Case Report

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Collision tumor comprising metastatic cholangiocarcinoma and seminoma in an undescended testis: a case report

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Abstract

Testicular metastasis of solid tumors is uncommon. Common primary sites of metastatic tumors to the testis are the lungs and prostate. Cryptorchidism is associated with a four-fold increase in the risk of a testicular germ cell tumor of which seminoma is the most common type. We report an extremely rare case of a collision tumor that comprised testicular metastasis of intrahepatic cholangiocarcinoma and a seminoma in an undescended testis. To the best of our knowledge, this is the first case of this type of tumor to be described. Awareness that metastatic intrahepatic cholangiocarcinoma may present as a testicular tumor may aid diagnosis and management of such patients.

Keywords

Collision tumor, cryptorchidism, testis, seminoma, metastasis, cholangiocarcinoma

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Introduction

Testicular metastasis of solid tumors is uncommon.[1] Common primary sites of metastatic tumors to the testis are the lungs and prostate.[2] Testicular metastasis usually presents as a complication of disease progression and rarely occurs as the first sign of an occult primary neoplasm.[1] There have been two case reports of testicular metastasis of intrahepatic cholangiocarcinoma (ICC).[3,4]

Cryptorchidism is associated with a fourfold increase in the risk of a testicular germ cell tumor (TGCT).[5] The most common type of TGCT in the cryptorchid testes is seminoma.[6] We describe an extremely rare case of a collision tumor that comprised testicular metastasis of ICC and a seminoma in an undescended testis. To the best of our knowledge, this is the first case of this condition to be described.

Case report

In June 2016, a 62-year-old man was referred to our hospital after losing 10 kg in weight over 2 months. A hypoechoic liver mass on ultrasonography was subsequently identified. Computed tomography (CT) showed an ill-defined, low-density lesion and a dilated intrahepatic duct in the left hepatic lobe (Figure 1). Laboratory tests showed an elevated carbohydrate antigen (CA) 19-9 level (146.27 U/mL; normal range, <37 U/mL), and normal carcinoembryonic antigen (1.78 ng/mL; normal range, <5 ng/mL) and alpha-fetoprotein (2.84 ng/mL; normal range, <20.0 ng/mL) levels. Left hepatectomy was performed because of suspicion of ICC. A gross examination showed an ill-defined, grayish-white, and focal yellowish solid tumor that was $3 \times 2.5 \times 2.3$ cm, with multiple black stones (Figure 2). Microscopically, the tumor consisted of a tubular or cord-like growth pattern of infiltrating atypical cells in an abundant fibrotic stroma. The tumor cells had ovoid nuclei and small nucleoli, and an eosinophilic cytoplasmic rim (Figure 3a). These cells stained positive for cytokeratin (CK) 7 and CK19, but they were negative for HepPar1, which is consistent with a diagnosis of ICC associated with hepatolithiasis (Figure 3b, c).

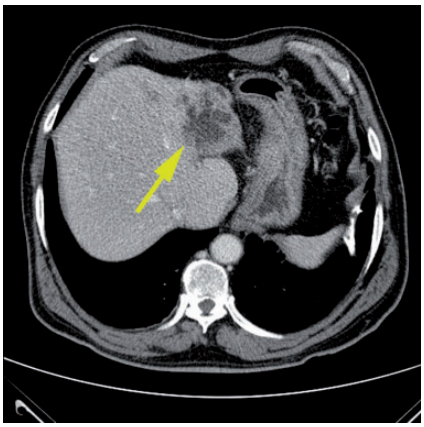

Figure 1. An ill-defined, low-density lesion (arrow) with a dilated intrahepatic duct in the left hepatic lobe was identified in the left hepatic lobe on abdominal computed tomography.

Following surgery, the patient received 5 months of postoperative chemotherapy that comprised six cycles of 5-fluorouracil and leucovorin. In February 2018, 14 months after chemotherapy was completed, his CA19-9 (869.65 U/mL) level had increased and he complained of lower abdominal pain. There was a palpable mass in the right inguinal area. The patient's history showed that he had no palpable testis in the right scrotal area from birth. Therefore, the right inguinal mass was a suspected undescended testis. Ultrasonography and abdominal CT showed a heterogeneous cystic and solid mass in the right inguinal area along with an inguinal hernia (Figure 4a). Furthermore, an ill-defined, low-density lesion was identified at the anastomosis site in the remnant liver, along with diffuse enhanced peritoneal wall thickening and a

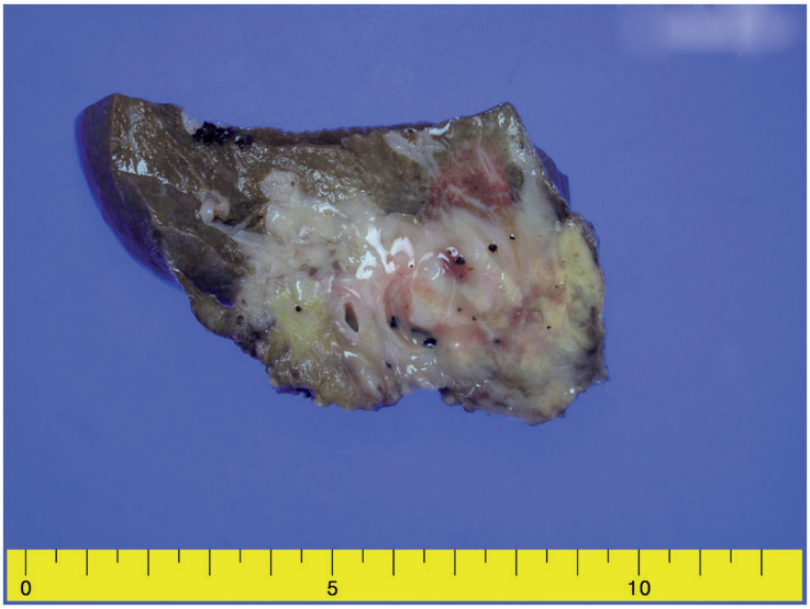

Figure 2. An ill-defined, grayish-white, and focal yellowish solid tumor with multiple black stones was observed.

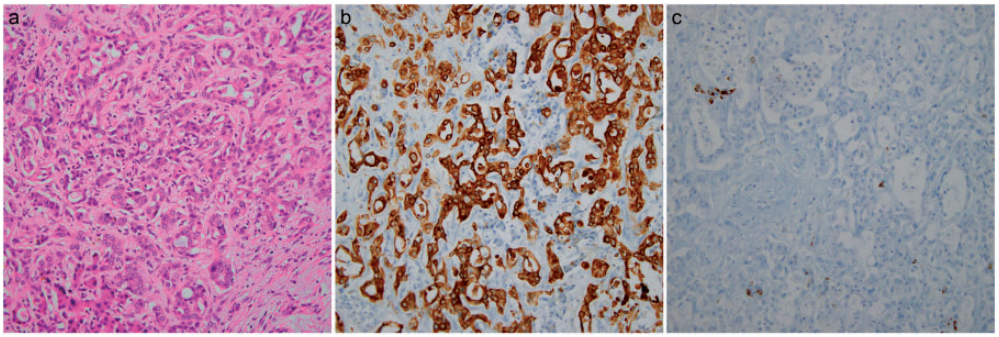

Figure 3. (a) Tumor cells show a tubular or cord-like growth pattern with ovoid nuclei and small nucleoli and an eosinophilic cytoplasm (magnification, ×200). (b) Immunostaining for CK7 is diffusely positive (magnification, ×200). (c) HepPar1 immunostaining is negative (magnification, ×200).

moderate amount of ascites. This was interpreted as local recurrence and peritoneal metastasis of ICC, respectively (Figure 4b, c).

Under suspicion of a TGCT arising from a cryptorchid testis, the patient underwent right radical orchiectomy. Gross examination of the right testis showed a well-encapsulated, grayish-white, firm mass of $4.2 \times 2.9 \times 1.8$ cm, with a cystic space (Figure 5). There was no other lesion involving the epididymis or spermatic cord. Microscopically, the mass comprised two tumor components that were separated by the cystic space (Figure 6a). The major tumor component showed histological features consistent with seminoma. Sheets of

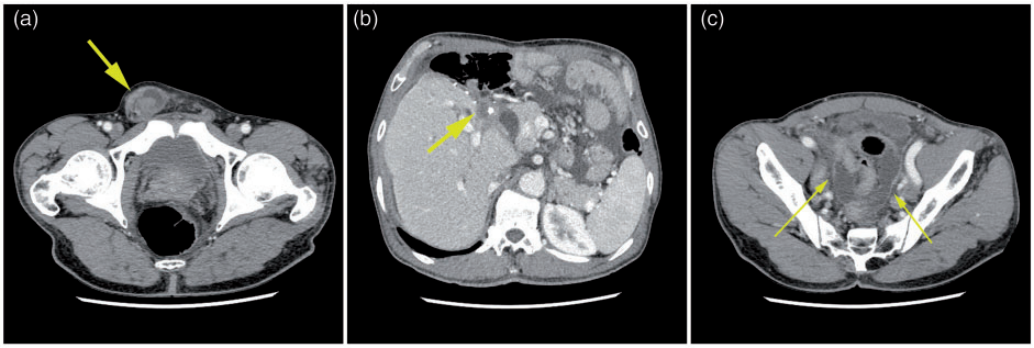

Figure 4. Abdominal computed tomography shows a heterogeneous cystic and solid mass (arrow) in the right inguinal area (a), an ill-defined, low-density lesion (arrow) at the anastomosis site in the remnant liver (b), and diffuse enhanced peritoneal wall thickening (arrows) (c).

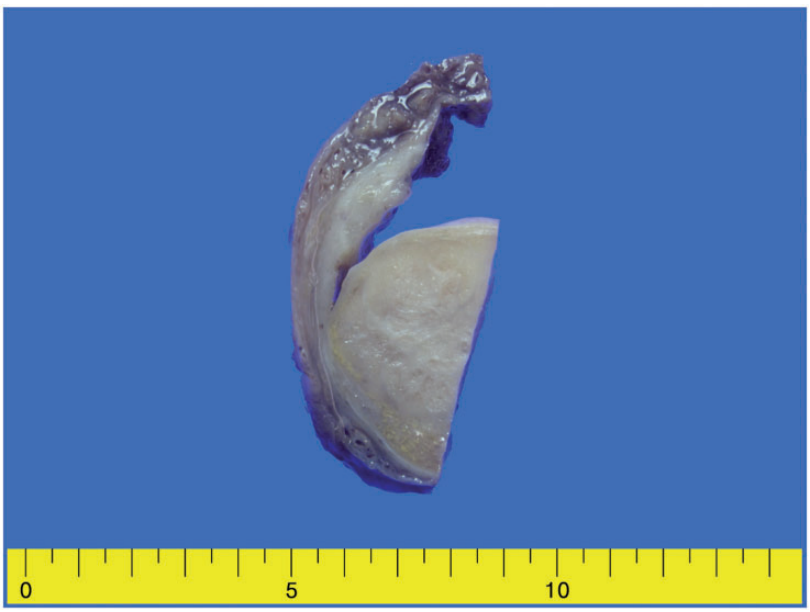

Figure 5. A photograph of the testis shows a well-circumscribed, grayish-white, firm mass with a cystic space.

relatively uniform tumor cells were divided into poorly demarcated lobules by fibrous septa. The tumor cells had an abundant clear cytoplasm, round-to-polygonal nuclei, and one or more prominent nucleoli (Figure 6b). The minor component showed a moderately differentiated adenocarcinoma with histological features reminiscent of ICC (Figure 6c). Immunohistochemical staining showed that the major component was positive for placental alkaline phosphatase (PLAP) and CD117, but negative for CK7 and CD30, which are markers of embryonal carcinoma (Figure 7a–c). Therefore, a diagnosis of seminoma was made. The minor component was positive

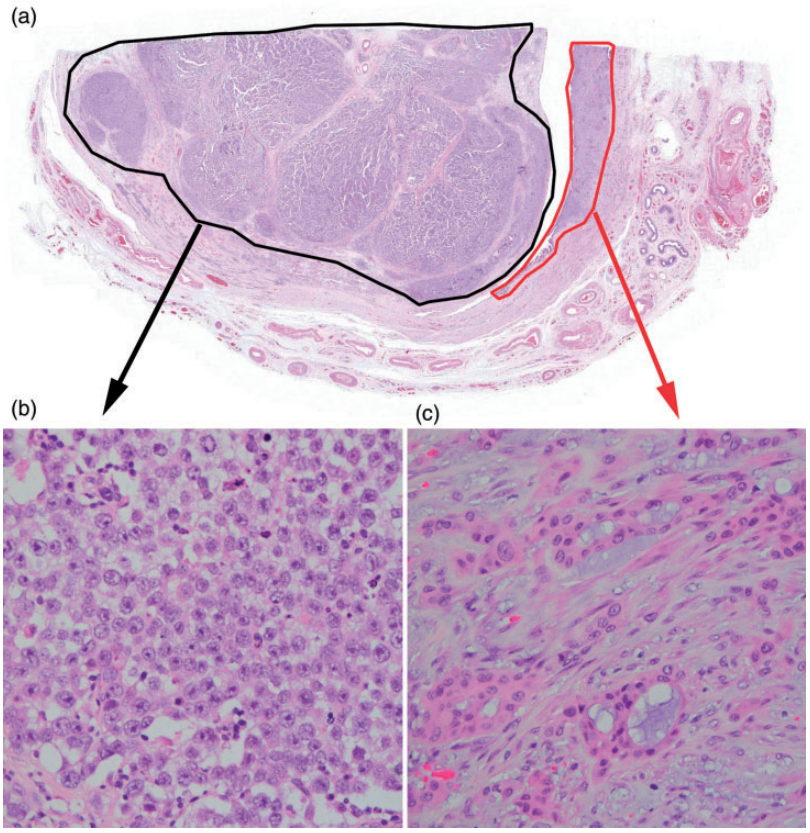

Figure 6. (a) Hematoxylin and eosin staining shows that the tumor is composed of two tumor components separated by the cystic space. The borders of the major tumor component and minor tumor component are marked in black and red, respectively (magnification, ×0.5). (b) Sheets of relatively uniform tumor cells are divided into poorly demarcated lobules by fibrous septa and the tumor cells have an abundant clear cytoplasm, round-to-polygonal nuclei, and one or more prominent nucleoli (magnification, ×400). (c) The tumor shows a tubular or cord-like growth pattern of moderately differentiated adenocarcinoma (magnification, ×400).

for CK7 and negative for PLAP, CD117, and CD30 (Figure 7d–f). On the basis of the history of ICC and the pathological findings, the minor neoplastic population was diagnosed as metastatic ICC. Finally, we concluded that the testis tumor was a collision of metastatic ICC and seminoma. The patient was treated with two cycles of palliative systemic chemotherapy, including gemcitabine and cisplatin. However, the symptoms of common bile duct obstruction and peritoneal metastasis progressed and the patient died 3 months after orchiectomy.

This study was approved by the Institutional Review Board of Chungbuk National University Hospital (2018-11-003). The patient provided informed consent in accordance with the Declaration of Helsinki.

Discussion

Solid tumor metastases involving the testis are rare.[3] A retrospective study of 738

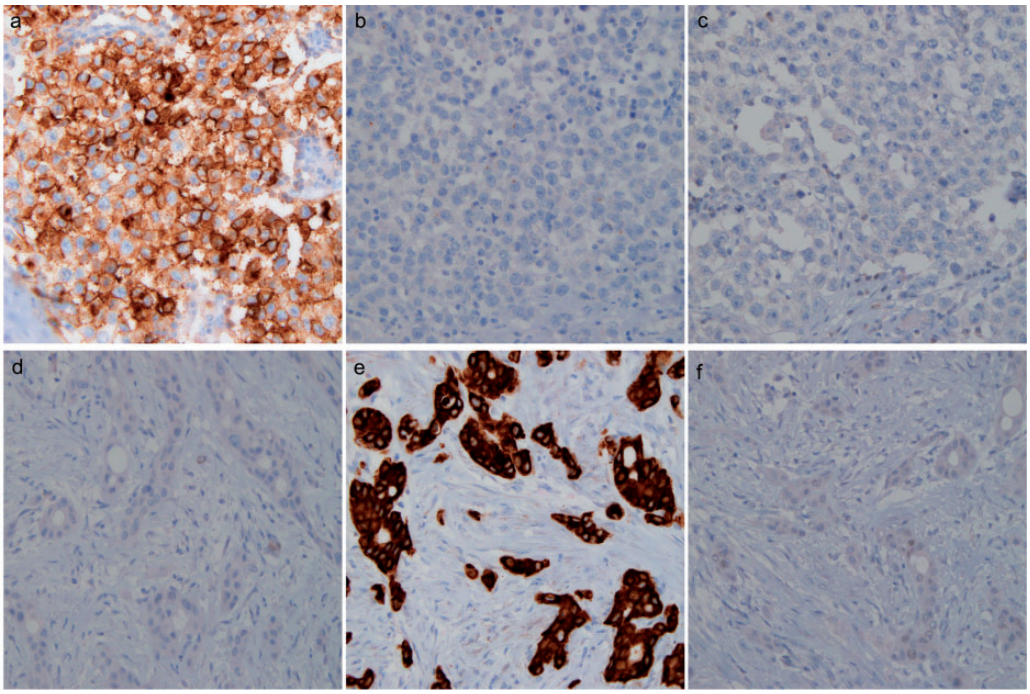

Figure 7. Immunohistochemical staining shows that the major component is positive for placental alkaline phosphatase (a), but negative for cytokeratin 7 (b) and CD30 (c). The minor component is negative for placental alkaline phosphatase (d), positive for cytokeratin 7 (e), and negative for CD30 (f) (magnification, all ×400).

autopsies of adult men with solid tumors reported that five (0.68%) had testicular metastases.[1] The most frequent primary sites of metastatic tumors to the testis include the lungs[1,2] and prostate.[7] Tozawa et al.[3] reviewed 30 cases of gastrointestinal cancer that had metastasized to the testis and reported that the majority of patients had other widespread metastases at the time of testicular tumor diagnosis. The common metastatic sites accompanying testicular metastasis are the peritoneum, lymph nodes, mesentery, skin, and lungs.

ICC is the second most common type of primary hepatic malignancy, comprising 5% to 15% of primary liver cancers.[8] Only a minority of patients (15%) present with resectable disease and the median survival is less than 3 years.[9] The most common metastatic sites of ICC include the lymph nodes, peritoneum, lungs, and pleura.[10] ICC metastasis to the male urogenital tract is rare;[11–13] only two cases of testicular metastasis of ICC have been reported.[3,4] Our patient was initially diagnosed with ICC, with no evidence of seminoma at that time. Fourteen months after surgical resection and adjuvant chemotherapy, the patient suddenly presented with seminoma and coexisting metastatic ICC in an undescended right testis. In this case, testicular metastasis of ICC was identified in the setting of disseminated disease (peritoneal metastasis and local recurrence of ICC in the remnant liver).

The metastatic routes to the testis are thought to include direct invasion from adjacent organs, transperitoneal seeding through a congenital hydrocele, or retrograde extension via the vas deferens.

Other mechanisms may include the blood-borne route or lymphatic extension.[14] Although no other metastatic tumor cell foci were identified in the vas deferens or outside of the scrotum in the radical orchiectomy specimen of our patient, the tumor cells had disseminated to the peritoneum. There was no microscopic evidence of lymphatic or vascular invasion. Therefore, we suspected that tumor cells had spread to the testis via transperitoneal seeding.

Colonization of a particular organ by metastatic tumor cells is related to the anatomical location, vascular drainage of the primary tumor, and tropism of particular tumor cells for specific tissues. Specific binding of tumor cells to the endothelium of certain organs, and/or the microenvironment within a distant organ may generate a site that is permissive for metastatic cell growth.[15] In the testis, the lower temperature of the intra-scrotal contents may impede the ability of disseminated tumor cells to become established.[16] In our case, the specific background of cryptorchidism may have provided a niche for testicular colonization by tumor cells due to an elevated temperature or disruption of a cellular regulatory pathway.[6]

The mechanisms underlying rapid progression of seminoma in our case are unknown. One hypothesis is that molecular pathways that are altered during progression and spread of ICC may induce pluripotent testicular germ cells to proliferate, resulting in tumorigenesis.

In conclusion, this report describes an extremely rare case of testicular metastasis of ICC and a coexisting seminoma in an undescended testis. Awareness that metastatic ICC may present as testicular tumor may aid diagnosis and management of such patients.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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