CLINICAL VIGNETTE

Primary Clear Cell Adenocarcinoma of the GU Tract

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A 53-year-old male with hypertension and DJD presented with cmplains of abdominal cramps, loss of appetite and abdominal bloating. CT of the abdomen and pelvis revealed a large right mid abdominal mass, measuring 10 x 14 x 16cm, extending into the lower pelvis, just above the bladder and displacing bowel loops. A smaller right lower pelvic mass measuring 3.7 x 5.7 cm was also noted. This was thought to be in the region of the right vas deferens, with extension and invasion of the seminal vesicle and prostate not excluded. Multiple pelvic, mesenteric and retroperitoneal lymph nodes also present, largest 12 mm. A 3 - 4 mm nodule in left lower lobe of the lung was noted. Fecal occult blood testing was positive, and recent HIV testing was negative. HCV antibody screen negative and labs also were suggestive of iron deficiency anemia.

Patient reported he could feel a right lower quadrant mass with discomfort. He had no changes in bowel movements or urination and no bleeding. He reported 4-5 pound weight loss in the last month with decreased appetite but no nausea, vomiting, diarrhea or fevers.

He was evaluated by Gastroenterology for a colonoscopy and the mass was thought to be extramural. No other mass or lesion identified in kidneys, ureters, bladder or prostate on multiple imaging. Interventional Radiology performed a CT guided biopsy. Pathology revealed adenocarcinoma with the top differential diagnosis being clear cell adenocarcinoma (of lower urinary tract, likely müllerian origin). The carcinoma was composed of single to multiple layers of cuboidal malignant epithelial cells, with amphophilic to focally clear cytoplasm, arranged in papillary and tubulocystic architecture. Focally lesional cells exhibited hobnail cytology. There was some hyalinization of papillary fibrovascular cores. Extensive tumor necrosis was present. Tumor cells were positive for PAX8, napsin A, HNF1β, and cytokeratin 7. Other differential diagnoses included adenocarcinoma arising in a germ cell tumor, and mesonephric adenocarcinoma. Given the absence of apparent mass in bilateral kidneys, metastatic renal cell carcinoma was unlikely.

Tumor makers including AFP, Beta HCG and CEA were all within normal range. He then presented to the hospital complaining of progressive abdominal pain. CT abdomen and pelvis revealed a 17.5 x 12.0 cm mass with necrosis and numerous gas bubbles, suspicious for fistulization. Patient underwent small bowel resection for bowel obstruction. Pathology revealed a 7.5 cm tumor classified as clear cell adenocarcinoma, with the morphology identical to the lesional cells detected by the biopsy. There was no precursor lesion seen. No associated müllerian remnant or nephrogenic adenoma identified. The Immunohistochemistry stains demonstrated a similar profile, showing tumor cells expressing PAX8, napsin A, cytokeratin 7 and wild-type pattern of p53 protein, negative for markers for mesonephric adenocarcinoma, germ cell tumor, urothelial carcinoma, and prostatic adenocarcinoma. The pathology diagnosis was clear cell adenocarcinoma, potentially originated from embryonic remnants or lower genitourinary tract. The resection specimen, included two regional lymph nodes with metastatic carcinoma.

This hospitalization was prolonged and complicated by BLE DVTs, DIC and acute renal failure requiring dialysis. Renal function recovered prior to discharge. He was placed on apixaban for BLE DVTs.

Repeat PET/CT after discharge revealed overall interval increase in size and number of multiple, at least 15, soft tissue masses and nodules within the pelvis and abdomen with broad base contact and mass effect of the adjacent structures with intense FDG uptake some demonstrating central photopenia compatible with necrosis. Many of the masses within the pelvis abut and demonstrate mass effect on the adjacent colon and small bowel with possible invasion and with limited evaluation due to the lack of intravenous contrast. Some of the nodules and masses are within nodal stations, for example left iliac and mesenteric, suggestive of nodal metastatic disease. Right posterior and inferior pelvic soft tissue mass measures 65 x 48 mm, previously 55 x 41 mm. Left upper quadrant soft tissue mass measures 36 x 25 mm, previously 14 x 10 mm.

Final diagnosis was of clear cell adenocarcinoma, potentially originated from embryonic remnants or lower genitourinary tract

Comprehensive cancer panel revealed TERT promoter site mutation c.-124 C>T, variant of unknown significance NOTCH3. MSI not detected and TMB low 3muts/Mb.

He was started on palliative carboplatin and paclitaxel. After 3 cycles, he was readmitted with intractable abdominal pain and

was found to have right hydronephrosis. This improved with placement of right nephrostomy tube. CT abdomen and pelvis revealed progressive disease. He was re-admitted several times, with multiple complications, including malfunctioning nephrostomy tube, abdominal pain and GU infections. His performance status continued to decline and opted for palliative care.

Primary clear cell adenocarcinoma of the GU tract is a rare variant of GU tract malignancies, mostly arising in the urethra or the bladder.[1] The mean age at presentation was 58 years. Although the female to male ratio varies among different sites, it exhibits strong female predominance.[2] The largest case series in males reported 15 cases, mostly arising in the bladder, urethra, and prostate.[3] They usually present with obstructive symptoms and hematuria. Two distinct characteristic histopathologic features of this carcinoma are hobnail cells and abundant clear cytoplasm.[1] Tumor cells typically express PAX8 and HNF1β. Due to the rarity of this malignancy, data regarding treatment is limited and there is no standard. When presentation is of early stage localized disease, surgical resection is the primary therapy. Platinum based chemotherapy has been generally utilized for advanced disease. The clinical course is generally aggressive. The 5-year overall survival rate in both genders were 39.3% -41%. In male patients, the mean time to death was 16 months (range: 6 to 39 mo).[3]

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