Case Report

Metastatic Adenocarcinoma of the Epididymis: A Case Report and Brief Literature Review

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Clinical Practice Points

- Epididymal adenocarcinomas are rare and little is known about their biology or natural history.
- Some epididymal adenocarcinomas can behave indolently, and close surveillance may be reasonable in some instances.

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Introduction

Neoplasms of the epididymis are rare, and benign tumors outnumber malignant ones by 3 to 1.[1] Of the benign neoplasms, adenomatoid tumors are most common. Less common neoplasms are leiomyomas, serous (non-papillary) cystadenomas, cavernous hemangiomas, and melanotic neuroectodermal tumors.[2] Primary malignant tumors of the epididymis include adenocarcinomas, mesotheliomas, and rhabdomyosarcomas. Herein, we report the case of a metastasizing adenocarcinoma of the epididymis − a clinical scenario that has been infrequently described in the literature.

Case Report

A 38-year-old male presented with painless right-sided scrotal swelling. He underwent spermatocelectomy, with pathology demonstrating a benign epididymal papillary cystadenoma. Five years later, the patient re-presented with recurrent swelling in the scrotum. A computed tomography (CT) scan demonstrated a 1.2-cm inguinal node, and he underwent a right epididymectomy for persistent pain. The mass consisted of an adenocarcinoma with papillary features and an associated papillary cystadenoma. A staging CT of the chest, abdomen, and pelvis demonstrated multiple sub-centimeter lung nodules and a 2.2 × 2.4 cm right inguinal mass. He subsequently underwent right radical orchiectomy, scrotectomy, resection of the inguinal mass, and inguinal lymph node dissection. Histologically, the mass was a low-grade adenocarcinoma involving 3 of 8 lymph nodes (Figure 1A). Immunohistochemically, the carcinoma cells were variably positive for CK7 and CD10 and positive for mesothelin and CAIX, but negative for PSA and PROSAP, CK20, CDX2, WT1, SALL4, Glypican 3, CK5, calretinin, and S100. UW-OncoPlex, a next-generation deep sequencing panel, was used to look for mutations that could be potential therapeutic targets.[3] A *TET3* frame-shift mutation was detected as was a low-level variant of a *MTHFR* splice site alteration.

Six months after his last surgery, the patient had another surveillance CT scan of the chest, abdomen, and pelvis that showed a right inguinal soft tissue density along the proximal femoral vessels. A positron emission tomography (PET)/CT scan revealed that the right inguinal mass was fludeoxyglucose-avid, as were several of the pulmonary nodules. Biopsy of the inguinal node confirmed metastatic adenocarcinoma. One year later, a repeat PET/CT scan demonstrated modest enlargement of the fludeoxyglucose-avid right inguinal node and stable pulmonary nodules (Figure 1B). The patient continues to have mild inguinal pain, but otherwise is doing well clinically in spite of no intervention in the preceding year.

Conclusion

Primary epididymal adenocarcinomas are rare. Only 25 cases have been reported in the English literature (Table 1).[1,4-18] The actual number of cases may be smaller, given that some authors contest the diagnosis of epididymal adenocarcinoma.[12] Given the rarity of these tumors, their pathogenesis remains in question. Because our patient had a component of cystadenoma in his tumor, we suspect that the tumor arose as a malignant transformation of a benign papillary cystadenoma. It is not clear

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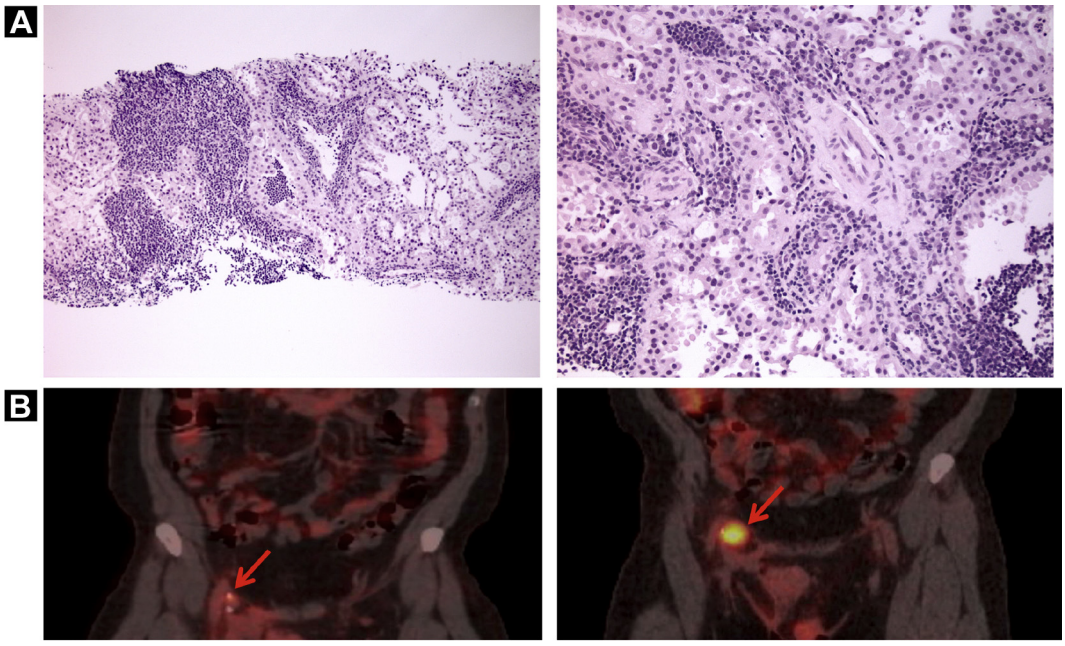
Figure 1 A, Hematoxylin-eosin Stain, 40× (Left Image) and 200× (Right Image) Magnification. Tumor Cells Form Glands and Have a Pale Eosinophilic Cytoplasm and Small, Punctate, Round Nuclei. B, Representative Positron Emission Tomography/Computed Tomography Images at Baseline (Left) and 1 Year Later (Right). Arrow Indicates Hypermetabolic Inguinal Lymph Node, Which Increased From 11 × 9 mm (max Standardized Uptake Value, 3.3) to 28 × 19 mm (3/280) (max Standardized Uptake Value, 5.9) Over This Time Period.



whether the observed *TET3* or *MTHFR* mutations were transforming events, although this seems somewhat unlikely, given that these mutations have not been associated with malignant transformation in other tumor types. It seems likely that mutations in genes not included in the targeted sequencing panel used may have influenced tumor biology. It is worth noting that only one other published case of epididymal adenocarcinoma reported sequencing data.[17] In this instance, a *TP53* mutation was revealed — a gene not altered in the present case.

These tumors have been reported in patients over a wide age range; from 24 to 82 years (Table 1).[12] Some tumors, which metastasized early, were fatal shortly after diagnosis, whereas in one case, the patient was alive 30 years after diagnosis despite the presence of para-aortic lymph node metastases at the time of diagnosis — paralleling the indolent course seen in our patient thus far.

As it stands, surgical resection of localized disease remains the mainstay for treatment of primary malignant epididymal tumors. In patients with metastatic disease, the optimal management approach has not been defined. A handful of cases have reported > 1 year progression-free survival with systemic chemotherapy (eg, platinum- and taxane-based). Whether these periods of prolonged disease stability resulted from effective cytotoxic therapy or are a reflection of an indolent natural history is unknown.[13,16]

Given the lack of data to guide clinical management, we opted for a conservative approach. Our patient has been monitored with serial CT scans and 2 PET/CT scans to evaluate for candidacy for metastasectomy. Although multidisciplinary consensus was that surgical resection of all metastatic disease was unlikely to be beneficial, we have not seen any evidence that his tumors are rapidly progressing, and he remains clinically stable. Because of a splice site alteration in the *MTHFR* gene, the tumor may respond to anti-folate chemotherapeutic agents. Consequently, we plan a trial of 5-fluorouracil-based chemotherapy if the tumor progresses more rapidly or he becomes symptomatic.