

C A S E R E P O R T

Lymphoepithelioma like carcinoma of the urinary bladder, treated with transurethral resection and intravesical Bacillus Calmette Guerin therapy only: A case report

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Abstract. Lymphoepithelioma-like urothelial carcinoma, which was first identified by Zukerberg, constitutes 0,4-1,3% of all urothelial carcinomas and has similar histomorphological features with nasopharyngeal lymphoepithelioma. We report a case of predominant lymphoepithelioma like bladder carcinoma in a 72 years old male patient. Transurethral resection of the bladder and adjuvant intravesical Bacillus Calmette Guerin treatment was applied. The patient is currently at the 16th month after diagnosis and no recurrence or metastasis has been observed in cystoscopic and radiological examinations. (www.actabiomedica.it)

Key words: Lymphoepithelioma like urothelial carcinoma, Transurethral resection, Bacillus Calmette Guerin

Introduction

Bladder cancers are the most common cancers of the urinary system. Over 90% of bladder cancers are urothelial carcinomas (UC) (1). In 25% of UC cases, many types of differentiation apart from classical UC morphology are seen (2) as a result of different embryological origins of the bladder and the high metaplastic capacity of the urothelium (3).

Lymphoepithelioma-like UC constitutes 0,4-1,3% of all UCs and has similar histomorphological features with lymphoepithelioma, which is the undifferentiated carcinoma of the nasopharynx (4). Lymphoepithelioma-like UC, first identified by Zukerberg et al in 1991, has different morphological and prognostic features and different treatment approaches than conventional UC cases (5).

In our study, we aimed to discuss a rare case of lymphoepithelioma-like UC with its clinical and pathological features.

Case Presentation

A 72-year-old male patient with hematuria referred to the urology clinic with contrasted abdominal MRI report which revealed a 30x18 mm contrast-enhanced mass lesion localized in the midline towards the superior of the bladder. No feature was observed in the patient's physical examination and medical history. The patient underwent cystoscopy with a preliminary diagnosis of bladder carcinoma, and transurethral resection (TUR) was performed.

TUR material was fixed in 10% formaldehyde for 24 hours and then paraffin block was prepared, and sections were taken. In hematoxylin eosin (HE) stained sections, tumoral infiltration forming layers and trabeculae, showing lamina propria invasion was observed in a background of dense mixed inflammatory cells. Tumor composed of undifferentiated cells with indistinct cytoplasmic borders and prominent large nucleolus, forming syncytial pattern (Fig. 1, 2). In

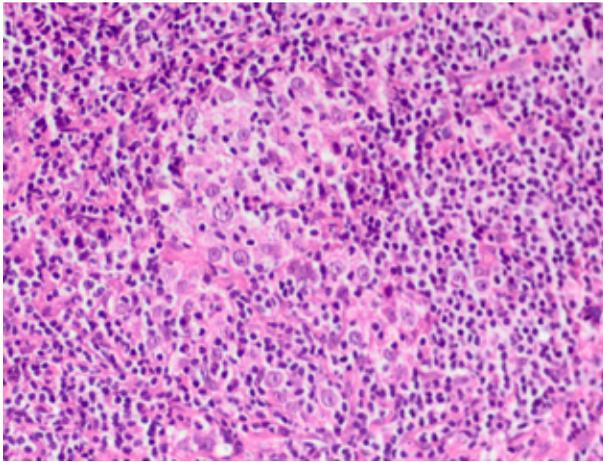


Figure 1. Hematoxylin Eosin (x40): Lymphoepithelioma like UC, tumoral cells with dense inflammatory cells

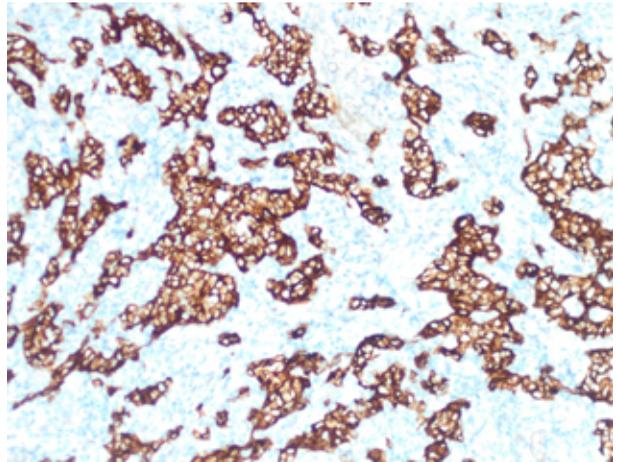


Figure 3. Immunohistochemical staining. Tumoral cells are positive for PANCK

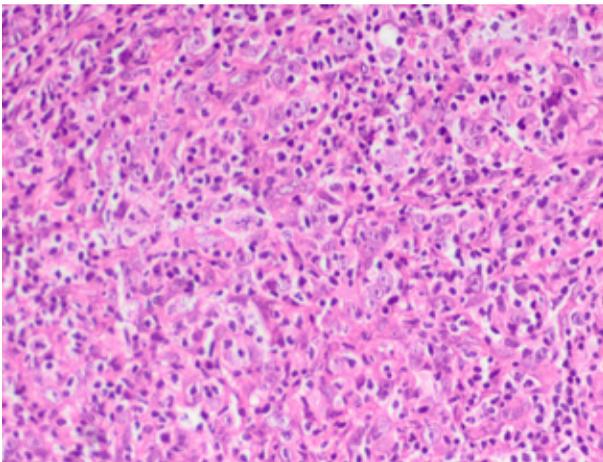


Figure 2. Hematoxylin Eosin (x40): Lymphoepithelioma like UC. Undifferentiated tumoral cells with syncytial pattern and prominent large nucleolus

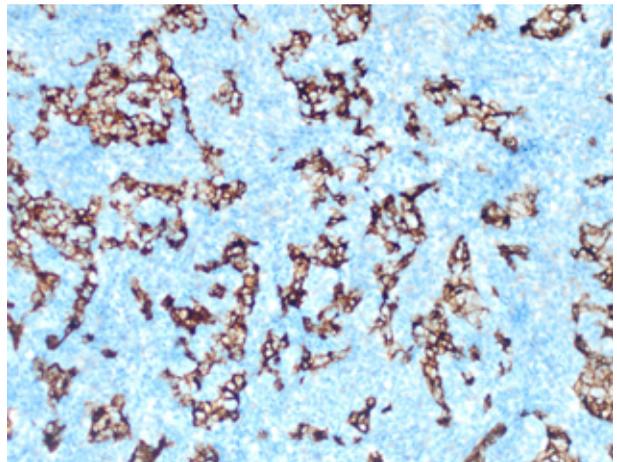


Figure 4. Immunohistochemical staining. Tumoral cells are positive for CK 7

the immunohistochemical study, tumoral cells were found positive with panCK (AE1 / AE3), CK7 and GATA-3 (Fig. 3, 4). Inflammatory cells were shown with CD3 and CD20, vascular structures were CD31 positive. A noninvasive UC component was present in less than 5% of the TUR material. Muscularis propria was not observed in the specimen. With the existing morphological, immunohistochemical and radiological findings, the case was reported as lymphoepithelioma-like UC showing lamina propria invasion.

Radiological examinations including chest CT and abdominopelvic CT including renal excretory phase revealed no perivesical and upper urinary tract involvement, lymphadenopathy or distant metastasis. Re-TUR was performed one month after the initial diagnosis. In the re-TUR material, chronic inflammation and foreign body-type inflammatory reaction were detected and muscularis propria layer was also present. Thus, the stage was determined as pT1N0M0.

Since lymphoepithelioma-like urothelial carcinoma is a variant histology and is at the highest risk group in terms of disease progression, radical cystoprostatectomy was primarily recommended. Upon the patient's refusal; intravesical BCG therapy with three-year maintenance and cystoscopic examination with an interval of 3 months was planned. Annual chest CT and abdominopelvic CT including the renal excretory phase were planned for radiological follow-up. Adjuvant intravesical Bacillus Calmette Guerin (BCG) treatment was applied at the 6th week, 3rd month, 6th month and 12th month after re-TUR. No lesion was observed in the 3rd, 6th, 9th and 12th months control cystoscopies and bladder washing cytology materials were reported as benign. The patient is currently at the 16th month after diagnosis and no recurrence or metastasis has been observed in cystoscopic and radiological examinations.

Discussion

The reasons for the large number of UC variants can be explained by the high variation capacity of urothelium, having origins from different embryological structures during embryological development, being capable of transforming into squamous, glandular and kidney epithelium experimentally, and the embryologic development from two different pathways (6,7).

Ten different variants are defined in the world health organization (WHO) 2016 classification (1). The variants show significant differences among themselves in terms of prognosis and treatment approaches and also create difficulties in differential diagnosis. While squamous differentiation, glandular differentiation and micropapillary variant are the most common ones among cases reported in the literature, lymphoepithelioma-like, large nested, large cell neuroendocrine variants are rarely encountered (2,4).

Lymphoepithelioma-like UC has morphological features similar to the lymphoepithelial carcinoma of the nasopharynx. This type of carcinoma has also been defined in breast, skin, lung, salivary gland organs and constitutes 0.4-1.3% of all bladder carcinomas. Although relation with Epstein Barr virus (EBV) was detected in nasopharyngeal lymphoepithelioma cases,

such relation was not observed in lymphoepithelioma-like carcinomas of the bladder (4,8).

Microscopically, lymphoepithelioma-like UC consists of tumor cells with indistinct cytoplasmic borders, showing syncytial pattern and infiltrating as nests, cords or layers which are accompanied by prominent lymphoid infiltration consisting of dense lymphocytes, plasma cells, histiocytes and to a lesser extent, neutrophils and eosinophils. Occasionally, lymphoid infiltration may be intense enough to suggest lymphoma. Necrosis and mitosis are frequently observed (2,9).

In the study by Amin et al., UC cases were divided into three classes according to the amount of their lymphoepithelioma-like component. If lymphoepithelioma-like component constituted all biopsy material it was classified as pure, if more than half it was classified as predominant, and if less than half it was classified as focal (9).

It has been reported in the literature that, as a result of the suppressive effect of prominent lymphoid infiltration and cytotoxic T lymphoid response on tumor cells, prognosis is better in patients with tumors classified pure and predominant, compared to focal (10,11). However, due to a limited number of cases, no definitive comment can be made about the prognosis of these cases.

In the differential diagnosis of lymphoepithelioma-like UC, lymphoproliferative diseases, chronic cystitis, UC with a pronounced inflammatory response and metastasis come first due to intense inflammatory background. Immunohistochemical staining may be helpful in differential diagnosis. In differentiation from lymphoproliferative diseases and chronic cystitis pankeratin and LCA can be used. Cytokeratin 7 can be used to distinguish from nasopharyngeal metastatic lesions. Nasopharyngeal carcinomas do not express cytokeratin 7, whereas bladder lymphoepithelioma-like carcinomas express. Morphological parameters, such as the syncytial pattern of the tumor cells, are more helpful in differentiation from conventional UCs with intense inflammation (8-10).

Due to the limited number of cases reported in the literature, a standard treatment approach has not yet been determined in these cases. Deep TUR, partial cystectomy and radical cystectomy have been reported as treatment modalities; and cisplatin-based

systemic chemotherapy, radiotherapy, intravesical chemotherapy, intravesical BCG regimens have been reported as adjuvant therapy options. It has been reported that, in cases in which only TUR was applied, disease-free survival was shorter in cases with focal lymphoepithelioma-like UC, compared to pure or predominant cases. It has also been reported that radical cystectomy is not required in all cases showing muscle invasion, especially pure and predominant lymphoepithelioma-like UC cases can be followed up by chemotherapy and/or radiotherapy after TUR or partial cystectomy, and radical cystectomy and adjuvant chemotherapy are required in muscle invasive cases with focal lymphoepithelioma-like UC (10-12).

In our case with predominant lymphoepithelioma-like UC, there was no progression or recurrence in the follow-up after TUR and intravesical BCG treatment. We think that this situation may be meaningful in the follow-up and treatment options of invasive lymphoepithelioma-like UC cases that do not show muscle invasion. However, long-term follow-up results are required for these cases to set an example in the treatment approach. Lymphoepithelioma-like UC is a rare variant of urothelial carcinoma, and many more cases and long-term follow-up results of these cases are needed to be able to determine the standard treatment approaches.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article”.

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Arrived: 15 May, 2020

Accepted: 29 July, 2020

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