papillary renal cell carcinoma [16]. Theoretically such a phenomenon could lead to macroscopic regions of fat attenuation on CT or frequency-selective suppression at MRI, but it is certainly uncommon, likely because the lipid-laden macrophages usually do not sufficiently exclude water molecules from the imaging voxels. However, radiologic–pathologic correlation showed that this mechanism could not provide an explanation of our patient's abundant regions of fat attenuation as the observed fatty regions were characterized by adipose tissue, or clusters of mature fat cells.

In conclusion, while it is recognized that renal cell carcinomas may contain imaging findings that suggest the presence of fat cell aggregates, or macroscopic fat, prior reports have only included renal masses with small amounts of fat that in all but two cases were adjacent to regions of tumoral calcification. Although additional clues such as tumor size, lack of marked enhancement, and presence of calcifications all warranted including renal cell carcinoma in the differential diagnosis, our patient is relatively unique in that the amount of fat was abundant and not in close proximity to the sparse calcifications seen on CT. Radiologic–pathologic correlation also allowed us to better understand the multiple pathophysiologic mechanisms of why renal cancer may contain fat cells or macroscopic fat.

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