CASE REPORT

# *Lymphoepithelioma-like carcinoma of the ureter discovered intraoperatively during a hysterectomy*

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MA P, LEONARD T, TRUSSELL JC. Lymphoepithelioma-like carcinoma of the ureter discovered intraoperatively during a hysterectomy. The Canadian Journal of Urology. 2008;15(6):4421-4424.

*We present a patient with a T2NXMX lymphoepithelioma-like carcinoma (LELC) of the lower third of her left ureter discovered incidentally during removal of a large uterine mass. This case of LELC is unique for its presentation in the context of fibroid mass and its distinct (incidental) manner of discovery. To our knowledge, this will be the sixth case report to describe LELC of the ureter. A review of available literature and summary of upper tract cases are provided.*

**Key Words:** lymphoepithelioma-like carcinoma, LELC, ureteral malignancy, incidental

## Introduction

Lymphoepithelioma-like carcinoma (LELC) of the ureter is rare and has only been described five times in the literature. This case is unique in that it was discovered incidentally during an abdominal hysterectomy. Knowing the characteristics of these readily treated tumors, and differentiating them from high grade lymphomas, is of great importance. Based on relatively limited data, long term follow-up for this condition should follow established guidelines for transitional cell carcinoma of the same location…with the caveat that upper tract LELC lesions do well with surgical intervention and typically do not require adjuvant therapy. Ureteral cases are rare and are often advanced at the time of diagnosis. Nonetheless, they have all been of the "pure" subtype (devoid of TCC components) and have been successfully treated solely through surgical intervention.

Accepted for publication June 2008

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## Patient presentation

A 64-year-old female patient with a single episode of painless gross hematuria had a hematuria work up at an outside facility that demonstrated left hydronephrosis and a large uterine mass. This hematuria work up demonstrated a negative cytology, a contrast enhanced CAT scan demonstrated left hydroureter, and a retrograde ureterogram of the involved side demonstrated absence of contrast in the proximal ureter (attributed to extrinsic, uterine compression). No ureteral mass was appreciated preoperatively. She presented to our institution for gynecological care of her uterine fibroids and was scheduled to undergo an exploratory laparotomy, bilateral salpingo-oophorectomy, and total abdominal hysterectectomy for an 11.1 cm x 6.5 cm x 8.8 cm, 253 gram uterus. During the gynecological portion of the procedure, though no ureteral injury occurred, the left distal ureter was noted to have a large intrinsic mass—located just below the common iliac vessels. Intraoperative urological consultation was obtained. A discussion occurred with the patient's representative during which consent for both an excisional biopsy and ureteral repair were obtained. The ureteral mass was isolated, excised, and sent for a frozen section. Frozen sections demonstrated

TABLE 1. **Ureter lymphoepithelioma-like carcinoma (LELC) neoplasm staining summary**

| Case | CD 20 | CD3** | Ck AE1/3 | CK 7 | CK20 | EBV | Other stains |
|---|---|---|---|---|---|---|---|
| Present case | (-) | N/A | (+) | (+) | (-) | (-) | |
| Terai[1] | (+)* | (+)* | (+) | (-) | (-) | (-) | |
| Oz and Sedmak[13] | N/A | N/A | N/A | N/A | N/A | N/A | |
| Roig[10] | N/A | N/A | (+) | N/A | N/A | (-) | P53 neu/c-erbB2 UCHL-1 |
| Ng[9] | N/A | (+)* | (+) | N/A | N/A | (-) | AE3 (-) |
| Chalik[8]*** | (+) | (+) | | (+) | (+) | (-) | CD68 histiocytes |
| TCC | (-) | (-) | (+) | (+) | (+) | (+) 31% | |

* = lymphoid infiltrates
** = CD 3 T-cells predominant in Terai and Ng cases
*** = CD 20 predominated CD3 by 2:1 ratio
N/A = results of stain not available
TCC = transitional cell cancer

the presence of a malignancy with negative ureteral margins. A left distal ureterectomy with bladder cuff, psoas hitch, and a stented, refluxing ureteral-vesical anastomosis was completed without complication. Postoperatively, no adjuvant therapy was performed. The patient is now 24 months post-op and has no evidence for recurrence—cytologies, cystoscopies, ureteroscopies, lymph node biopsy, and CT urograms have all been negative.

## Histology

LELC's are readily identified histologically by characteristic syncitial nests of undifferentiated malignant cells in a background of lymphocytes.[1] The World Health Organization (WHO) recognizes such tumors as an independent subcategory of urothelial carcinoma, distinct from transitional cell carcinomas.[2] Unlike lymphoepitheliomas that occur in other sites, such as the nasopharynx, evidence of Epstein-Barr viral protein synthesis is not detected by in situ hybridization in urinary tract LELC's. To further distinguish these tumors from TCC, 31% of conventional transitional cell carcinomas of the urinary bladder demonstrate evidence of active Epstein-Barr viral protein synthesis.[1]

### *Macroscopic*

Left ureter specimen measured 3.0 cm X 1.1 cm X 1.0 cm with a pink-red, smooth and glistening external surface. Tumor mass was firm, yellow, and obstructing and obliterating the entire internal ureter portion and expanding the normal ureter dimensions.

### *Microscopic*

Hisotologic sections demonstrated essentially complete obliteration of the ureteral lumen by tumor, which was composed of nests and irregular cords of

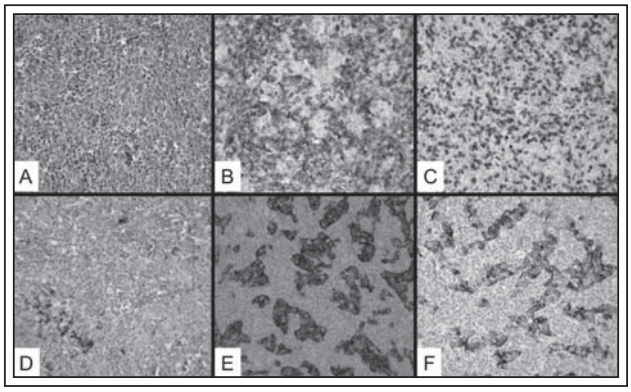


**Figure 1.** Photomicrographs (200x total magnification) of ureteral LELC. Routine hematoxylin and eosin staining (A) shows nests and irregular cords of undifferentiated carcinoma within a pronounced lymphoid stroma. The lymphoid stroma is highlighted by the brown membranous staining in the leukocyte common antigen (LCA, CD45 rb) immunoperoxidase stain (B). The polymorphous lymphoid stroma shows a preponderance of lymphocytes with a T-cell immunophenotype (C, CD3 immunoperoxidase stain) with fewer scattered B-cells (D, CD20 immunoperoxidase stain), in keeping with a reactive lymphoid infiltrate. The undifferentiated carcinoma is highlighted by mixed cytokeratin (E, AE1/AE3) and cytokeratin 7 (F) immunoperoxidase stains.

undifferentiated cells with large, pleomorphic nuclei, many with prominent nucleoli. These cells had poorly defined cytoplasmic borders and were present within a background of a dense polymorphous lymphoid stroma. Neoplastic (epithelial) cells showed positive immunohistochemical staining for cytokeratin AE1/3 and CK7; a cytokeratin 20 stain was essentially negative. The lymphoplasmacytic infiltrate stained strongly for leukocyte common antigen (LCA), while the neoplastic cells were LCA negative. While the lymphocytic background showed both CD3 and CD20 positive staining cells, the majority were CD3-positive, in keeping with the reactive nature of the lymphoid stroma, Table 1. These histologic findings are consistent with the diagnosis of a lymphoepithelial-like carcinoma. There was no distinct component suggestive of a conventional transitional cell carcinoma, Figure 1.

## Discussion

LELC is most commonly found in the nasopharynx and other foregut structures, with rare presentations in other locations, including the urothelial lining. When present urologically, bladder lesions predominate.

TABLE 2. **Summary of lymphoepithelioma-like carcinoma (LELC) cases in the renal pelvis and ureter**

| Case report | Year | Site | Sex age | Chief complaint | Stage | Treatment | Follow up | Outcome |
|---|---|---|---|---|---|---|---|---|
| Present case | 2008 | U | F 64 | Gross HU uterine mass | T2NXMX | Ureterectomy | 24 mn | NED |
| Terai[1] | 2005 | U | M 72 | Gross HU | pT2pN0 | Neph-U | 30 mn | NED |
| Oz and Sedmak[13] | 2005 | U | F 71 | Unknown | Unknown | Neph-U | Unknown | Died of pancreatic CA 3 yr postop |
| Roig[10] | 2001 | U | M 58 | Gross HU | Unknown | Neph-U | 18 mn | NED |
| Ng[9] | 1999 | U | F 62 | Micro HU | T2N0M0 | Neph-U | 18 mn | NED |
| Chalik[8] | 1998 | U | M 75 | Gross HU, intermittent flank pain | T3N0M0 | Ureterectomy psoas hitch | 12 mn | NED |
| Yamada[6] | 2007 | RP | F 75 | Gross HU | T3N0M0 | Nephrectomy | 6 mn | NED |
| Perez-Motiel[7] | 2006 | RP | F 72 | Unknown | T3 | Unknown | N/A | DWT |
| Perez-Motiel[7] | 2006 | RP | M 68 | Unknown | T3 | Unknown | N/A | DWT |
| Cohen[12] | 1999 | RP | F 79 | Macroscopic HU | T3N0M0 | Neph-U | 6 mn | NED |
| Fukunaga[11] | 1998 | RP | M 70 | HU | unknown | Nephrectomy Partial cystectomy Adrenalectomy Splenectomy Adj radiotherapy (50 Grey) | 72 mn | NED |

Modified from Yamada Y, Fujimura T, Yamaguchi T, Nishimatsu H, Hirano Y et al. Lymphoepithelioma-like carcinoma of the renal pelvis. Int J Urol 2007;14:1093-1094. Used with permission.

U = ureter; RP = renal pelvis; HU = hematuria; Neph-U = nephroureterectomy; Mn = months; NED = no evidence of disease; DWT = dead with tumor

To date, LELC arising from the renal pelvis has been described only five times and six times in the ureter, Table 2. To further characterize this malignancy, LELC is subdivided histologically based upon the percentage of non-LELC components—most commonly transitional cell carcinoma. The sub-types include pure (100%), predominant (> 50%), or focal (< 50%)—depending on the extent of involvement by LELC cells.[1,3] Greater percentages of non-LELC cells worsens prognosis. The "focal" subtype has a particularly poor prognosis with 0% disease free and 0% disease specific survival. Improved prognosis is noted with the "pure" and "predominate" subtypes having 81% and 82% disease free survivals, and 93% and 93% disease specific survival rates, respectively.[4] Of note, in its "pure" form, LELC (of the bladder) has been chemotherapy responsive.[3,5] All of the six reported cases of ureteral LELC, including the case we report here, are of the "pure" subtype.

In four out of five previous cases, LELC of the ureter presented initially with hematuria—three of which had gross hematuria (as did the present case). One ureteral LELC case failed to report the initial presentation.

This patient's ureteral LELC was discovered as an incidental finding during a TAH-BSO. Diagnosis was made in the context of a concomitant uterine fibroma which was reportedly obscured the LELC on prior radiographs (CT scan and IVP). In contrast, prior LELC-cases involving the ureter and renal pelvis have been diagnosed successfully using CT, IVP, retrograde pyelogram, cystogram, or combinations of these modalities.

Recurrence free follow-up has been reported at 18 and 30 months in ureteral LELC cases, and up to 6 years in renal pelvis cases.[6,7] Unlike cases involving the bladder, adjuvant chemotherapy and radiotherapy has not been used for treatment of ureteral LELCs. Surgical excision has successfully treated all reported ureteral LELC cases to date.[1,6,8-10] In contrast, a single renal pelvic LELC case reported a 6-year survival with adjuvant radiation therapy.[11]

Pure-type LELC of the bladder are reported by Porcaro et al to have disease free survival and disease specific survival of 81% and 93% respectively (n = 17) with a single fatality.[4] Transurethral resection bladder tumor (TURBT) alone or with adjuvant chemotherapy can be effective treatment for "pure" and "predominant" bladder LELC. Of note, Porcaro et al report no clear benefit for adjuvant therapy was demonstrated for "pure" and "predominant" subtypes.[4] Amin et al reported that bladder LELC treated with adjuvant chemotherapy following TURBT resulted in disease free follow-up reported from 9 to 72 months.[3]

To date, all reported ureteral LELC cases have been of the "pure" subtype and have been successfully treated with surgical intervention alone. In contrast, LELC of the bladder can present with the "predominant" or less favorable "focal" subtypes—which may require adjuvant chemotherapy. □

References


1. Terai A, Terada N, Ichioka K, Matsui Y, Yoshimura K et al. Lymphoepithelioma-like carcinoma of the ureter. Urology 2005;66:1109.
2. Eble JN, Sauter G., Epstein JI, Sesterhenn IA (Eds): World Health Organization. Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. IARC Press: Lyon 2004.
3. Amin MB, Ro JY, Lee KM, Ordóñez NG, Dinney CP et al. Lymphoepithelioma-like carcinoma of the urinary bladder. Am J Surg Pathol 1994;18:466-473.
4. Porcaro AB, Gilioli E, Migliorini F, Antoniolli SZ, Iannucci A et al. Primary lymphoepithelioma-like carcinoma of the urinary bladder: report of one case with review and update of the literature after a pooled analysis of 43 patients. *Int Urol Nephrol* 2003;35:99-106.
5. Dinney CP, Ro JY, Babaian RJ. Lymphoepithelialioma of the bladder: a clinicopathological study of 3 cases. *J Urol* 1993;149:840-841.
6. Yamada Y, Fujimura T, Yamaguchi T, Nishimatsu H, Hirano Y et al. Lymphoepithelioma-like carcinoma of the renal pelvis. *Int J Urol* 2007;14:1093-1094.
7. Perez-Montiel D, Wakely PE, Hes O, Michal M, Suster S. High-grade urothelial carcinoma of the renal pelvis: clinicopathologic study of 108 cases with emphasis on unusual morphologic variants. *Mod Pathol* 2006;19:494-503.
8. Chalik YN, Wieczorek R, Grasso M. Lymphoepithelioma-like carcinoma of the ureter. J *Urol* 1998;159:503-504.
9. Ng KF, Chen TC, Chang PL. Lymphoepithelioma-like carcinoma of the ureter. *J Urol* 1999;161:1277-1278.
10. Roig JM, Amérigo J, Velasco FJ, Giménez A, Guerrero E et al. Lymphoepithelioma-like carcinoma of ureter. *Histopathology* 2001;39:106-107.
11. Fukunaga M, Ushigome S. Lymphoepithelioma-like carcinoma of the renal pelvis: a case report with immunohistochemical analysis and in situ hybridization for the Epstein-Barr viral genome. *Mod Pathol* 1998;11:1252-1256.
12. Cohen RJ, Stanley JC, Dawkins HJ. Lymphoepithelioma-like carcinoma of the renal pelvis. *Pathology* 1999;31:434-435.
13. Oz Z, Sedmak B. Lymphoepithleioma-like carcinoma of the ureter – A Case report. *Zdrav Vestn* 2005:74:711-712.