CASE REPORT

Testicular Swelling as an Initial Presentation of a Patient With Metastatic Gastric Cancer

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While signet-ring cell morphology in the testes might represent metastatic spread from an extragonadal adenocarcinoma, a rare variant of primary testicular neoplasms should be considered in a differential diagnoses as was seen in this rare occurrence of a testicular swelling as an initial presentation for a patient with metastatic gastric cancer.

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Gastric cancer is one of the most common cancers and the second most common cause of cancer-related death worldwide.[1] Patients with an early-stage gastric cancer are often asymptomatic, and about 30% to 40% of patients present with distant metastases.[2] The most common sites of metastasis are the liver, peritoneum, and the lymph nodes. In more advanced stages, gastric cancers spread to the lungs, brain, bones, soft tissues, and other sites. Krukenberg tumors are classic but rare occurrences of gastric cancer metastasis to ovaries in females. In men, it is rare for gastric cancer to metastasize to the testes. Only a few cases of testicular metastasis from gastric cancer have been reported in the literature.[3-5]

Primary testicular neoplasms typically present with unilateral testicular swelling. In rare instances, testicular swelling can be an initial presentation of a metastatic cancer. In this article, we report a man who initially presented with right testicular swelling and was eventually diagnosed with a secondary testicular cancer from an aggressive metastatic gastric adenocarcinoma.

CASE PRESENTATION

A 43-year-old male presented to his primary care physician with a 6-month history of right testicular swelling and unintentional weight loss of 33 pounds. An ultrasound of the scrotum and the testes showed a 4.5-cm hypoechoic and predominantly cystic mass in the right testis. Serum levels of β-human chorionic gonadotropin, α-feto protein and lactate dehydrogenase were within normal limits.

A primary testicular neoplasm was suspected. The patient underwent a right-sided inguinal orchiectomy. The pathology of the resected testis revealed an intestinal type adenocarcinoma with mucinous and signet-ring cell features (Figure). The characteristic morphology led to further investigations for a gastrointestinal (GI) primary cancer. An upper GI endoscopy revealed a 4-cm fungating mass at the junction of body and fundus of the stomach that extended along the lesser curvature. A biopsy of the mass revealed poorly differentiated adenocarcinoma with signet-ring cell features similar to that in the testicular specimen.

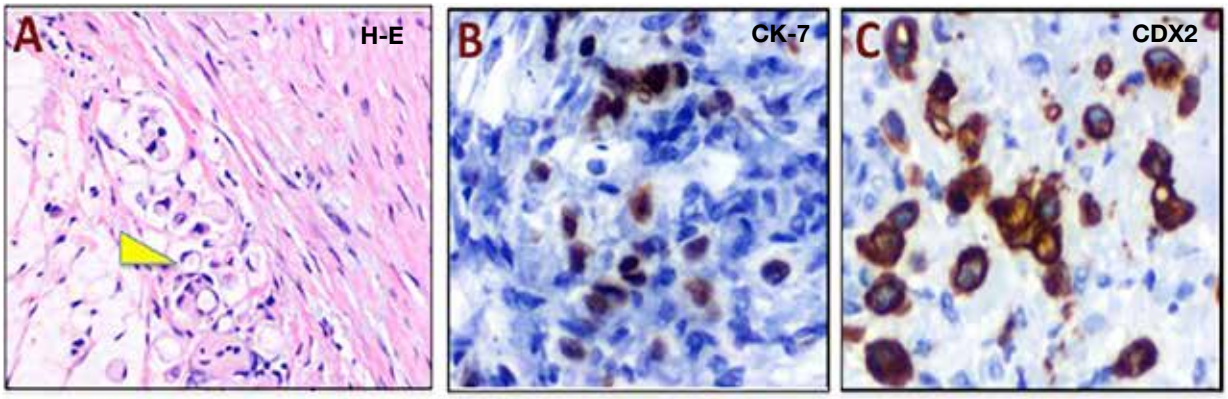
A staging Fluorine-18 fluorodeoxyglucose positron emission tomography scan revealed extensive hypermetabolic peritoneal nodules consistent with peritoneal carcinomatosis. The patient started palliative chemotherapy with 5-fluorouracil and oxaliplatin but rapidly declined with progressive abdominal symptoms after completion of 2 cycles. He discontinued chemotherapy and eventually opted for supportive care focusing on comfort.

DISCUSSION

Testicular neoplasm is the most common solid tumor in men aged 20 to 34 years in the US.[6] More than 90% of testicular neoplasms are germ-cell tumors and originate from the testes.[6] Secondary neoplasms of the testes from solid tumors are rare. In an autopsy series, secondary neoplasms from solid tumors represented 4.6% of all testicular neoplasms.[7] The reported frequencies of primary sites of origin vary based on the report. In a relatively large series, the most

FIGURE

Metastatic Signet-Ring Cell Adenocarcinoma of the Testis



(A) Hematoxylin-eosin staining of the orchiectomy specimen shows signet-ring cells characterized by large cytoplasmic vacuoles indenting the nucleus, appearing either empty/clear or containing a droplet of mucin (yellow arrowhead). Adenocarcinoma is suggested by pools of extravasated mucin surrounding the metastatic signet-ring cells, coalescing into larger mucin pools at the left/lower aspect of the panel. (B) Cytokeratin-7 (CK-7) and CDX2 (C) positivity by immunohistochemistry confirmed the epithelial and gastrointestinal origin, respectively.

common solid tumors of origin were the prostate (35%) and lungs (20%).[8] Among hematologic malignancies, lymphomas may originate from or secondarily involve the testes. Primary testicular lymphomas account for approximately 5% of testicular neoplasms and commonly occur in men aged > 60 years.[9] Testicular involvement of acute myeloid or lymphoid leukemia may happen at diagnosis, but relapses of acute leukemia in a testicular site are more common and well recognized.[10,11]

Our report shows a rare occurrence of a testicular swelling as an initial presentation of an aggressive metastatic gastric adenocarcinoma. When a patient presents with a testicular swelling, a testicular neoplasm is suspected based on the clinical examination, serum tumor markers, and ultrasonographic examination of the testes. Inguinal orchiectomy is the initial standard of care, and pathologic examination of a resected testis renders the confirmatory diagnosis. The overwhelming majority of these patients have primary testicular neoplasms, predominantly testicular germ-cell tumors. A small group may have atypical and rare tumors requiring additional workup to establish a diagnosis.

Metastatic spread of a solid tumor to a testicular site is rare. A testis is somewhat protected by the distinct anatomy that is offered by the blood-testis barrier. The tunica vaginalis, an external fibrous covering sheath of the testis, separates the testis from the peritoneal cavity and provides additional protection. Nevertheless, possible routes of secondary metastatic spread may include hematogenous and lymphovascular spread, cavitary dissemination and peritoneal seeding. Among gastric cancers, diffuse gastric cancer subtype is commonly associated with signet-ring cells. These cells lack adhesion and invade as single cells or small groups, leading to scattered tumor cells and a higher probability of seeding.

Our patient exhibited extensive peritoneal carcinomatosis, so peritoneal seeding likely played a dominant role in disseminating the cancer to the testis. It should be noted that possible primary sites of signet-ring cell metastatic adenocarcinomas are broad and may include the stomach and other GI and pancreaticobiliary sites, as well as the lung, bladder, breast, and gynecologic tract. Immunohistochemistry is often of limited value in establishing the primary site. Diagnosis is best established on clinical grounds, as was done in our patient.

When signet-ring cells are encountered in an orchiectomy specimen and a primary extratesticular site of origin cannot be identified, it is important to consider rare variants of primary testicular tumors in the differential diagnosis. A number of primary testicular tumors have signet-ring morphology. These include primary signet-ring cell stromal tumor of the testis (PSRST),[12] seminoma with signet-ring cell predominance,[13] and a primary signet-ring cell germ-cell carcinoma of the testes (PSRGCT).[14]

Seminoma and PSRST variants generally are differentiated from adenocarcinoma by a lack of mucin production and the absence of

keratin expression. PSRGCT is considered a malignant somatic-type transformation of a testicular germ-cell tumor and germ-cell clonality is established by abnormal 12p chromosome through fluorescent in situ hybridization testing.[13] PSRST is a benign tumor with excellent prognosis. Seminoma variants with signet-ring cell predominance and PSRGCT are managed as germ-cell tumors and are also considered to have good outcome. In contrast, testicular involvements from metastatic adenocarcinomas, including gastric cancers, are managed with multidisciplinary approach, including systemic chemotherapy. Despite this, patients have a poor outcome with a median survival of about 1 year.[2]

CONCLUSION

Advanced gastric adenocarcinoma can metastasize to the testes, and patients may present with a testicular swelling as an initial presentation. It is important to differentiate secondary testicular cancers from rare variants of primary testicular tumors because the prognosis and management vary substantially.

Author disclosures

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Disclaimer

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