Synchronous transitional cell carcinoma and metastatic hepatocellular carcinoma in the urinary bladder: a case report

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An 83- year-old male presented with intermittent hematuria and obstructive symptoms. A CT scan of the abdomen and pelvis showed diffuse thickening of the urinary bladder and a large 10 cm liver mass. Histopathological examination of bladder biopsy demonstrated two distinct lesions. The surface showed non-invasive urothelial carcinoma and the submucosa demonstrated metastatic hepatocellular carcinoma showing bile pigment and expressed Hep Par 1 and CD10. To the best of our knowledge, this is the first case report of synchronous transitional cell carcinoma and metastatic hepatocellular carcinoma of the urinary bladder.

Key Words: transitional cell carcinoma, hepatocellular carcinoma, hepatoid adenocarcinoma, metastasis, urinary bladder

Introduction

Secondary tumors of the bladder account for 15% of malignant bladder tumors excluding lymphoma and leukemia. Most commonly, they arise from the female genital tract (30%), prostate and seminal vesicles (26%) and rectosigmoid (24%).[1] Metastatic hepatocellular carcinoma (HCC) to the urinary bladder is distinctly rare. Only two previous cases have been reported.[2,3] We describe a case of synchronous noninvasive papillary urothelial cell carcinoma and metastatic HCC in an 83-year-old male. To the best of our knowledge, these two synchronous tumors in the urinary bladder have not been previously described in the literature.

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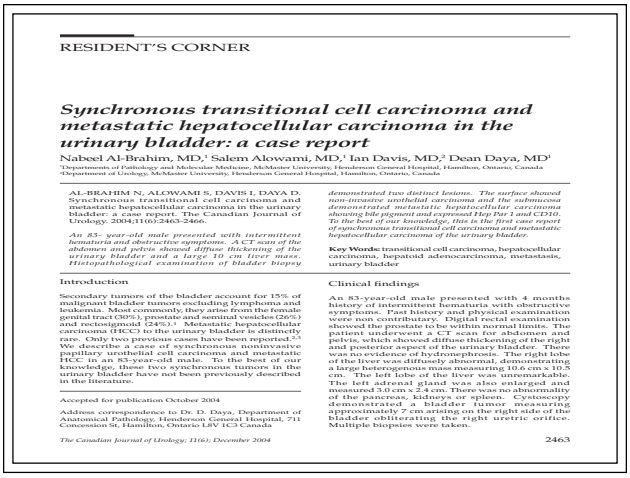
Clinical findings

An 83-year-old male presented with 4 months history of intermittent hematuria with obstructive symptoms. Past history and physical examination were non contributary. Digital rectal examination showed the prostate to be within normal limits. The patient underwent a CT scan for abdomen and pelvis, which showed diffuse thickening of the right and posterior aspect of the urinary bladder. There was no evidence of hydronephrosis. The right lobe of the liver was diffusely abnormal, demonstrating a large heterogenous mass measuring 10.6 cm x 10.5 cm. The left lobe of the liver was unremarkable. The left adrenal gland was also enlarged and measured 3.0 cm x 2.4 cm. There was no abnormality of the pancreas, kidneys or spleen. Cystoscopy demonstrated a bladder tumor measuring approximately 7 cm arising on the right side of the bladder obliterating the right uretric orifice. Multiple biopsies were taken.



RESIDENT'S CORNER

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Figure 1. Two distinct lesions papillary transitional carcinoma (left side) and hepatocellular carcinoma (HCC) (right side).

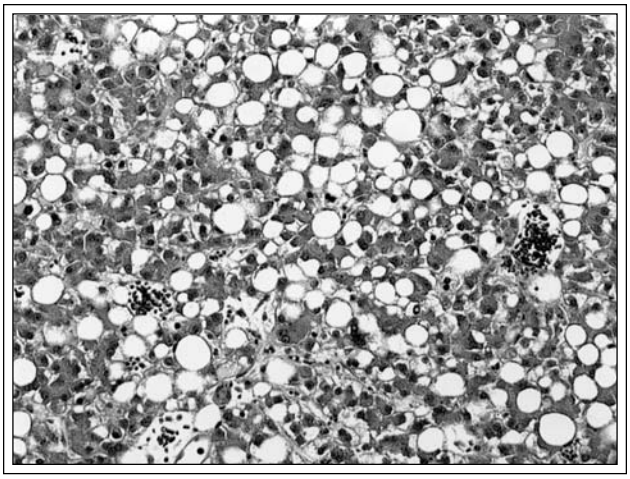

Figure 2. High power view of HCC.

Pathological findings

Multiple soft, pink-tan, hemorrhagic fragments in aggregate measuring 6.o x 6.0 x 1.0 cm were submitted for histological examination. Formalin-fixed, paraffin-embedded blocks were sectioned at 5 μm for hematoxylin and eosin (H&E) and 3 μm sections were also done for immunohistochemical (IHC) stains.

Histological examination revealed two distinct lesions. The surface showed a papillary lesion, with typical features of a non-invasive high grade urothelial carcinoma. Within the submucosa and muscularis propria, a histologically distinct second lesion was noted Figure 1. The second lesion was formed by polygonal cells with well-defined cell membrane and moderate to abundant amounts of esinophilic, fine granular cytoplasm arranged in trabeculae, nests and sheets. Moderate nuclear atypia with some large prominent nucleoli were noted. A distinctive feature of this lesion was the presence of steatosis Figure 2 and both intracellular and extracellular bile pigment as confirmed by histochemical stain.

The following immunohistochemical stains were performed: antibodies, dilutions and results were noted

TABLE 1. **Summarized IHC results**

Antibodies	**Source**	**Dilutions**	**Results**	**Pattern**
Cam5.2	Becton & Dickinson	1:50	+	cytolasmic
CK7	DAKO	1:50	+*	cytoplasmic
CK20	DAKO	1:100	+*	cytoplasmic
AE1/AE3	DAKO	1:25	+*	cytoplasmic
p-CEA	DAKO	1:6000	+**	canalicular
CD10	Nova Castro	1:40	+**	membranous
Hep-par 1	Phoenix Biotech	1:100	+**	cytoplasmc
AFP	DAKO	1:5000	-	-
Kappa	DAKO	1:10,000	-	-
Lambda	DAKO	1:30,000	-	-
LCA	DAKO	1:200	-	-
S100	DAKO	1:5000	-	-

*Antibodies expressed only in urothelial tumor.
**Antibodies expressed only in the metastatic hepatocellular carcinoma.

in Table 1. Both the urothlial and metastatic hepatocellular carcinoma were positive for Cam5.2, but only the former was diffusely positive for AE1/AE3, CK7 and CK20. The metastatic lesion was strongly positive for CD10 and CEA demonstrating a canalicular pattern of CEA staining, typical for hepatic carcinoma. Hep Par 1 was also strongly positive Figure 3. The histological features including the presence of definite bile stain within the metastatic focus and the immunohistochemical results are indicative of metastatic hepatocellular carcinoma with synchronous noninvasive papillary urothelial carcinoma.

Discussion

Secondary tumors of the urinary bladder are not uncommon.[1] However, metastatic HCC to the urinary bladder is very rare.[2,3] The first case was initially suspected clinically to be a bladder tumor with metastasis to the liver. However, pathological examination proved it to be hepatocellular carcinoma with metastasis to the bladder.[2] The second case was of a 51-year-old male who was found to have incidental hepatocellular carcinoma at the time of orthotopic liver transplantation due to hepatitis C and alcoholic cirrhosis. Two years later, he presented with painless hematuria and histological examination revealed metastatic hepatocellular carcinoma.[3]

Recently, hepatoid adenocarcinoma (HA) has been described[4-7] which can mimic metastatic hepatic carcinoma. HA is a rare extrahepatic tumor showing areas morphologically similar to HCC. It has been reported in a variety of organs commonly in the stomach,[4] ovary,[5] and rarely in the urinary bladder.[6,7] In a series of HA of the urinary bladder,[7] the histological examination revealed a variable proportion of tubular glands and trabecular structures were identified in all the cases. The glands lined by columnar cells with clear cytoplasm. The hepatoid foci characterized by polygonal cells separated by sinusoids. The cells are arranged in solid sheet and anastomosing trabeculae with abundant esinophilic cytoplasm and prominent nucleoli. Three cases showed bile pigment within the cytoplasm of scattered malignant cells. However none of the cases showed synchronous transitional cell carcinoma. In series of HA arising from different organs,[8] the majority of cases also showed tubular differentiation.

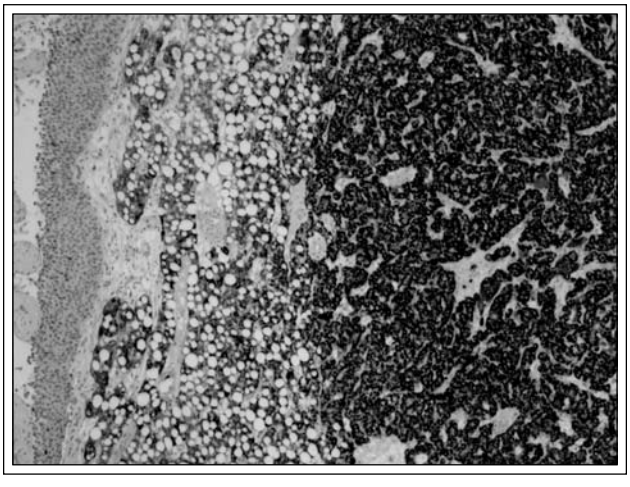

Figure 3. IHC demonstrate strong expression of Hep-Par 1 in HCC (right side) and no expression in the transitional cell carcinoma (left side).

Immunohistochemically, HAs demonstrate expression of low molecular weight cytokeratins, alpha-fetoprotein (AFP), epithelial membrane antigen (EMA) and canalicular staining for (p-CEA).[7] These antigens are also expressed in HCC.[9] Further more, most reported cases of HAs showed elevated serum AFP.[7] Therefore, HA is a mimicker of HCC and it is extremely difficult to differentiate between them based on morphology, histochmical stains and standard immunohistochemical stains.

Hepatocyte-Paraffin-1 (Hep Par 1) is a monoclonal antibody recently introduced that reacts with hepatocyte specific epitope.[10] Several studies[11-13] demonstrated that Hep Par 1 has sensitivity and specificity of 82% and 92% respectively, suggesting that it is the most sensitive and specific marker for HCC. A recent study[8] showed that 7/8 of HAs were negative for Hep Par 1. regardless the site of origin of HA. In addition, the series of urinary bladder HAs,[9] three cases showed only focal expression of Hep Par 1. On the other hand, the case of metastatic HCC to the bladder reported by Franks,[3] the tumor showed strong expression of Hep Par 1. Similarly, the case reported herein showed strong expression of Hep Par 1 and clinically a large liver mass supporting the diagnosis of metastatic HCC and excluding primary HA of the bladder.

In conclusion, the liver is a common site for metastatic tumors. However, the possibility of primary HCC metastasize to another organ should be considered. Metastatic HCC to the urinary bladder is very rare and not to be confused with primary HA of the bladder. □

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