Case report

Primary lymphoepithelioma-like carcinoma of the urinary bladder: Case report and literature review

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1. Introduction

A lymphoepithelioma is an undifferentiated epithelial carcinoma of the nasopharynx, histologically distinct due to the prominent lymphoid infiltration. Carcinomas with similar histological features arising outside the nasopharynx are called lymphoepithelioma-like carcinomas (LELCs), which have been described in the lungs, thymus, salivary glands, cervix, and bladder. A primary LELC of the urinary bladder was first reported in 1991. To date, fewer than 75 cases have been reported in the literature. The pure form of LELC is considered to have a favorable prognosis and may respond well to chemotherapy and radiotherapy. It is important to differentiate an LELC from a lymphoma, poorly differentiated urothelial carcinoma, and poorly differentiated squamous cell carcinoma with a lymphoplasmacytic background, because an LELC of the urinary bladder can be managed with bladder preservation in some cases. Herein, we report a case of an LELC of the urinary bladder in a 71-year-old man, to highlight its possibility despite its rarity.

2. Case report

A 71-year-old man presented with intermittent painless gross hematuria for several weeks. An initial examination with intravenous urography (IVU) revealed a filling defect in the bladder wall. Cystoscopy showed a 2 cm sessile tumor located in the bladder dome (Fig. 1). Computed tomography (CT) of the abdomen and pelvis showed no evidence of perivesical tumor invasion or distant metastasis. Thus, the patient received transurethral resection (TUR) and fulguration of the bladder tumor. However, follow-up cystoscopy showed a recurrent bladder tumor from the original tumor bed 6 months later. A partial cystectomy with pelvic lymph node dissection was performed for the solitary bladder tumor.

Histopathology showed that the tumor consisted of high-grade tumor cells admixed with lymphoid tissue, resulting in a picture reminiscent of a nasopharyngeal carcinoma (Fig. 2). The tumor showed transmural infiltration, but no invasion of the perivesical fat (Fig. 3). Therefore, the tumor was assessed as stage T2 disease. Immunohistochemical studies showed that the neoplasm was positive for cytokeratin (AE1/AE3) (Fig. 4) but negative for vimentin (Fig. 5), high-molecular-weight cytokeratin (34betaE12), cytokeratin 5/6, cytokeratin 20, and CD141. The morphologic features and the immunoprofile of the tumor supported a diagnosis of a pure LELC of the urinary bladder. The surgical margins and dissected lymph nodes were tumor-free.

The Foley catheter was removed 2 weeks after the partial cystectomy. No tumor recurrence was identified by cystoscopy performed at 3, 6, 12, 18, and 24 months. CT scans showed no evidence...
of tumor recurrence or metastasis during follow-up. The patient is currently alive and free of disease.

3. Discussion

An LELC of the urinary bladder is an extremely rare tumor first described by Zukerberg et al in 1991. In 1994, Amin et al categorized LELCs of the urinary bladder into three subgroups: pure, predominant (>50% lymphoepithelial component), and focal (<50% lymphoepithelial component). To date, fewer than 75 cases have been reported. The largest study was by Porcaro et al, who pooled 43 cases from several sources. According to their pooled analysis, an LELC of the urinary bladder is a male-predominant tumor with a male-to-female ratio of 3:1. The average age was 68.4 (52–84) years. Most patients present with painless gross hematuria. During a mean follow-up of 37.7 months, the disease-specific overall survival was 71%. It was noteworthy that survival of the pure and predominant forms of LELC of the urinary bladder was >90%. Most previous studies suggested that patients with an LELC, especially of the pure and predominant forms, have a relatively better prognosis compared to patients with a stage-matched urothelial carcinoma. An intense immunological response by infiltrating lymphoid cells against the tumor may play an important role. Moreover, inflammatory infiltration may cause early symptoms, such as gross hematuria, frequency, and urgency, which should promptly alert patients.

The Epstein-Barr virus (EBV) is sometimes associated with a lymphoepithelioma of the nasopharynx, but EBV was not detected in any of the cases of LELC of the urinary bladder. Increased expression of the p53 protein, which is not related to the p53 mutation, was demonstrated. Histopathological features of LELCs closely resemble those of lymphoepitheliomas of the
nasopharynx. LELCs are composed of nests, sheets, or cords of large undifferentiated malignant epithelial cells within a dense inflammatory background. Tumor cells have large vesicular nuclei with prominent nucleoli and scant cytoplasm. The differential diagnosis includes poorly differentiated squamous cell carcinoma, small-cell carcinoma of the urinary bladder, and a lymphoma. Immunohistochemical studies for cytokeratin and lymphoid markers can help in resolving the differential diagnosis. Identification of epithelial markers, such as epithelial membrane antigen (EMA) and several cytokeratins (AE1/AE3, CK7, and CK8), can confirm the epithelial origin of the LELC and exclude a diagnosis of a lymphoma. LELCs of the urinary bladder are typically negative or focally positive for CK20. In contrast, a traditional urothelial carcinoma may show high positivity for CK20.4,8 Vimentin, a protein found especially in connective tissues, is used as a sarcoma tumor marker. Negative staining for vimentin can exclude a diagnosis of a sarcoma. A poorly differentiated urothelial carcinoma with lymphoid infiltrate is another differential diagnosis that should be considered. However, urothelial carcinomas are typically positive for cytokeratin 20, high-molecular-weight cytokeratin (34βE12), and CD141.3 In our patient, the initial pathological analysis from TUR showed an undifferentiated carcinoma, which was negative for CD141, prostate-specific antigen, and prostatic acid phosphatase. The final diagnosis of an LELC was confirmed, after complete tumor resection, by the histological pattern and immunohistochemistry, which showed that the tumor was positive for cytokeratin (AE1/AE3) (Fig. 4) and negative for vimentin (Fig. 5), high-molecular-weight cytokeratin (34βE12), cytokeratin 5/6, cytokeratin 20, and CD141. According to the 2004 World Health Organization classification (Table 1), undifferentiated carcinomas are a category including small-cell carcinoma, large-cell neuroendocrine carcinoma, lymphoepithelioma-like carcinoma, osteoclast-rich carcinoma, giant-cell carcinoma and otherwise unspecified carcinomas. Because urothelial neoplasia has a pronounced ability for divergent differentiation, it is important that surgical pathologists be aware of this potential for multidirectional differentiation and make a precise diagnosis.

To date, the histogenesis of atypical cells of LELCs is unknown. A recent study by Williamson et al15 found characteristic chromosomal abnormalities in LELCs compared to traditional urothelial carcinomas, using UroVysion fluorescence in situ hybridization. Those findings indirectly suggest that pathogenesis of urinary LELCs and traditional urothelial carcinomas may be similar.

Owing to limited experience, standard therapeutic approaches for LELCs of the urinary bladder are not well established yet. In cases of small tumors without deep invasion, TUR of the bladder tumor with adjuvant therapy may be sufficient. A partial or radical cystectomy may be necessary in cases of large or muscle-invasive tumors. The pure and predominant forms of LELCs may respond well to cisplatin-based chemotherapy. Dinney et al reported a complete response to chemotherapy and TUR of bladder tumors in three cases of muscle-invasive LELCs, with no evidence of recurrence after 6 years of follow-up.10 Radiotherapy and intravesical chemotherapy are also used as adjuvant therapies. However, the survival benefit is not well documented, due to the limited number of cases. Because most LELCs of the urinary bladder present as solitary sessile masses and the rate of metastasis is low, bladder preservation may be possible. However, some authors suggested that conservative treatment should be considered only in cases of pure or predominant LELCs.9 Our patient is well without evidence of disease 24 months after a partial cystectomy.

In conclusion, LELCs of the urinary bladder are rare. It is important to differentiate them from other tumors because of their relatively favorable prognosis. Although standard treatment has not been established, a combination of a bladder-preserving approach and adjuvant therapy may be appropriate.

Conflicts of interest statement

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References


