

Lymphoepithelioma-like carcinoma of the ureter

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Abstract

We report an extremely rare case of lymphoepithelioma-like carcinoma of the ureter. A 73-year-old man presented with asymptomatic gross hematuria. Based on the clinical diagnosis of a left ureteral tumor, the patient underwent left nephroureterectomy. Histological examination showed lymphoepithelioma-like carcinoma of the ureter with a unique growth pattern of submucosal spread, in which cytokeratin immunohistochemistry clearly demonstrated the cluster of neoplastic cells within the dense lymphocytic infiltrates. The tumor cells showed negative results for the presence of Epstein-Barr virus by Epstein-Barr virus-encoded ribonucleic acid in situ hybridization. The patient was free of tumor recurrence and metastasis 15 months after the operation. To avoid misdiagnosis as chronic inflammation, recognition of this type of tumor is important.

INTRODUCTION

Lymphoepithelioma is an undifferentiated carcinoma with intense lymphoid infiltrates arising in the nasopharynx.¹ Carcinomas that histologically resemble lymphoepithelioma of the nasopharynx are called lymphoepithelioma-like carcinoma (LELC). Only five patients with LELC of the ureter have been reported in English literature previously²³⁴⁵⁶. Here, we report an additional case of LELC of the ureter which showed a unique spreading lesion, and discuss about potential diagnostic pitfalls for this rare type of ureteral carcinoma, LELC.

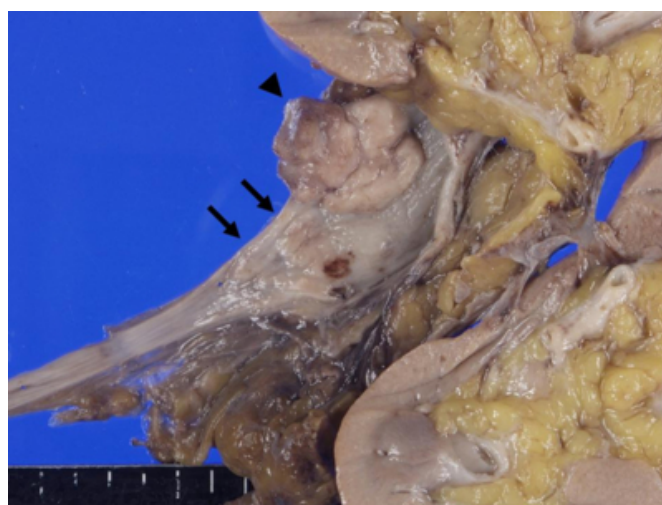
CASE REPORT

A 73-year-old man presented with asymptomatic gross hematuria. Retrograde pyelography revealed a defect in the upper ureter. Magnetic resonance imaging showed a mass in the left upper ureter that measured about 2 cm in its greatest dimension. Based on the clinical diagnosis of a left ureteral tumor, the patient underwent left nephroureterectomy.

Macroscopically, a solid tumor measuring 2.2×1.8 cm was protruding into the dilated upper ureteral lumen near the ureteropelvic junction (Fig 1). The distal ureteral wall was thickened for 1.6 cm in length, continuously with the solid tumor.

Figure 1

Figure 1: Solid tumor measuring 2.2×1.8 cm is protruding into the dilated upper ureteral lumen (arrow head). Distal ureteral wall is thickened for 1.6 cm in length, continuously with the solid tumor (arrows)



Microscopically, the tumor consisted of invasive nests of large undifferentiated cells in a dense lymphoid stroma (Figures 2 and 3). In the region of the solid tumor, neoplastic cells were admixed with lymphoid infiltrates and grow expandingly into the deep muscularis propria of the ureter (Fig 2). Tumor cells had large vesicular nuclei and prominent nucleoli with indistinct cytoplasmic membranes, which formed syncytium-like nests (Fig 3, inset). In the region of ureteral wall-thickening, the surface was covered with non-neoplastic urothelium, and there were massive lymphoid infiltrates in the lamina propria (Fig 3). Higher

magnification demonstrated scattered small tumor nests within the infiltrates (Fig 3, inset), which might provide an impression of aggregates of macrophages or abortive germinal center. There was no component of conventional urothelial carcinoma, neither flat nor papillary type.

Figure 2

Figure 2: Low-power view of the central region of the tumor. Tumor cells and lymphoid infiltrates are mixed together and grow expansively. Arrows: muscularis propria of the ureter. (hematoxylin-eosin, original magnification $\times 20$)

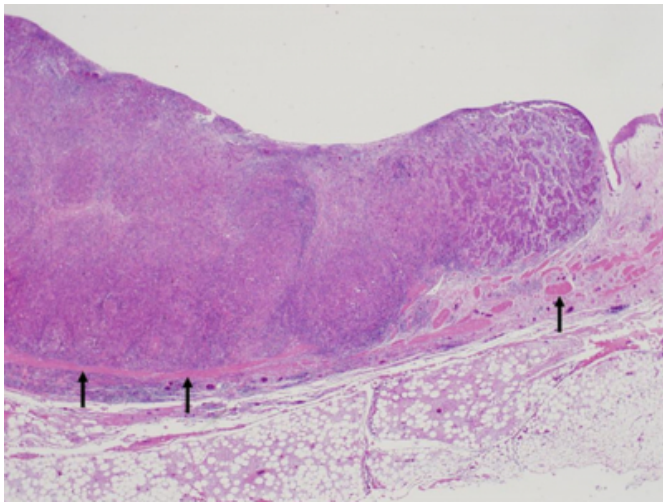
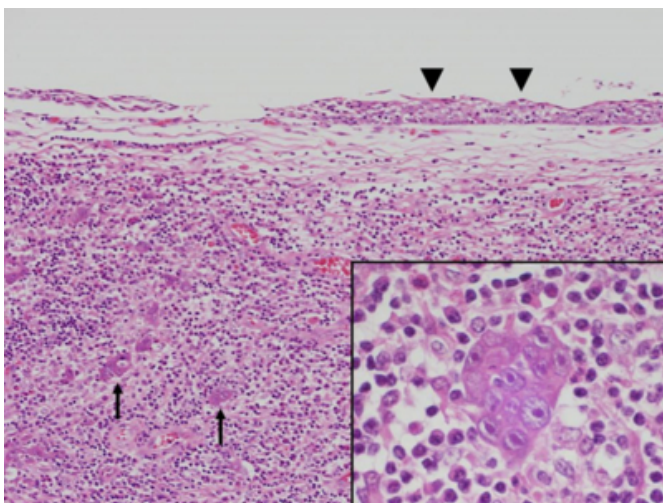


Figure 3

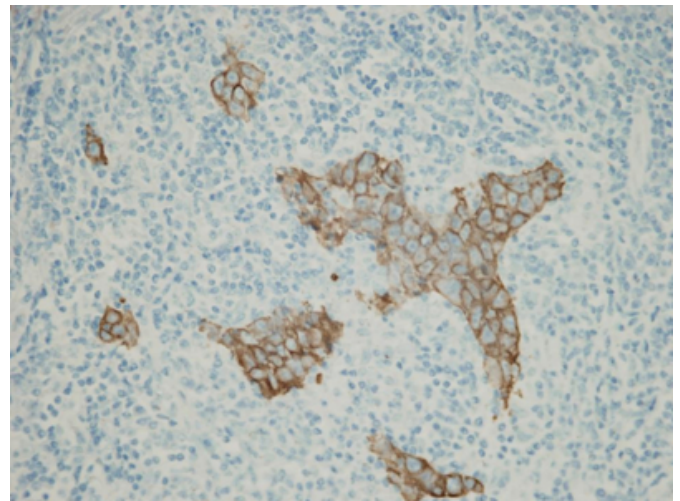
Figure 3: Histopathology of the region of ureteral wall-thickening (Figure 1, arrows). Ureteral surface is covered with non-neoplastic urothelium (arrow heads). Massive lymphoid infiltrates are observed in the lamina propria, with scattered tumor nests (arrows). (hematoxylin-eosin, original magnification $\times 200$). Inset: high-power view of the tumor cells. Tumor cells form a syncytium-like small nest. (hematoxylin-eosin, original magnification $\times 1000$)



Immunohistochemically, tumor cells were strongly positive for cytokeratin AE1/AE3, which confirmed their epithelial origin (Figure 4). The stromal lymphoid cells showed a predominance of CD3-positive T cells compared to CD20-positive B cells, mixed with a small number of plasma cells and eosinocytes. In situ hybridization using an Epstein-Barr virus (EBV)-encoded ribonucleic acid probe failed to demonstrate the presence of EBV in the tumor cells.

Figure 4

Figure 4. Immunohistochemical staining of tumor cells for cytokeratin AE1/AE3. (original magnification $\times 400$)



Pathological diagnosis was LELC of the left ureter, pT2b N0. Neither lymphatic vessel nor blood vessel invasion was identified. Surgical margins were negative. Postoperatively, no adjuvant therapy was performed. The patient was free of tumor recurrence and metastasis 15 months after the operation.

DISCUSSION

LELC has been described in various organs including the stomach, salivary glands, lung, thymus and urinary tract. LELC of the upper urinary tract remains extremely rare. Only five and seven patients, respectively, with LELC of the ureter²³⁴⁵⁶ and renal pelvis⁷ have been reported in English literature previously. The five cases of LELC of the ureter reported in the literature are summarized in Table 1.

Figure 5

Table 1. Summary of LELC cases of the ureter

References	Year	Sex-Age	Chief complaint	Stage	Treatment	Follow up	Outcome
Chalik ²	1998	M-75	Gross hematuria, flank pain	T3N0M0	Ureterectomy + psoas hitch	12 mn	NED
Ng ³	1999	F-62	Voiding difficulty	T2N0N0	Nephroureterectomy	18 mn	NED
Roig ⁴	2001	M-58	Gross hematuria	Unknown	Nephroureterectomy	18 mn	NED
Terai ⁵	2005	M-73	Gross hematuria	T2N0M0	Nephroureterectomy	30 mn	NED
Ma ⁶	2008	F-64	Gross hematuria	T2N0Mx	Ureterectomy	24 mn	NED
Present case	2009	M-73	Gross hematuria	T2N0M0	Nephroureterectomy	15 mn	NED

mn, months; NED, no evidence of disease.

Most patients with LELC of the ureter present with asymptomatic gross hematuria²⁴⁵⁶. Histologically, LELC is characterized by syncytium-like nests of undifferentiated carcinoma associated with a prominent lymphoid infiltrate. Our case showed typical histological findings of LELC. However, the growth pattern of ureteral submucosal spread was unique to this case (Figure 3), which has not been previously reported. Since LELC can be present as a submucosal tumor covered by non-neoplastic epithelium, LELC of the urinary tract can be misdiagnosed as chronic inflammation, especially when only small specimens (i.e., ureteroscopic biopsy specimens) are available for the diagnosis. Appropriate sampling and careful observation with immunohistochemistry for cytokeratins are necessary for correct diagnosis.

EBV infection is closely associated with lymphoepithelioma of the nasopharynx and LELC of some organs⁸. Concerning LELC of the urinary tract, however, no reported case has shown any association of EBV, as in our case¹⁷. Despite the morphological similarity to lymphoepithelioma of the nasopharynx, there may be an alternative etiology for LELC in the urinary tract, such as an exaggerated host immune response.

It has been proposed that LELC of the urinary tract has a

relatively favorable prognosis in pure or predominant forms⁹. Concerning LELC of the ureter, all the five previously reported cases showed no evidence of disease after surgical resection²³⁴⁵⁶. Expanding rather than infiltrative growth pattern, (Figure 2), absence of lymphovascular invasion, and complete resection of the tumor suggested a favorable prognosis in our case. However, the follow-up period of the reported cases was relatively short (range 12 to 30 months). Moreover, contrary to previous reports, a recent study by Tamas et al. demonstrated that LELC of the urinary bladder treated by cystectomy had a similar prognosis to ordinary urothelial carcinoma, and did not differ between pure and mixed cases⁷. Since there is sparse data regarding the prognosis of LELC of the ureter, further large scale studies are needed to elucidate its prognosis.

In conclusion, we reported a case of LELC of the ureter. Recognition of this type of tumor is important to avoid misdiagnosis.

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