Case Report
A case of predominant lymphoepithelioma-like carcinoma of the renal pelvis and literature review

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Abstract: Lymphoepithelioma, as is well known, is a form of undifferentiated epithelial tumor, which is primarily described in the nasopharynx and characterized by syncytial sheets of malignant epithelial cells with a prominent reactive lymphoid infiltrate in background. A carcinoma that shows similar histological features but arises outside the nasopharynx is called lymphoepithelioma-like carcinoma (LELC). Primary LELC of the renal pelvis is very rare and there is only limited information in the published reports. We managed a case of a 59-year-old man, who presented with asymptomatic gross hematuria for more than one month. MRI showed that right kidney accounted for a soft tissue signal mass with a diameter of 2.3 cm in renal pelvis. He was treated with the Robot assisted Radical resection of the right tumor and was diagnosed with a pT3 N0 cM0, the high grade of renal invasive urothelial carcinoma, with predominant Lymphoepithelioma-like carcinoma differentiation. Unlike nasopharyngeal lymphoepithelioma, in situ hybridization analysis of this urinary LELC was negative for the Epstein-Barr virus. Here we report on one more case of primary LELC of the renal pelvis, and review of the published reports, particularly those describing the expression of Epstein-Barr virus.

Keywords: Lymphoepithelioma-like carcinoma, renal pelvis, Epstein-Barr virus

Introduction
Lymphoepithelioma is a form of undifferentiated epithelial tumor, characterized by syncytial nests of malignant epithelial cells with a prominent reactive lymphoid infiltrate in background, and primarily described in the nasopharynx [1]. Tumors that show the similar histological features but arise outside the nasopharynx are called lymphoepithelioma-like carcinoma (LELC). According to some reports, lymphoepithelioma-like carcinoma may be pure, predominant, or focally admixed with typical urothelial carcinoma or other variants [2, 3]. Other organs include the tonsil, salivary glands, thymus, lungs, stomach, skin, uterine cervix, breast, prostate, and the urinary tract [4]. In most cases, lymphoepithelioma-like carcinoma is related to Epstein-Barr virus (EBV), especially in the thymus gland (thymoma with lymphoid hyperplasia), but no association has been reported between lymphoepithelioma-like carcinoma of the bladder and EBV [5, 6]. To the best of our knowledge, this is the tenth case of lymphoepithelioma-like carcinoma of the renal pelvis in the English literature [1, 4, 7-12].

Case report
A 59-year-old man, who presented with asymptomatic gross hematuria for more than one month. Cystoscopy showed hematuria spurring from the left ureteral orifice. MRI (Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School) showed that right kidney accounted for a soft tissue signal mass with a diameter of 2.3 cm in renal pelvis. (Figure 1). The patient was treated with the Robot assisted laparoscopic radical resection of the right tumor, then treated with GC (Gemcitabine+Cisplatin, GC) chemotherapy regimens. And a cytological examination of urine showed malignant cells. Intraoperative pathology showed undifferentiated carcinoma and the origin was not diagnosable. The pathological stage was pT3 NO cM0. Histopathological examination showed sheets of undifferentiated cells with large pleomorphic nuclei and promi-
Predominant lymphoepithelioma-like carcinoma of the renal pelvis

![Figure 1](image1.png)

**Figure 1.** MRI showed that right kidney accounted for a soft tissue signal mass with a diameter of 2.3 cm in renal pelvis.

![Figure 2](image2.png)

**Figure 2.** Histopathological examination showed sheets of undifferentiated cells with large pleomorphic nuclei and prominent nucleoli, indistinct cytoplasmic borders.

...nent nucleoli, indistinct cytoplasmic borders (Figure 2). These cells were composed of malignant cells with the syncytial appearance, the background consists of a prominent lymphoid infiltrate that includes T and B lymphocytes, plasma cells, histiocytes, surrounding individual tumor cells. The histological picture was compatible with lymphoepithelial carcinoma. From these findings, this tumor was diagnosed as predominant LELC (> 50%) of the renal pelvis. The epithelial cells of this tumor expressed P63 and GATA3 by immunohistochemistry examination (Figure 3). The stromal lymphoid cells showed positive stains for CD3, CD20 (Figure 4). Epstein-Barr virus encoded ribonucleic acid (RNA, EBER) in situ hybridization study was carried out using fluorescein labeled oligo probes, but confirmed negative in the tumor or adjacent stromal lymphoid cells (Figure 5).

![Figure 3](image3.png)

**Figure 3.** The epithelial cells of this tumor expressed P63 (A) and GATA3 (B) by immunohistochemistry examination.

...No recurrence of this case has been seen for about 6 months.

**Discussion**

Lymphoepithelioma usually presents as undifferentiated carcinoma of the nasopharynx and comprises the largest category of neoplasms within the spectrum of nasopharyngeal carcinoma. Tumors that show similar features but occurring in diverse anatomical locations are called “lymphoepithelioma-like carcinoma” (LELC). Other sites of the body include the tonsil, salivary gland, thymus, lung, stomach, skin and cervix. It is rarely seen in the urinary tract, especially in the renal pelvis, with only isolated cases involving the urinary bladder, ureter, and kidney [1].

LELC has been recently described as a distinct variant of urothelial carcinoma in the latest 2016 World Health Organization Classification of Tumors [6]. It is more common in men and occurs in late adulthood, with a mean patient...
Predominant lymphoepithelioma-like carcinoma of the renal pelvis

The age of 69 years (range: 44-90 years). As with other urological malignancies, hematuria is the most common sign, and most patients present with stage pT2-3 disease [6]. Amin et al, described a classification system, determined by the percentage of LELC morphology within the tumor, characterizing pure (100%), predominant (> 50%) and focal (< 50%) disease [13], this case represents a predominant form of LELC. Some scientists have suggested that pure or predominant lymphoepithelioma-like carcinoma has a relatively better prognosis and response to chemotherapy than traditional urothelial carcinoma, allowing for preservation of bladder functions; but when the component of the lymphoepithelioma-like carcinoma is only focal or less, these tumors, however, will behave similarly to conventional urothelial carcinoma [14].

Histologically, the tumor is composed of nests, sheets, and cords of undifferentiated cells with large pleomorphic nuclei, and has high nuclear to cytoplasmic ratios, vesicular chromatin and prominent nucleoli, indistinct cytoplasmic borders, and a syncytial appearance. The background consists of a prominent lymphoid infiltrate that includes T and B lymphocytes, plasma cells, histiocytes, and occasional neutro-

Figure 4. (A) The corresponding HE staining of (B-D). The stromal lymphoid cells showed positive stains for CD20 (B), CD3 (C) and the epithelial cells of this tumour also expressed CK7 (D).

Figure 5. Epstein-Barr virus encoded ribonucleic acid (RNA, EBER) in situ hybridization was negative in the tumour or adjacent stromal lymphocytes.
Predominant lymphoepithelioma-like carcinoma of the renal pelvis

Table 1. The clinicopathological characteristics of reported LELC of the renal pelvis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Symptom</th>
<th>Location</th>
<th>Size (cm)</th>
<th>T</th>
<th>S</th>
<th>EBV status</th>
<th>HC</th>
<th>Follow-up</th>
<th>Outcome</th>
<th>Year</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>70</td>
<td>Hematuria</td>
<td>UN</td>
<td>UN</td>
<td>RN+RT</td>
<td>UN</td>
<td>N</td>
<td>Pre</td>
<td>6 years</td>
<td>NED</td>
<td>1998</td>
<td>Fukunaga et al [7].</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>79</td>
<td>Hematuria</td>
<td>R</td>
<td>4</td>
<td>NU</td>
<td>T3N0M0</td>
<td>N</td>
<td>Pre</td>
<td>6 months</td>
<td>NED</td>
<td>1999</td>
<td>Cohen et al [8].</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>72</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>RN</td>
<td>T3</td>
<td>N</td>
<td>Pre</td>
<td>3 months</td>
<td>DWD</td>
<td>2006</td>
<td>Perez-Motiel et al [9].</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>68</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>RN</td>
<td>T3</td>
<td>N</td>
<td>Focal</td>
<td>12 months</td>
<td>DWD</td>
<td>2006</td>
<td>Perez-Motiel et al [9].</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>75</td>
<td>Hematuria</td>
<td>L</td>
<td>3.5</td>
<td>NU</td>
<td>T1N1M0</td>
<td>N</td>
<td>Pure</td>
<td>36 months</td>
<td>NED</td>
<td>2007</td>
<td>Haga et al [1].</td>
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<tr>
<td>6</td>
<td>UN</td>
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<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>UN</td>
<td>6 months</td>
<td>NED</td>
<td>2007</td>
<td>Tamas et al [10].</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>75</td>
<td>Hematuria</td>
<td>L</td>
<td>3.7</td>
<td>RN</td>
<td>T3N0M0</td>
<td>N</td>
<td>UN</td>
<td>6 months</td>
<td>NED</td>
<td>2014</td>
<td>Ahn et al [12].</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>75</td>
<td>Hematuria</td>
<td>R</td>
<td>4.5</td>
<td>NU</td>
<td>T3N1M0</td>
<td>UN</td>
<td>Pre</td>
<td>6 months</td>
<td>NED</td>
<td>2013</td>
<td>Modi et al [4].</td>
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<tr>
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<td>F</td>
<td>65</td>
<td>Hematuria</td>
<td>R</td>
<td>5.3</td>
<td>RN</td>
<td>T3N0M0</td>
<td>N</td>
<td>Pre</td>
<td>7 months</td>
<td>NED</td>
<td>2016</td>
<td>Present case</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>59</td>
<td>Hematuria</td>
<td>R</td>
<td>2.3</td>
<td>RN</td>
<td>T3N1M0</td>
<td>N</td>
<td>Pre</td>
<td>6 months</td>
<td>NED</td>
<td>2016</td>
<td>Present case</td>
</tr>
</tbody>
</table>

T: treatment; S: stage; EBV: Epstein-Barr virus; HC: histological classification; M: male; F: female; R: right; L: left; UN: unknown; RN: radical nephrectomy; RT: radiation therapy; N: negative; NU: nephroureterectomy; Pre: predominant; NED: no evidence of disease; DWD: died with disease.

phils or eosinophils, with eosinophils being prominent in rare cases. The epithelial cells of this tumor are immunoreactive with several cytokeratin markers and often express p63 and GATA3.

Unlike in the head and neck location, no association has been reported between the urinary tract LELC and Epstein-Barr virus [5]. In our case, EBV encoded ribonucleic acid (RNA, EBER) in situ hybridization study was also negative. In most of the published cases, EBV was reported to be positive in the organs which have direct external exposure such as nasopharynx, and negative in the organs which are completely internal, such as kidney. This may contribute further evidence to no association between EBV and the urinary tract LELC [15].

LELC of the urinary tract is usually diagnosed in less-advanced clinical stages [16]. The prognosis is favorable well for patients presenting with the pure and predominant forms with a diploid DNA pattern and very poor for patients presenting with focal LELC [5].

Clinico-pathological characteristics of patients with LELC of the renal pelvis are shown in Table 1. Including this case, there have been ten reported cases of LELC of the renal pelvis in the English literature. Of these ten patients, six were female and the mean age was 72. Most patients presented with painless hematuria and had an advanced stage (pT3) of disease. Almost all tumors were negative for EBV examination. Seven patients were managed with radical surgery, three were treated with nephroureterectomy and two patients also had auxiliary radiotherapy. Due to the rarity of LELC of the renal pelvis, there are no better guidelines regarding the management of this disease, it is interesting to note that from the case series in Table 1, two of the three patients who underwent radical nephrectomy alone died with the disease. However, all those who underwent radical nephroureterectomy and auxiliary chemotherapy or radiotherapy had no evidence of disease on follow-up.

This may support the theory that it is related to urothelial carcinoma, LELC of the urinary tract requires radical resection of the entire upper urinary tract. This conclusion has been supported by Haga and colleagues [1].

Disclosure of conflict of interest

None.

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Predominant lymphoepithelioma-like carcinoma of the renal pelvis


