Case Report

GATA-3 expression in primary pure choriocarcinoma of the bladder

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Abbreviations & Acronyms
CT = computed tomography
H&E = hematoxylin and eosin
MRI = magnetic resonance imaging

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Introduction: Primary pure choriocarcinoma of the bladder is extremely rare and should be distinguished from urothelial carcinoma. GATA-3 is a zinc finger transcription factor and a known sensitive immunostaining marker for urothelial carcinoma. However, its accuracy in the detection of urothelial carcinoma is moderate and it is also an important factor in trophoblast differentiation.

Case presentation: A 78-year-old man presented with asymptomatic gross hematuria for 6 months. Cystoscopy and clinical imaging revealed local bladder carcinoma. He underwent a radical cystectomy and histological diagnosis revealed pure choriocarcinoma (pT2aN0M0) with positive immunostaining, indicating GATA-3 was present. Systemic chemotherapy could not be applied due to his poor general condition, and he died 7 months after surgery.

Conclusion: We reported the first case of pure choriocarcinoma of the bladder, which showed positive immunostaining results indicating the presence of GATA-3.

Key words: bladder, case report, choriocarcinoma, GATA-3, immunohistology.

Keynote message

Choriocarcinoma of the bladder has an aggressive malignant potential and results in a poorer prognosis than urothelial carcinoma. GATA-3 may be expressed in both urothelial carcinoma and choriocarcinoma. Choriocarcinoma of the bladder should be correctly distinguished from urothelial carcinoma by recognizing its immunostaining pattern and careful interpretation of the results.

Introduction

Choriocarcinoma is a rare neoplasm that mainly occurs in the uterus and ovaries following a molar pregnancy in females. In males, testicular choriocarcinoma is most common among patients in their 20s and 30s.[1] Extragonadal choriocarcinoma usually develops in midline structures like the mediastinum, retroperitoneum, and pineal gland but rarely occurs in other organs such as the lungs, gastrointestinal tract, breasts, or urinary bladder.[1] To date, only 42 cases of primary choriocarcinoma of the bladder have been reported, and 67% of those included urothelial carcinoma.[2–7] Thus, primary pure choriocarcinoma of the bladder is extremely rare.

In recent years, GATA-3 has been known as a useful immunohistochemical marker in the detection of urothelial and breast carcinomas. GATA-3 combined with other related markers such as uroplakins[8] may enable us to distinguish urothelial carcinoma from other malignancies of the bladder.

In this study, we report on the first case of primary pure choriocarcinoma of the bladder with an immunohistological staining pattern showing GATA-3 and other markers.

Case presentation

A 78-year-old man presented with asymptomatic gross hematuria for 6 months. He had a history of smoking 80 cigarettes per day for 32 years, hypertension, and brain infarction. Cystoscopy revealed a large nodular mass partially covered by a necrotic surface in the left bladder wall (Fig. 1). Fluorodeoxyglucose-positron emission tomography/CT scans showed hydronephrosis of the left kidney; however, no enlarged lymph nodes or distal metastases

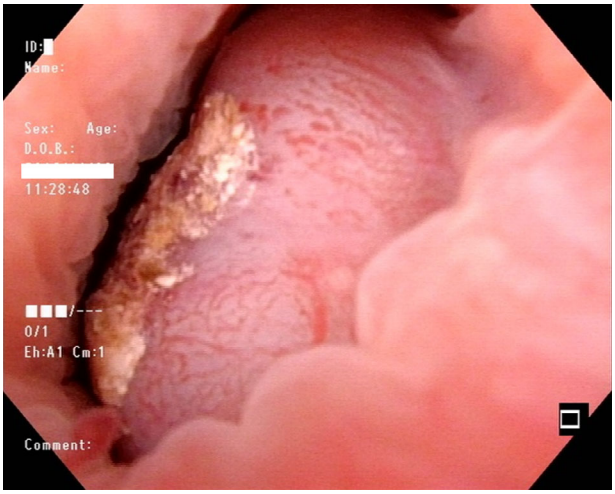

Fig. 1 Cystoscopy showing a nodular tumor in the left bladder wall.

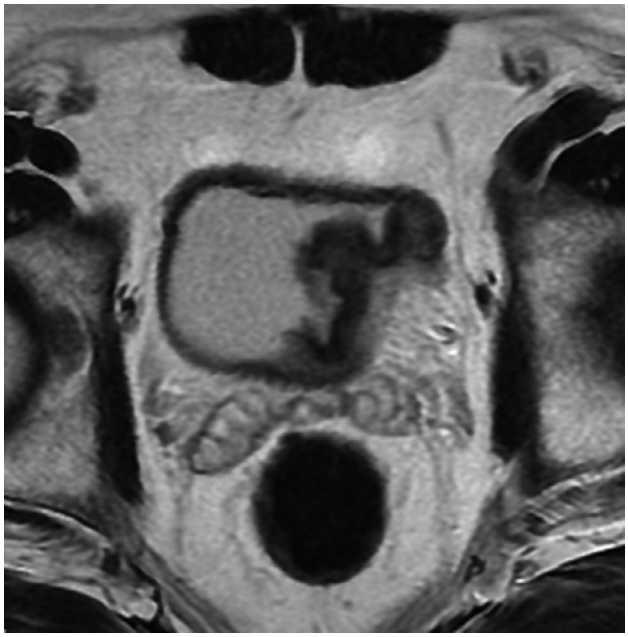

Fig. 2 MRI T2 weighted axial plane. The mass located at the left bladder wall.

were seen. MRI scans indicated T2 bladder cancer (Fig. 2). A transurethral resection of the tumor was performed, and the histological findings of H&E staining indicated potential muscle-invasive high-grade urothelial carcinoma. Subsequently, he underwent a laparoscopic radical cystectomy, pelvic lymph node dissection, and bilateral cutaneous ureterostomy. Histologically, the tumor showed pleomorphic nuclei and atypical syncytial trophoblastic cells. Immunohistochemical analyses showed that the tumor cells were positive for β-hCG, GATA-3, AE1/AE3, and CK7, but negative for uroplakin II, uroplakin III, CK20, and hPL (Fig. 3). There was no evidence of any urothelial carcinoma component morphologically and immunohistochemically. The diagnosis was given as pure choriocarcinoma of the bladder (pT2a, INFβ, ly0, v0, u-rt0, u-lt0, RM0, pN0). His serum β-hCG level was not preoperatively measured. His serum LDH level was within normal range before and after surgery. Two weeks after total cystectomy, his serum β-hCG level was 0.3 ng/mL (normal range <0.1 ng/mL). No other primary lesions or residual tumors were detected by systemic CT scans, testicular MRI, or ultrasonography. However, at 11 postoperative weeks, CT scans revealed multiple lung, liver, and pelvic lymph node metastases and peritoneal dissemination. His serum β-hCG level gradually increased to 2000 ng/mL. Any systemic chemotherapy could not be applied due to his poor general condition, and he died 7 months after surgery.

Discussion

To the best of our knowledge, only 11 cases with detailed clinical information of primary pure choriocarcinoma of the bladder have been reported.[2–7] In the 11 patients, the mean age was 62.9 years (range 19–81). Of these patients, 72.7% (8/11) were men, and this trend was consistent with the cases of urothelial carcinoma of the bladder. Interestingly, 81.8% (9/11) of the cases were reported from Asian countries. Of the cases, four were reported to undergo cystectomy and seven were administered systemic chemotherapy as treatment. However, 63.6% (7/11) were already dead at the time of publication after a relatively short follow-up period. This indicates that primary pure choriocarcinoma of the bladder harbors an aggressive malignant potential and results in a poorer prognosis than urothelial carcinoma. Thus, pure choriocarcinoma of the bladder should be correctly distinguished from urothelial carcinoma for proper treatment to be provided.

β-hCG is a well-known biomarker of choriocarcinoma that can be used for immunohistological evaluation and clinical follow-up of disease progression by monitoring of the serum level. Elevated serum β-hCG levels may require additional postoperative chemotherapy even without the positive imaging results of metastasis.[9] Cisplatin-based chemotherapy such as methotrexate, vinblastine, doxorubicin, and cisplatin and bleomycin, etoposide, and cisplatin have shown a potential increase in survival rates. However, the optimal regimen of chemotherapy for extragonadal choriocarcinoma of the bladder is still unclear.

The histogenesis of extragonadal choriocarcinoma is uncertain, and choriocarcinoma of the bladder often contains varying degrees of urothelial carcinoma components.

To prove the existence of urothelial carcinoma, uroplakins have been used to diagnose with urothelial carcinoma. As to immunohistochemical expression for bladder invasive urothelial carcinoma, uroplakin Ⅱ has sensitivity of 63% and specificity of 95%, and uroplakin III has sensitivity between 19% to 53% and specificity of 100%.[10] In this case, immunohistochemical expressions of uroplakin II and uroplakin III are negative and no morphological feature of urothelial carcinoma, so we ruled out urothelial carcinoma. For diagnosis of urothelial carcinoma, GATA-3 has been recently used in the histopathological evaluation as a specific immunostaining marker positive for urothelial cells, in addition to the use of uroplakins. GATA-3 is a transcription factor that binds to the consensus DNA sequence to aid the development of several

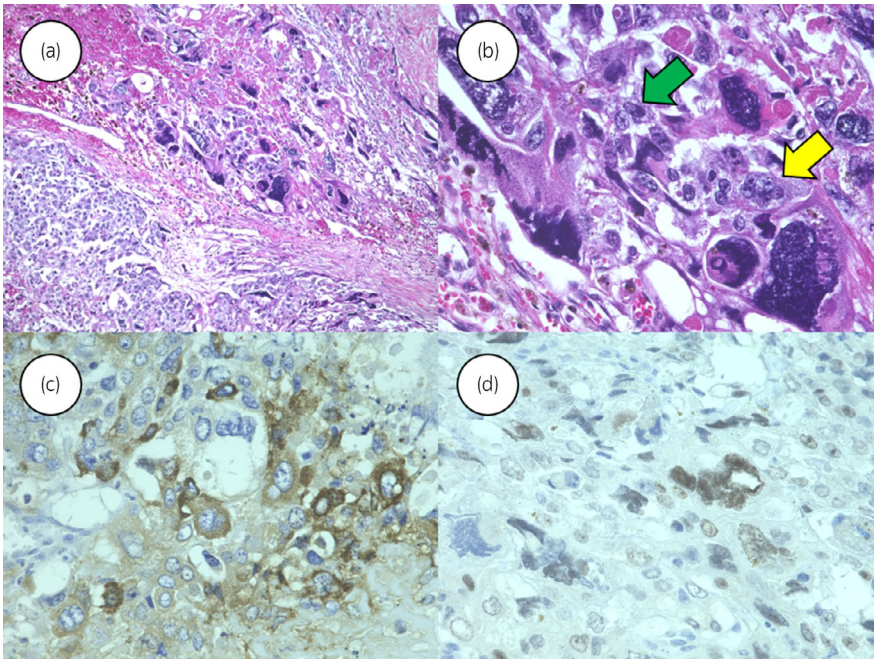

Fig. 3 Microscopic examinations of the tumor. (a,b) Hematoxylin–eosin stained section at 10× and 40× magnification, in which two types of tumor cells (syncytiotrophoblast giant cell [yellow arrow] and cytotrophoblast cell [green arrow]) are visible. The tumor cells are positive for (c) β-hCG and (d) GATA-3.

tissues and cell lineages,[8,11] and is known as a useful immunohistochemical marker, particularly for urothelial and breast carcinomas. In high-grade tumors, the expression of GATA-3 is positive in 67–86% of urothelial carcinomas and 48–94% of breast carcinomas.[11]

Recent reports have demonstrated the positive expression of GATA-3 in trophoblastic neoplasms, and 78% of choriocarcinomas showed positive immunostaining for GATA-3.[11] Thus, it was concluded that GATA-3 may act as a diagnostic marker for trophoblastic tumors.

In this case, morphological evaluation in H&E staining suggested the presence of pure choriocarcinomas. However, the existence of urothelial carcinomas could not be completely excluded. Therefore, additional immunohistochemical examinations were done. As a result, β-hCG and GATA-3 tests were broadly positive, but tests for uroplakins in the tumor cells were negative. Thus, we reached a diagnosis of pure choriocarcinoma of the bladder without a urothelial carcinoma component.

The primary limitation of this report is that the results were derived only from a single case. However, primary pure choriocarcinoma of the bladder is extremely rare. Though we monitored serum β-hCG level for clinical follow-up of disease progression, we did not examine preoperative markers of gonadal tumors, such as β-hCG and α-fetoprotein. Therefore, gonadal tumor staging and the International Germ Cell Consensus Classification could not be evaluated. But, to our best knowledge, previous reports stage a bladder choriocarcinoma as bladder cancer or have no information to stage.[4]

Choriocarcinoma of the bladder should be correctly distinguished from urothelial carcinoma, but GATA-3 may be expressed in both urothelial carcinoma and choriocarcinoma. As such, both appropriate recognition of immunostaining patterns and careful interpretation of the results are needed.

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Conflict of interest

The authors declare no conflict of interest.

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