



Pathology Page

Primary lymphoepithelioma-like carcinoma of the urinary bladder

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Received : 20-12-2016

Revised : 24-01-2017

Accepted : 02-02-2017

A 74-year-old male with diabetes mellitus and hypertension complained of lower urinary tract symptoms, including urinary frequency, incontinence, and weak stream for 1 month. Intermittent painless gross hematuria was also noted. He went to a local hospital for help. Physical examination was unremarkable. However, bladder sonography showed a large hyperechoic bladder mass. Computerized tomography revealed huge bladder tumors with irregular borders, bladder wall thickening, and contrast enhancement. The tumors almost occupied the whole bladder. Diagnostic transurethral bladder tumor biopsy showed a poorly differentiated carcinoma. Herein, the patient was transferred to our hospital, where radical cystoprostatectomy, bilateral ureterocutaneostomy, and pelvic lymph node dissection were performed. During the operation, the urinary bladder had huge papillary tumors and indurated left lateral wall with palpable lymph nodes at the left pelvic wall. No prostatic or intestinal involvement was grossly found. After operation, the patient recovered uneventfully. However, because of the poor performance status of the patient, he did not receive any adjuvant chemotherapy. He eventually died of urosepsis after 9 months.

Microscopic examination revealed extensive infiltration of almost poorly and undifferentiated tumor cells, densely packed in solid nests and sheets with pale cytoplasm, ill-defined cytoplasmic borders, large nuclei, vesicular chromatin, and prominent nucleoli [Figures 1 and 2]. The background revealed dense accumulation of inflammatory cells, including mature lymphocytes, plasma cells, histiocytes, neutrophils, and eosinophils. Tumor invasion to perivesical soft tissue was present, while no prostate involvement or metastasis of lymph node was found. Immunohistochemically, tumor cells were positive for 34 β E12, CK7, p63, p40, and p53, while negative for CK20, GATA-3, Uroplakin III, AMACR, and CD45. EBV *in situ* hybridization was negative.

Lymphoepithelioma-like carcinoma (LELC) is an undifferentiated carcinoma with histological features similar to undifferentiated, nonkeratinizing carcinoma of the nasopharynx. LELC occurs in various organs, including salivary glands, thymus, lung, skin, stomach, uterine cervix, and breast. Its occurrence in the urinary system is rare [1]. The reported incidence rate of LELC of the bladder (LELCB) ranges

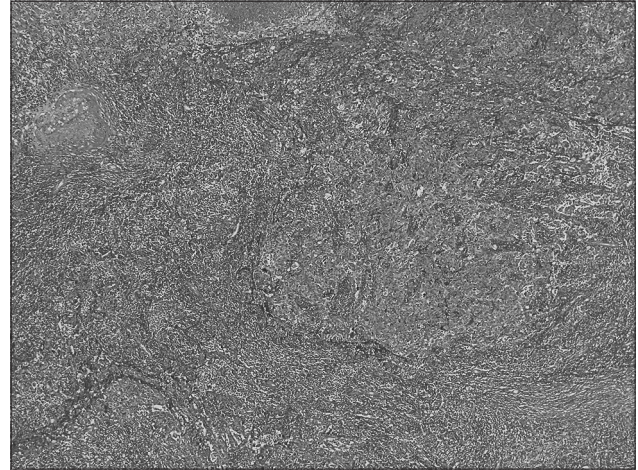


Figure 1: Microscopically, there were solid nests and sheets of poorly and undifferentiated tumor cells accompanying with dense inflammatory infiltration (H and E, $\times 40$)

from 0.3% to 1.3% of all bladder cancers [2-4]. The primary urothelial LELC was described for the first time by Zukerberg *et al.* in 1991 [5]. Until 2014, only 93 cases with LELCB were reported. Most cases of LELCB occurred in their seventh decade with male predominance [1,6]. The presenting symptoms of LELCB were similar to urothelial carcinomas. Gross hematuria and irritative voiding disorders were the most common complaints of these patients.

It is clinically difficult to distinguish bladder tumor variants. The pathological differential diagnosis includes malignant lymphoma, undifferentiated urothelial carcinoma with prominent lymphoid infiltrate, chronic cystitis, and small cell carcinoma [1]. LELC is classified histologically according to lymphoepithelioma component as pure (100%), predominant ($\geq 50\%$), or focal ($< 50\%$). Most cases of LELCB have muscle-invasive T2 or T3 disease regardless of histological

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How to cite this article: Chen CC, Loh TW. Primary lymphoepithelioma-like carcinoma of the urinary bladder. Tzu Chi Med J 2017;29(2):125-126.

| Access this article online | |
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| Quick Response Code:  | Website: www.tcmjmed.com |
| | DOI: 10.4103/tcmj.tcmj_28_17 |

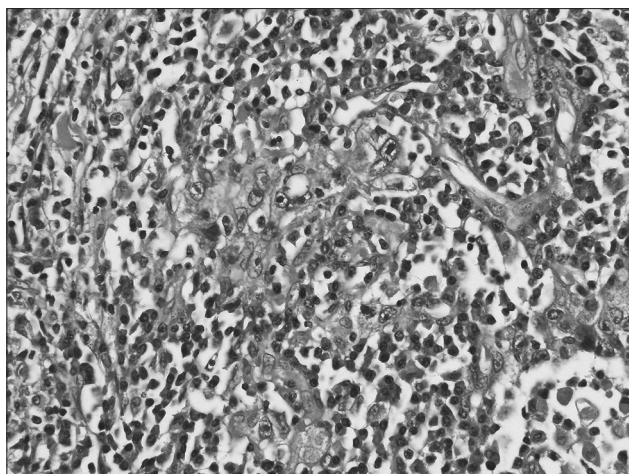


Figure 2: Morphologically, the neoplastic cells have large nuclei, pale cytoplasm, irregular cellular borders, prominent nucleoli, and active mitoses (H and E, $\times 400$)

classification [1]. The metastatic potential of LELC seems low [2,7]. No evidence of a viral etiology for LELCB is proven. The immunohistochemical profile of LELCB seems to include positivity for high molecular weight CK34bE12, CK7, and p63, coupled with negativity for CK20 in most cases. The predominance of lymphoepithelial component might be a good prognostic factor. Some authors contribute the causes to the intense host inflammatory reaction against tumor, or earlier diagnosis and better chemotherapy response than conventional urothelial carcinoma [1,6,8].

Owing to the rarity of LELCB, there is no treatment guideline for these patients. Treatments of LELCB often consist of transurethral endoscopic resection, or partial cystectomy, or radical cystectomy. Cisplatin-based chemotherapy plus radiation therapy is usually the adjuvant treatment [6]. Due to the huge bladder tumor burden and poor performance status of our patient, he received radical cystoprostatectomy and ureterocutaneostomy diversion without any following chemotherapy or other treatments. In summary, LELCB is an enigmatic entity with a unique histologic appearance and incompletely understood biological behavior. From reported

cases, it has been concluded that it typically responds well to transurethral resection followed by chemotherapy.

Declaration of patient consent

The authors certify that the patient has obtained appropriate patient consent form. In the form the patient has given the consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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