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Case Report

Bladder Lymphoepithelioma-Like Carcinoma: Case Report and Literature Review

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Abstract

Urinary Lymphoepithelioma-like carcinoma are rare tumours classified according to Lymphoepithelioma component as pure (100%), predominant (≥50%) or focal (<50%), that is correlated with prognosis.

We present here an original case of a 54 year-old man who was diagnosed with a high-grade T2 transitional cell carcinoma associated with LELC >50%. Four cycles of neoadjuvant gemcitabine and platinum-based chemotherapy were carried out with a good tolerance. After completed chemotherapy, the patient underwent a radical cyst prostatectomy with lymph nodes dissection and orthotropic urinary diversion. One year after surgery the patient remains free from relapse.

It's difficult to define the optimal strategy, literature reporting only small series. Nevertheless, the benefit of chemotherapy is certain.

The outcome is good in the pure and predominant forms and poorer in focal subtypes.

Keywords: Bladder cancer; Lympho-epithelial; Carcinoma; Chemotherapy

Introduction

Lymphoepithelioma-Like Carcinoma (LELC) is a rare tumour, which has a close link to Epstein-Barr virus. (EBV) It's commonly found in nasal pharyngea, stomach, cervix, lung, hepatobiliary tract and ovary [1].

Its occurrence in the urinary system is very rare. LELC of the urinary bladder was first described by Zuckerberg in 1991 [2]. It represents between 0,4 and 1,3% of all bladder cancers. These tumours are classified according to Lymphoepithelioma component as pure (100%), predominant (≥50%) or focal (<50%) [3].

We present here an original case of a 54 year-old man who was diagnosed with a LELC of the urinary bladder and discuss its management regarding the lake of data in the literature.

Case Report

A 54 year-old Caucasian man presented few weeks history of haematuria associated with urinary frequency and dysuria. He had no medical history. He underwent surgery for discal hernia and appendicectomy a long time ago. He was a smoker since he was 15 year-old and stopped for fifteen years.

He underwent transurethral resection for its bladder tumour.

The results of histological examination confirmed a high-grade T2 transitional cell carcinoma with LELC >50%. On immunohistochemical staining the CKAE1/AE3, p53, was positive and CK7 and CD20 were negative.

In order to classify this tumor, the patient got a CT scan of the chest and the abdomens as well as a bone scan showing no evidence of loco regional extension or metastases. Blood tests showed a moderate anemia and normal kidney and hepatic functions. The tumor was classified according TNM classification of urinary bladder cancer (2009) as a stage T2b, N0, M0.

After discussion of the case during a multidisciplinary GU round, treatment with neoadjuvant gemcitabine and platinium-based chemotherapy was carried out. The patient received four cycles with a good tolerance (no grade 3 or more toxicity).

After completed chemotherapy, the patient underwent a radical cystoprostatectomy with lymph nodes dissection and orthotopic urinary diversion.

The final pathological evaluation of the tumour was predominant transitional cell carcinoma with LELC, classified ypT2R0pN0 tumour, and a low-risk Gleason 6 prostate adenocarcinoma.

The patient is under close observation with regular clinical and radiologic follow-up. He is for now considering in remission for 6 months.

Discussion

Lymphoepithelioma-like carcinoma of the bladder is a rare variant, often manifesting in T2-T3 (usually muscle-invasive) stages and occurring in male patients of 60 year-old.

They are revealed most of the time by haematuria, generally accompanied with urgency.

These tumours have a favorable prognosis with a five-year survival of 59%, achieving 62% in the pure type, compared to transitional cell carcinoma [4].

They respond better to chemotherapy than transitional cell carcinoma. The exact pathogenesis of this tumour is not well

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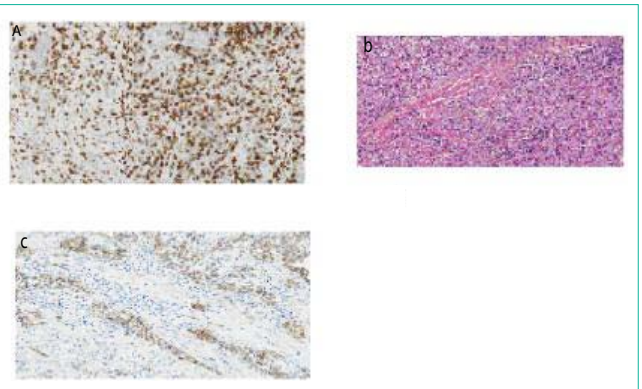

Figure A: Immunohistochemistry for CD3.
Figure B: Hematein Eosin Safran X10.
Figure C: Keratin.

established. Epstein-Barr virus is frequently associated with Lymphoepithelioma of the nasopharynx but has not been found in the LELC of the urinary bladder. Abnormality of p53 regulation might be a part of the pathogenesis [5]. These tumours are characterized by a prominent lymphocytic infiltration. They may occur in an association with transitional cell carcinoma.

Kenichi et al. reported a case of LELC of the bladder and a review of the literature [6].

The total 103 cases with LELC of urinary tract were reported between 1991 and 2012. Seventy-three males (70,9%) and 30 females (29,1%) with mean 68,9 years (ranged from 44 to 90 years) were included.

Regarding the histological type, the pure type was 41/103 cases (39,8%), the mixed type was 47/103 cases (45,6%). The others were not shown. In addition to LELC, the coexistent Gleason 3+3 (n=1), 3+4 (n=1) and 4+3 (n=3) adenocarcinoma in the prostate was found.

The tumors were diagnosed at high stages: 14/98 cases T1 (14,3%); 49/98 cases T2 (50%); 30/98 cases T3 (30,6%); 2/98 (2%).

Treatment consisted of radical cystectomy in 34/98 cases (34,7%), partial cystectomy in 7/98 cases(7,1%), transurethral resection in 46/98 cases (46,9%), nephroureterectomy in 6/98 cases (6,1%), nephrectomy in 2/98 cases (2%), ureterectomy in 1/98 cases (1%) and the others were unknown.

Adjuvant therapies were chemotherapy in 28/98 (28,6%), radiotherapy in 17/98 (17,3%), and intravesical chemotherapy in 3/98 (3,1%).

The mean follow up was 21,7 months. 61/92 cases (66,3%) had no evidence of disease, 14/92 cases (15,2%) were tumor death, 9/92 (9,8%) had metastasis (lung, lymph nodes, skin, and abdomen), and 8/92 cases (8,7%) were death of other cause.

Amin et al. described a classification system, based on the percentage of LELC morphology: pure (100%), predominant (≥50%) and focal (<50%) disease. Both lymphocytic (CD20, CD21, CD68, CD79a, CD45R0) and epithelial (CK7, CK20, AE1, AE3, EMA) markers can be over expressed [7].

In their pooled analysis of 56 patients, Serrano et al. concluded that focal disease is more aggressive and requires a radical cystectomy; pure or predominant tumors could benefit from a bladder-preserving treatment [8].

The benefits of chemotherapy are recognized, especially in infiltrative disease. In the Serrano study, patients with pure/predominant LELC who received chemotherapy followed by surgery showed a 100% disease-free survival, compared with 53% disease-free survival in those who did not (median follow up of 34 and 25 months respectively).

Platinium-based agents have shown promising outcomes. In fact, Dinney et al. used cisplatin as neoadjuvant chemotherapy for three patients with LELC. All patients remained free of recurrence after six years of follow-up [9].

Ziouziou et al. nevertheless described the case of a patient treated only by radical surgery for a LELC of bladder [10].

In our case the patient was treated with four cycles of neoadjuvant chemotherapy with cisplatin. The response was excellent after chemotherapy and the patient underwent surgery. No adjuvant treatment was delivered because of the N0, R0 status.

However it's difficult to define the optimal strategy, literature reporting only small series. The benefits of chemotherapy are certain. Multiple chemotherapy regimens have been used, but platinum-based agents have shown good outcomes.

Differential diagnoses are: lymphoma or inflammatory lesions like chronic cystisis. Evidence suggests that transitional cell carcinoma have poorer prognosis than LELC. Focal LELC is expected to be more aggressive than pure form.

It can be explained by the immune response due to the lymphoid cells against the tumour.

Conclusion

In summary our case is an original report, it underlines many questions.

First of all the problem of differential diagnosis, which can need the help of experiences pathologists.

Then, no guidelines exist due to a few case-reports and studies.

Other studies are needed to better understand the pathology and help the management.

The outcome is good in the pure and predominant forms and bad in focal subtypes. That suggests that in the first case, patients could be treated with a sparing approach, while, and in the other case, cystectomy and systematic adjuvant treatment seem to be the best choice.

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