Case Report

Collecting-duct carcinoma of the kidney with prominent signet ring cell features

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ABSTRACT

Collecting-duct carcinomas (CDCs) comprise approximately 1% of renal epithelial malignancies. We report a case of collecting duct carcinoma with prominent signet ring cell features in a 60-year-old man. Grossly, the tumor measured 7.5 cm in greatest dimension, occupied the entire lower pole of the kidney, and was well-circumscribed. Microscopically, it displayed a predominant tubulopapillary pattern of growth with a desmoplastic stroma. The tumor tubules were lined by a single layer of cells with large, pleomorphic nuclei, some of which had a hobnail appearance. Large intracytoplasmic vacuoles with compression of nuclei (signet ring cells) were present throughout the tumor. Alcian blue, mucicarmine, and periodic acid–Schiff stains failed to identify intracellular mucin or glycogen in the signet ring cells. The tumor cells were immunohistochemically positive for cytokeratin (cytokeratin 7) and vimentin. To the best of our knowledge, this is the second reported case of renal CDC with prominent signet ring cell features.

Keywords: Collecting-duct carcinoma, intracellular edema, kidney, signet ring cell

INTRODUCTION

Collecting duct carcinoma is a recently recognized, rare histological variety of renal carcinoma (RC) considered to arise from the epithelium of the collecting ducts. Diagnosis of this entity depends on well-defined gross and microscopic criteria and is supported by a characteristic immunostaining pattern. The clinical features of these patients, the natural course of the disease and its response to treatment have not been clearly established. We report an additional case of CDC in a 60-year-old male. To the best of our knowledge, this is the second reported case of renal CDC with prominent signet ring cell features.[1]

CASE REPORT

A 60-year-old male presented to a surgical OPD with complains of pain in abdomen and lower back ache since 1 year. There were two bouts of hematuria since then. As per abdominal examination, there was a ill-defined lump in the right lumbar region. Abdominal ultrasonography and CT scan revealed a tumor measuring 7 × 7 cm in the lower pole of the right kidney. Radiological diagnosis of renal cell carcinoma was made. The patient underwent right radical nephrectomy.

Gross examination revealed a well-circumscribed, firm tumor measuring 7.5 × 7.0 × 7.0 cm occupying almost the entire lower pole of the right kidney. The cut surface of the tumor was whitish yellow with focal areas hemorrhage and microcysts. Normal renal parenchyma was identified at the upper pole. The tumor was confined to the kidney and did not invade the renal vessels or the pelvis. Microscopically, the tumor was well-demarcated from the surrounding kidney and partially surrounded by dense, fibrous tissue. It displayed predominantly a tubulopapillary pattern of growth [Figure 1]. The tubules were lined by a single layer of cuboidal to columnar cells. Pale luminal secretion was infrequently present. The nuclei were intermediate to large in size and varied from round to oval with moderate pleomorphism and prominent nucleoli. The most prominent feature was the presence of variably sized intracytoplasmic vacuoles, some of which compressed the nuclei, resulting in a signet ring appearance in many tumor cells [Figure 2]. The amount of cytoplasm in the cells without cytoplasmic

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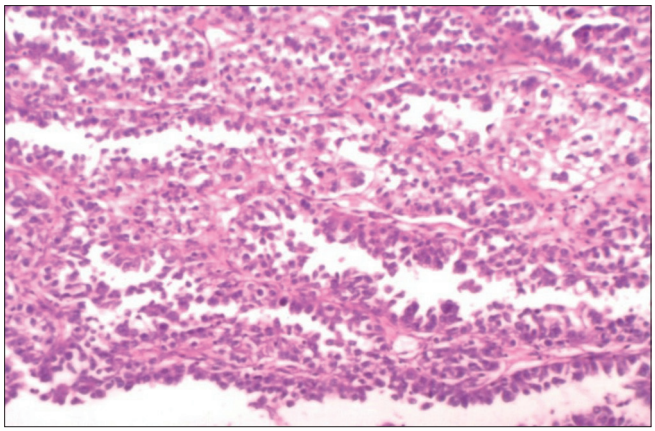

Figure 1: Photomicrograph showing tumor cells arranged in tubulopapillary pattern (H and E, 20x)

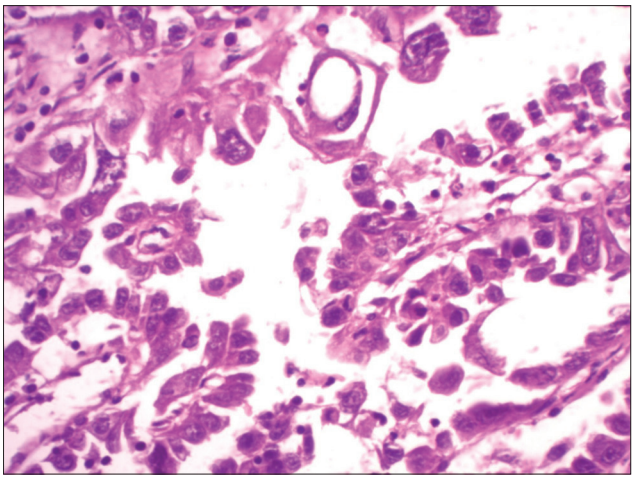

Figure 2: Higher magnification revealing hobnail cell lining the tubules and a signet ring cell (H and E, 40x)

vacuoles was scanty to moderate, and some cells lining the tubules displayed a hobnail appearance [Figure 2]. A minor solid pattern (about 10% of the tumor) was present in several areas and associated with slightly spindled tumor cells and pleomorphic nuclei (Fuhrman Grade 4). Mitoses were only infrequently seen. Areas of tumor necrosis and aggregates of foamy histiocytes, lymphocytes, and plasma cells were present throughout the entire tumor. There was a marked desmoplastic reaction.

DISCUSSION

Collecting-duct carcinoma was first described in 1949 and was recognized as a separate entity of renal cell carcinoma in 1986.[2] Collecting-duct carcinomas comprise approximately 1% of renal epithelial malignancies.[3] These tumors are now being recognized as an aggressive form of renal neoplasia and are often present with advanced stage disease.[3]

They have been described as occurring in a wide patient age range, but generally affect patients in the 4th to 7th decades (mean age 55 years), with a male predominance of approximately 2:1. These tumors are frequently symptomatic, with typical presenting features being one or more of the classic renal tumor triad of hematuria, abdominal mass and intermittent flank/back pain, and also fatigue and weight loss. The frequency of symptomatic presentation of these tumors reflects their rapid growth and early metastatic spread, with approximately one-third of patients being shown to have metastases at the time of diagnosis.

Evidence of a collecting-duct origin for these tumors is that when small, the primary tumor was usually confined to the renal medulla. Despite this, these tumors are usually of large size when diagnosed and involve both the renal cortex and medulla. Typically CDCs are white to gray and have a firm consistency on sectioning. Tumor necrosis is typically present although hemorrhage is not usually seen macroscopically. These tumors may extend into the renal pelvis.

The microscopic features of CDC may be somewhat variable, however, the morphologic criteria for diagnosis are the presence of an infiltrative tubular or tubulopapillary pattern, associated with a desmoplastic stromal reaction. The tumor cells typically exhibit a high grade of nuclear pleomorphism and nuclear atypia is seen in the epithelium of adjacent renal tubules.[4] Mitotic figures are frequently present and histochemically both acid and neutral mucin may be seen.[5] In addition to the tubulopapillary architecture, these tumors may also contain compact papillary structures, solid sheet-like areas of tumor cells and microcysts. Occasionally foci of spindle cells may be present, however, if this is more than a rare occurrence, the tumor should be considered to be a sarcomatoid carcinoma arising within a collecting-duct carcinoma. There is usually an associated chronic active inflammatory cell infiltrate in and adjacent to the tumor, and in some cases a neutrophilic infiltrate can be quite pronounced. Tumor architecture may be recapitulated in extra-renal metastases.

Although mucin production, either intraluminal or intracellular, has been reported in most CDC's,[1] to the best of our knowledge, signet ring cells have not been described in renal cell carcinoma, including CDC. To our surprise, the signet ring cells did not contain mucin, as evidenced by the negative staining for mucicarmine, Alcian blue, and periodic acid–Schiff and by the absence of mucinogens ultrastructurally. In a similar case described by Li *et al.*,[1] no significant number of fat droplets or glycogen granules was detected in electron microscopy to account for the empty cytoplasmic vacuoles. The pathogenesis of these intracytoplasmic vacuoles is not entirely clear. One possible

cause is artifact. Signet ring-like changes attributable to biopsy and formalin fixation have been found in lymphocytes and smooth muscle cells in transurethral resection specimens of the prostate, gastric lymphoma, and gastrointestinal stromal tumor.[6] We cannot completely rule out the possibility of retraction artifact in our case because tissue sections taken for both histological and ultrastructural studies were formalin fixed. The fact that similar change was not present in the non-neoplastic cells, including the benign tubular epithelium, and that signet ring morphology has not been observed by other authors in the same type of tumor suggests that this is a very rare phenomenon. Li *et al*.[1] favor an interpretation that the intracytoplasmic empty spaces revealed by light and electron microscopy are probably the results of intracellular edema and degeneration, which displaced most of the organelles.

The differential diagnosis of collecting-duct carcinoma includes papillary renal cell carcinoma, renal medullary carcinoma, metastatic carcinoma and urothelial carcinoma with glandular differentiation. Papillary renal cell carcinoma usually only poses a problem if it is of high grade, but usually lacks the desmoplasia and infiltrative pattern typical of CDC. Immunohistochemical staining can be useful in differentiating between these two tumor types with papillary renal cell carcinoma frequently showing positivity for CD10, AMACR and RCC antigen. Medullary carcinoma may show a morphologic overlap with CDC, but usually exhibits reticular and solid patterns of growth. The constant association with sickle cell trait and young patient age at diagnosis are further indicators in favor of a diagnosis of medullary carcinoma. Metastatic adenocarcinoma should always be considered in the differential diagnosis of these tumors, as there is usually a marked desmoplastic response to tumor associated with a brisk inflammatory cell infiltrate. A previous history of malignancy may be of diagnostic assistance and appropriate clinical and immunohistochemical investigations should be undertaken to further characterize tumors as metastatic rather than primary.

The immunohistochemical expression of CDC reflects the origins of the tumor from the collecting duct of the distal nephron. Tumors usually show positive reactions to lectins such as *Ulex europeaus* agglutinin-1 and peanut lectin, also e-cadherin, c-KIT, and both high and low molecular weight cytokeratins. Vimentin staining of tumor cytoplasm may also be present. There is a variable expression of Leu M1 and EMA, whereas markers of proximal renal tubules (CD10, RCC antigen, and AMACR) are almost always negative.[7]

Most CDCs are clinically aggressive, frequently resulting in death.[8,9] However, a group of low-grade CDC with favorable outcome has also been proposed,[10] suggesting a morphological as well as biological spectrum of the tumor.[9]

For the majority of patients surgical treatment will not result in a cure. Previously recommended chemotherapy and/or immunotherapy appears to have a limited role in treatment of this disease, and early detection may be the best method for prolonging patient survival.[11]

CONCLUSION

Identification of the CDC has important diagnostic and potentially prognostic ramifications. The diagnostic process should involve meticulous attention to the architectural, histologic, and immunohistochemistrical findings. Caution should be exercised when infiltrative nature, stromal desmoplasia, dysplasia in adjacent collecting ducts, and expression of high molecular weight cytokeratin are present, and their acceptance should be contingent on the presence of otherwise characteristic histoarchitectural features of CDC.

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