

Metastatic Collecting (Bellini) Duct Carcinoma Presented in a Young Patient: A Case Report and Review of the Literature

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Collecting (Bellini) duct carcinoma (CDC) of the kidney is a highly aggressive tumor with an extremely poor prognosis. It arises from the distal segments of the collecting ducts of Bellini in the renal medulla, unlike conventional renal cell carcinoma (RCC), which occurs in the epithelial cells of the proximal tubules of the renal cortex. CDC accounts for less than 2% of all renal masses [1].

CDC occurs more frequently in males. Tokuda and colleagues [2] conducted the largest CDC study in Japan involving 81 histologically confirmed cases and found the median age at presentation to be 58.2 years. Clinical presentation includes abdominal pain, flank mass, and hematuria. Associations with deep vein thrombosis, syndrome of inappropriate antidiuretic hormone secretion, and leukocytosis secondary to increased granulocyte-colony stimulating factor production have also been reported.

In diagnosis of CDC, it is important to distinguish between invasive papillary RCC and urothelial carcinoma. Positive immunohistochemical staining for distal tubules and collecting duct markers is helpful to discriminate CDC from the more commonly diagnosed clear cell

RCC, which is of proximal nephron origin [3].

In about 40% of cases, CDC is metastatic at presentation. Common metastatic sites include the lungs, liver, adrenal glands, bones, and lymph nodes. The overall 2 year survival of CDC is unfavorable, ranging from about 20% to approximately two-thirds of cases [1].

We present a case of metastatic CDC in a young patient. To the best of our knowledge, this is the fifth such case occurring in a patient younger than 35 years of age.

PATIENT DESCRIPTION

A 32 year old male with no prior relevant clinical history presented to the emergency department of the Sheba Medical Center (Israel) with complaints of intermittent fever, back pain, and pain in his right leg for 2 weeks. Physical examination was generally unremarkable. Initial laboratory inves-

tigations revealed hemoglobin 8.8 mg/dl, C-reactive protein 236 mg/L, and D-dimer 2163. A contrast enhanced computed tomography (CT) scan of the abdomen showed multiple hypodense lesions ranging from 0.5–2.5 cm in the liver and spleen and a focal poorly defined infiltrative mass involving the right kidney [Figure 1], multiple retroperitoneal lymph nodes and thrombi in the inferior vena cava as well as in the common iliac and right internal iliac veins. A chest CT showed numerous pulmonary nodules and small bilateral pleural effusions. In addition, whole body ¹⁸fluorodeoxyglucose-positron emission tomography/CT (¹⁸FDG-PET/CT) showed evidence bone marrow involvement. Magnetic resonance imaging of the brain was reported as normal.

The patient proceeded to have a liver biopsy, which was inconclusive. A splenic biopsy demonstrated poorly differentiated adenocarcinoma of renal origin.

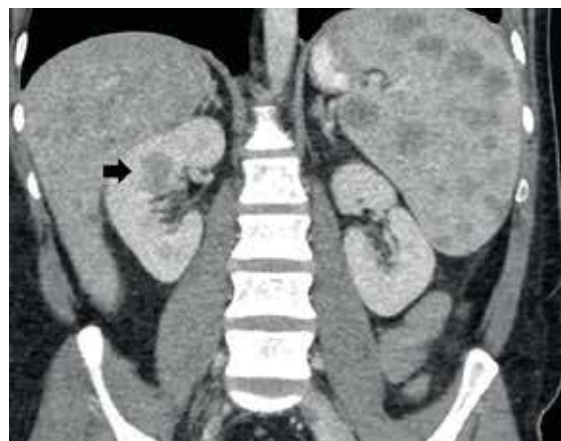


Figure 1. Coronal computed tomography image reformation showing multiple hypodense metastases in the liver and spleen. The right kidney shows an infiltrating hypodense lesion (arrow) in the renal medulla, extending to the cortex

Immunohistochemical analysis revealed the tumor cells to be strongly positive for CK19, MNF116, and PAX8, and focally positive for CK7, MUC1, and vimentin. CK20, TTF1, PSA, CEA, P501s, HEPA, inhibin, napsin A, GATA3, mammaglobin, CDX2, and MUC2 were all negative. The immune profile was concluded as being compatible with CDC of the kidney.

Based on the clinical, radiological, and immunohistochemical analyses, the patient was started on gemcitabine and cisplatin combination chemotherapy. No significant clinical improvement was seen after completion of chemotherapy.

COMMENT

CDC is a rare type of renal cell carcinoma, with a tendency toward early dissemination and metastasis. The clinical presentation is nonspecific and could apply to any renal malignancy. In a multi-center nationwide study conducted by Tokuda and co-authors, 37% of patients presented with gross hematuria, 23.5% with back pain, and 8.6% general fatigue. The median age of presentation was 58.2 years [2]. CDC has been reported in patients ranging from 11 to 82 years of age, males being the predominant gender affected. After reviewing the literature, we found only four other cases in patients younger than 35 years of age [3,4].

Metastasis at presentation can be found in up to 40% of patients with CDC [1]. Our patient had metastasis to his liver, lungs,

spleen, bone marrow, and lymph nodes, with tumor thrombus in the vena cava and iliac veins.

Cross-sectional imaging findings may suggest the diagnosis of collecting duct carcinoma. This includes CT scan findings of a hypodense infiltrating renal mass, typically involving the renal medulla with a true cystic component as opposed to most renal tumors which are expansile and show the presence of a pseudocapsule.

Due to the nonspecific nature of the clinical presentation and imaging findings, a definite diagnosis of collecting duct carcinoma is therefore made by histology and immunohistochemistry. Immunohistochemical markers include lectin *Ulex europaeus*, epithelial membrane antigen, and high-molecular weight cytokeratins. Vimentin reactivity is variable. These stains were used to make a definitive diagnosis in our case.

Tumors of the lung and breast commonly metastasize to the kidneys. However, this is uncommon in young patients. Metastasis from lymphoma to the kidneys is the third most common after lung and breast cancer, and should be included in the differential diagnosis of young patients with collecting duct carcinoma.

Treatment options for CDC include surgery, chemotherapy, and immunotherapy. In our case, chemotherapy was the option chosen, using the gemcitabine and cisplatin regimen. The effectiveness of a gemcitabine-cisplatin regimen has been demonstrated to induce a 26% (95%

confidence interval 8%–44%) objective response rate in CDC. Given the lack of any other beneficial agent, a gemcitabine-cisplatin regimen should be considered the standard of care for first-line systemic treatment of metastatic CDC [5].

CONCLUSIONS

CDC is a rare subtype of RCC, which usually presents at an advanced stage and has a very poor prognosis. In young patients presenting with extensive metastatic disease involving the kidneys, CDC should be included in the list of differential diagnoses.

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Capsule

Unintentional immunotherapy inhibition

Metastatic spread depends on lymphangiogenesis, and mediators of this pathway are targeted clinically for cancer treatment. **Fankhauser** and colleagues used mouse models of melanoma to show that blocking lymphangiogenesis disrupted recruitment of naïve T cells and subsequent antitumor immunity. Data from patients enrolled in clinical

trials confirmed that indicators of lymphangiogenesis were associated with robust T cell responses. These findings have important implications for using and predicting responses to immunotherapy.

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Eitan Israeli

“My country, right or wrong; if right, to be kept right; and if wrong, to be set right”

Carl Schurz, (1829–1906), German revolutionary, American statesman and reformer