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Mucin-secreting clear cell renal cell carcinoma. A rare variant of conventional renal cell carcinoma☆

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ABSTRACT

We report herein one case of conventional renal cell carcinoma (RCC) producing extensive extracellular mucinous secretion in a 71-year-old man. To the best of our knowledge, the presence of mucinous secretion in this tumor has not been documented. Mucin production, despite its low frequency, can be considered an additional feature of conventional RCC. Therefore, clear cell RCC should be added to the list of parenchymal renal tumors that can show significant mucin secretion; and it should be included in the inventory of morphologic variations of this tumor, which may cause diagnostic difficulties. It is of primary importance to distinguish mucin-secreting clear cell RCC from the metastasis of a mucin-secreting tumor to conventional RCC. Presence of mucin in a clear cell carcinoma does not exclude a renal origin.

1. Introduction

Clear cell (conventional) renal cell carcinoma (RCC) may present unusual morphologic features including intra- and extracellular hyaline globules [1], structures resembling Mallory bodies [2], neuromelanin [3], melanin-like pigment [4], basophilic cytoplasmic granules [5], myospherulosis [6], rhabdoid morphology [7], intranuclear inclusions and nuclear grooves [8], syncytial giant cells [9], focal papillary/pseudopapillary architecture [10], heterotopic bone formation [11], sarcoid-like granulomas [12], lymphomatoid features [13], colonization by metastatic tumor [14], and presence of Gamna-Gandy bodies [15].

We report herein one case of clear cell RCC producing diffuse extracellular mucinous secretion. To the best of our knowledge, the presence of extensive mucinous secretion in this tumor has not been documented.

2. Case report

A 71-year-old man was referred to the urology service for a large right renal neoplasm diagnosed by ultrasound examination. Medical history was remarkable for type 2 diabetes mellitus, pulmonary tuberculosis, and essential arterial hypertension. The patient had been a severe smoker. Computed tomography scan of the abdomen and thorax showed a solitary, circumscribed, nonhomogeneous, 10-cm mass located in the upper pole of the right kidney and various nodules in both lungs suggestive of tumor metastases. A right nephrectomy was performed, and the patient was discharged without complications.

2.1. Pathologic findings

The surgical specimen weighed 1020 g with attached perinephric adipose tissue and measured 18 × 9 × 6 cm. The upper pole was distorted by a 10 × 8.5 × 8 cm, well-circumscribed, bulging tumor variegated in color, from yellow to tan and brown with dark areas of hemorrhage and whitish areas of stroma. The tumor invaded adipose perirenal tissue and extended into renal vein (Fig. 1).

The renal specimen was fixed in 10% buffered neutral formalin and embedded in paraffin after standard procedure. Deparaffinized sections were stained with hematoxylin and eosin. Selected sections were stained with Mayer's mucicarmin, Alcian blue–periodic acid Schiff (PAS), pH 2.5, Alcian blue, pH 0.4, and Mowry's colloidal iron stain. Other selected sections were immunostained using the Dako FLEX Ready-to-Use System (Dako, Glostrup, Demmark) and an automated immunostainer (AutostainerLink 48, Dako). The primary antibodies used were: CD10 (clone 56C6, prediluted, Dako), epithelial membrane antigen (EMA, clone E29, prediluted, Dako), cytokeratin (clone AE1/AE3, prediluted, Dako), cytokeratin 7 (CK7, clone OV-TL 1230, prediluted, Dako), RCC marker (clone SPM314, prediluted, Dako), AMACR (P504S, clone 13H4, prediluted, Dako), and vimentin (clone V9, prediluted, Dako). For pretreatment, a retrieval solution (Dako) at pH 9 was used. Appropriate controls were included.

Conventional histopathologic preparations showed a neoplasm with clear cells arranged in alveolar nests, small aggregates, and tubules interspersed by a prominent network of delicate blood

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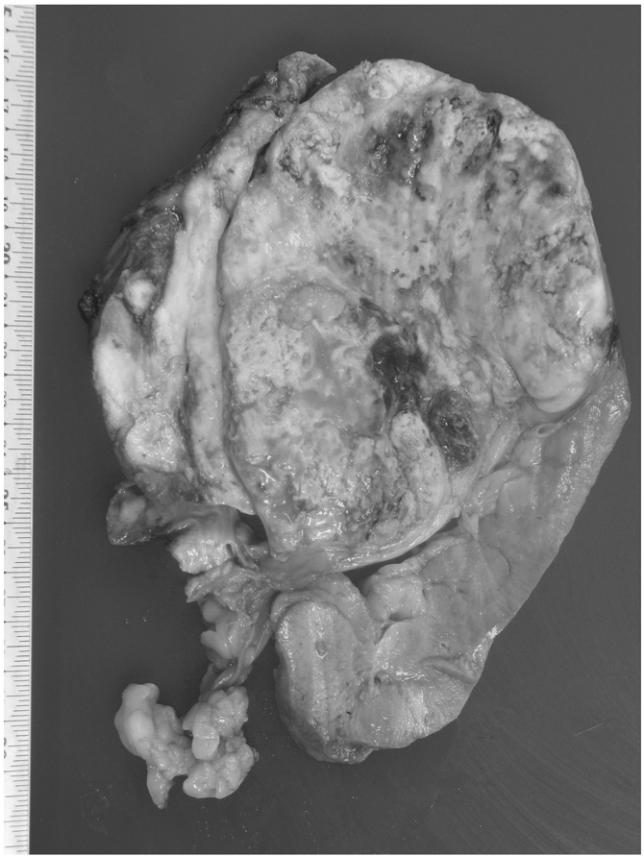

Fig. 1. Clear cell RCC. A large polar tumor with a variegate appearance is bulging into the perinephric adipose tissue.

vessels. Alveoli often had spaces containing abundant basophilic mucin (Figs. 2 and 3A). Intracytoplasmic mucin was occasionally observed. Tumor cells had clear-water cytoplasm surrounded by a distinct cell membrane. Nuclei had finely granular chromatin and conspicuous nucleoli. Prominent nuclear pleomorphism, hyperchromasia, and macronucleoli were seen in some areas. Necrosis occurred in 25% of the neoplasia.

Presence of mucin secretion was observed in most of the slides obtained (60%). The mucin stained strongly in dark rose with Mayer's mucicarmin (Fig. 3B), and in blue with Alcian blue-PAS at pH 2.5 (Fig. 3C), and Mowry's colloidal iron (Fig. 3D). The presence of strongly acidic sulfated mucosubstances was demonstrated with Alcian blue at pH 0.4.

Tumor cells showed intense, diffuse, membranous immunoreaction for CD10 (Fig. 4A) and EMA; intense, diffuse positivity of membrane and cytoplasm for AE1/AE3 cytokeratin and RCC marker; focal positivity for AMACR in high-grade areas; and scattered cytoplasmic reactivity in groups of cells for vimentin (Fig. 4B). CK7 was negative.

3. Discussion

Presented here is a unique case of mucin-secreting clear cell RCC. The mucin was strongly acidic, sulfated, extracellular, and diffuse. The type of mucin is similar to that of the colonic epithelium, but the tumor cells did not display morphology of intestinal cells. Mucin secretion on this tumor can be ascribed to cellular modulation [16]. Under appropriate stimuli, these modulated cells are adapted to secrete mucin and remain recognizable as members of their cell type. However, the stimulus for this change was not apparent in our case.

Renal adult tumors with significant extracellular mucin production include tubulo-papillary adenoma [17], oncocytoma [18], papillary RCC [19], mucinous tubular and spindle cell carcinoma [20], collecting duct carcinoma [21], low-grade collecting duct (tubulocystic) carcinoma [22], renal medullary carcinoma [23], and unclassified carcinoma [24,25].

Therefore, clear cell RCC should be added to the list of renal tumors that can show significant mucin secretion. Besides, some of these tumors such as papillary RCC [10], mucinous tubular and spindle cell carcinoma [26], or low-grade collecting duct (tubulocystic) carcinoma [27] can show focal clear cell features. Furthermore, mucinous tubular and spindle cell carcinoma may be tubular predominant [26]. All these features must be considered and evaluated in the differential diagnosis. On the other hand, classic chromophobe RCC may show strong diffuse cytoplasmic positivity with colloidal iron stain, indicating a content of mucopolysaccharides unique to this type of RCC. Besides, the histologic pattern and the immunohistochemical profile are different from conventional RCC.

Tumor-to-tumor metastases are uncommon. RCC is by far the most common recipient of metastases. Differential diagnosis between clear cell RCC with mucin secretion and metastasis of mucin-secreting tumors to conventional RCC [14] can be challenging, but it is crucial from the point of view of postoperative therapy and prognosis. Clinical information and immunohistochemical panel studies are requisite [14].

Mucin is at most rare in conventional RCC and some would categorize the present tumor as unclassified. However, both the histologic appearance and the immunohistochemical pattern correspond with the features of the common clear cell RCC.

Clear cell RCC represents approximately 90% of the renal carcinomas that metastasize. Thus, the presence of mucin in a metastatic tumor does not exclude a possible renal origin.

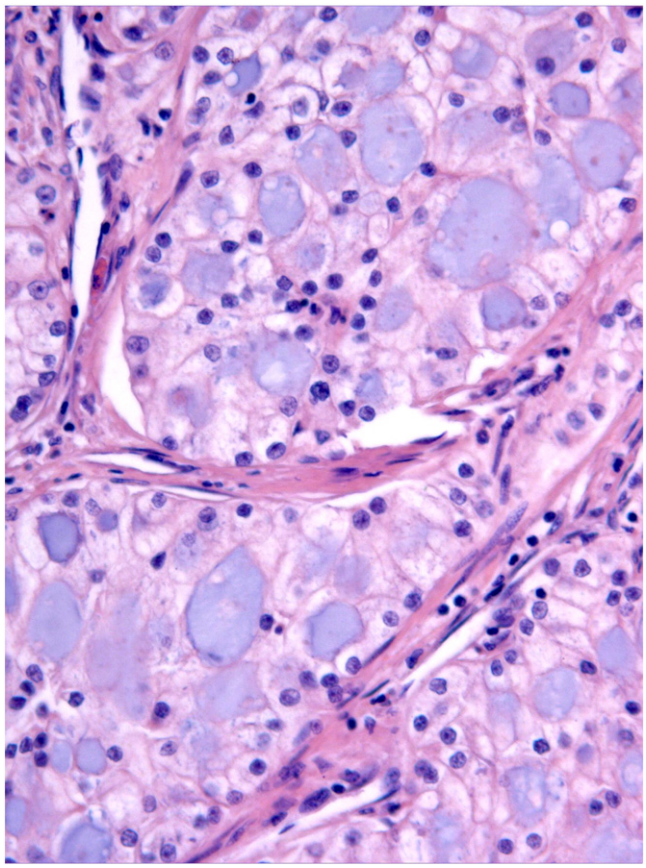

Fig. 2. Mucin-secreting clear cell RCC. Presence of intraluminal mucin (hematoxylin and eosin stain, original magnification ×200).