Spotting the Deceiver: Metastatic Urothelial Carcinoma to the Liver Masquerading as a Well-Differentiated Neuroendocrine Tumor Histologically

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Introduction

- Urothelial carcinoma is a highly lethal malignancy in the metastatic state and is the sixth most common cancer in the United States, which is likely due to exposure to multiple known risk factors such as, aromatic amines, tobacco smoke, and benzene.
- Metastatic urothelial carcinoma (UC) of the bladder is generally considered an aggressive disease with the potential to metastasize to lymph nodes, bones, lungs, liver, and peritoneum.
- Metastatic disease also carries a worse prognosis compared to non-muscle invasive disease, with a 5-year overall survival of 6% vs. 90%, respectively.
- Platinum-based chemotherapy has been the backbone of first line treatment for patients with advanced UC and single-agent immune checkpoint inhibitors (ICI) are the standard of care for patients following progression on chemotherapy.
- To further complicate the matter, the treatment landscape of metastatic disease, especially that which is unresponsive to first-line platinum-based chemotherapy agents, is largely still an area without clearly defined guidelines.
- The accurate diagnosis of metastatic urothelial carcinoma is challenging especially in the setting of histological mimickers.
- Without pathological expertise and additional immunohistochemistry, metastatic tumors could remain incorrectly diagnosed and delay therapeutic intervention.

Case Report

- Herein, we describe a 62-year-old man who presented with jaundice, elevated LFTs, diffuse abdominal pain, and early satiety.
- MRI imaging of the abdomen revealed a hilar hyperintense mass involving the common bile duct, bilateral hepatic ducts causing narrowing, a 1.1 cm mass in segment 6, and hydroureteronephrosis with thickening of the renal pelvis.
- The clinical differential diagnosis included cholangiocarcinoma and other tumors including a metastatic neuroendocrine tumor (NET).

Results

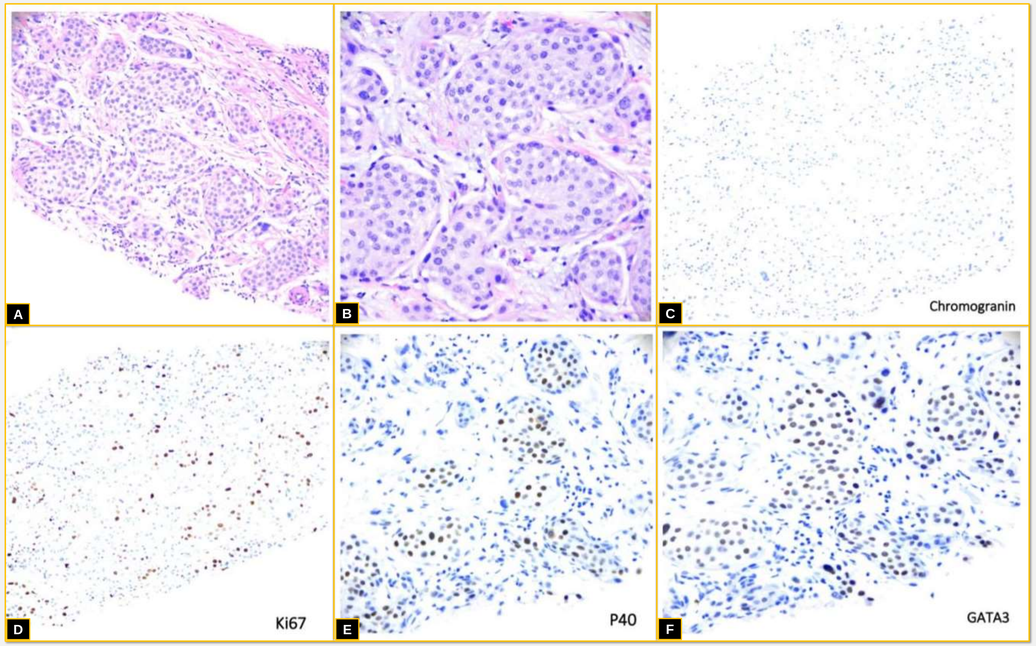

Figure A. H&E section of metastatic UCa in the liver (l4x)

Figure B. H&E section of metastatic UC in the liver (20x)

Figure C. Chromogranin negative

Figure D. Ki-67 37%

Figure E. p40 positive

Figure F. GATA3 positive

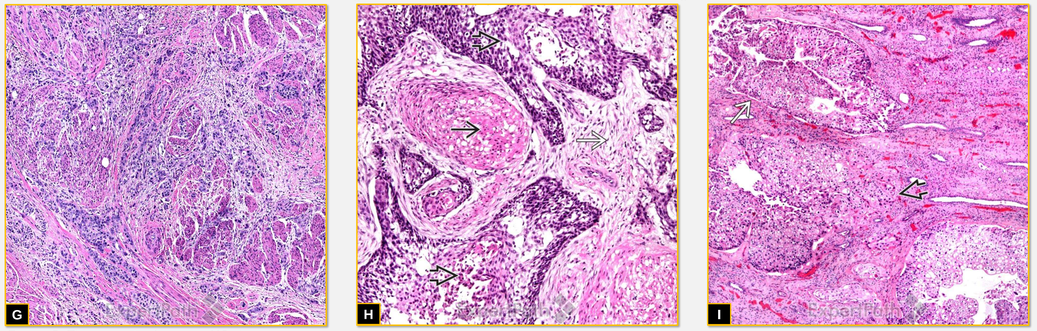

Figure G. This example of invasive UC shows prototypical invasion of the muscularis propria, which is characterized by infiltrating tumor cells that surround large confluent aggregates of compact smooth muscle.

Figure H. This invasive UC (black open arrow) contrasts the eosinophilic muscle bundles of the muscularis propria (black solid arrow) with the more myxoid and spindled reactive myofibroblastic proliferation (white solid arrow).

Figure I. There is unequivocal invasion of the renal parenchyma in the form of irregular tumor clusters (black open arrow) to warrant a pT3 stage.

Discussion

- Microscopic evaluation of liver mass biopsy revealed an insular growth pattern with monotonous epithelioid cells arranged in nests, morphologically suggestive of a well-differentiated neuroendocrine tumor (WDNET) (See Figures A & B).
- However, neuroendocrine immunohistochemical stains, including synaptophysin, chromogranin, and CD56, were all negative, and the Ki-67 staining was 37%, higher than expected for a WDNET (See Figures C & D).
- This prompted broadening of the differential and consideration of other entities.
- Following further workup, a diagnosis of metastatic urothelial carcinoma was confirmed by immunopositivity for immunohistochemical markers P40 and GATA3 (See Figures E & F).

Conclusion

Familiarity with tumors that are histologically identical is critical.

Considering an appropriate differential diagnosis and following a stepwise immunohistochemical approach will be crucial in spotting the mimickers and rendering appropriate management promptly.

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