Clinical Course of Plasmacytoid Urothelial Carcinoma of the Upper Urinary Tract: A Case Report

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Key Words

Cadherins · Chemotherapy · Immunohistochemistry ·
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Abstract

Plasmacytoid urothelial carcinoma of the bladder represents a rare and aggressive variant of urothelial carcinoma, which is usually diagnosed at an advanced pathologic stage. Until now, no reports exist on this rare tumor type in the upper urinary tract. Herein, we present the first report on the clinical course of a metastatic plasmacytoid urothelial carcinoma of the renal pelvis and show its unfavorable outcome despite multimodal therapy.

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Background

Plasmacytoid urothelial carcinoma (PUC) is a rare variant of urothelial carcinoma (UC), which accounts for about 3% of all muscle-invasive UCs. PUC is characterized by distinct clinical and histopathological features and patients with this disease have a poor prognosis because it is usually diagnosed at an advanced pathological

stage. Notably, loss of E-cadherin expression seems to be constitutive for this particular tumor. Herein, we present the first clinical experience reported in metastatic PUC of the upper urinary tract treated with multimodal therapy.

Case Presentation

A 72-year-old female presented with a history of recurrent urinary tract infections that had been treated repeatedly with antibiotics during the past months. Intermittent gross and permanent microscopic hematuria led to an additional sonographic examination, which revealed a solid tumor mass in the right renal pelvis. Cystoscopy showed no abnormal findings. Computed tomography (CT) confirmed the diagnosis of a solid mass in the right renal pelvis measuring 3 cm in diameter. There were also enlarged retroperitoneal lymph nodes in the para-aortal and interaortocaval areas with a maximum size of 2.7 cm. Open standard nephroureterectomy with ipsilateral lymph node dissection (hilar and limited interaortocaval with a removal of 5 lymph nodes) and removal of a bladder cuff was performed revealing a macroscopic white-to yellow-colored tumor of the right renal pelvis with a knotty appearance that infiltrated the renal calices.

Microscopy showed a tumor with solid and papillary areas with cells exhibiting prominent nucleoli with eosinophilic cytoplasm, leading to a plasma cell like appearance (fig. 1, 2). Tumor cells invaded the peripelvic fat as well as the lymphatic and blood vessels, leading to a tumor classification of pT3 L1 V1 G3 pN1 (ac-

Fig. 1. Tumor cells of PUC of the upper urinary tract infiltrating the peripelvic fat of the specimen. HE. $\times 100$.

Fig. 2. PUC of the upper urinary tract showing medium-sized tumor cells with a single cell growth pattern exhibiting prominent nucleoli with an eosinophilic cytoplasm, leading to a plasma cell-like appearance. HE. $\times 400$.

cording to the TNM classification of 2004). Additionally, tumor invasion was detectable. Immunohistochemistry showed negative staining for E-cadherin, CK20, and CD138, whereas staining was positive for PAN-CK and CK7. No pathological findings were apparent with bone scanning for skeletal metastasis.

Owing to the advanced tumor stage, adjuvant chemotherapy with two courses of gemcitabine ($1,250 \text{ mg/m}^2$ days 1 and 8) and carboplatin (area under the curve 5) was initiated. Chemotherapy was well tolerated. A restaging CT 2 weeks after chemotherapy showed no residual cancer. The maximum diameter of the formerly enlarged lymph nodes was described as 1 cm after palliative chemotherapy.

Five months after the first courses of gemcitabine and carboplatin, radiological follow-up of the patient revealed recurrent lymph node enlargement, and another three courses of gemcitabine and carboplatin were planned because of the good initial response. However, a restaging CT after completing these courses revealed progressive lymph node metastasis, so that the chemotherapy with gemcitabine and carboplatin was stopped. Sixteen months after the initial diagnosis, the patient developed symptomatic osseous metastases in the pelvis. Palliative combined radiochemotherapy using paclitaxel as a radiosensitizer and a subsequent total radiation dose of 36 Gy was performed and led to temporary local and symptomatic control. However, after another three months, cerebral and cerebellar metastases were diagnosed owing to persistent headache and swindle. During the further disease course, the patient's consciousness worsened (Glasgow Coma Scale score 10), and a cerebral shunt was performed leading to considerable symptomatic relief. Radiation therapy of the diagnosed cerebellar metastasis followed, but was not tolerated by the patient. At this time, the patient refused further therapies and died after a total clinical course of 20 months.

Discussion

PUC is a rare histologic variant of UC with an incidence of 3% of all muscle invasive bladder carcinomas [1]. This frequency was confirmed by our own studies as recently reported [2]. We also characterized this rare variant on a molecular level in the largest series described so far [3].

PUC is a high-grade tumor characterized by a poor patient prognosis because it is usually diagnosed at an advanced pathologic stage, probably owing to its specific cellular growth pattern. In a subgroup analysis of the AUO-AB-05/95 study, patients with PUC seemed to have a less favorable outcome compared with patients with conventional muscle-invasive UC of the bladder [3]. However, an exact diagnosis is of crucial therapeutic and prognostic value because systemic chemotherapy in a neoadjuvant setting seems to have a beneficial effect on survival, at least in a subset of patients. Complete response after two courses of neoadjuvant chemotherapy for locally advanced but nonmetastatic PUC (T4 N0 M0) with methotrexate, adriamycin, vinblastine and cisplatin has been reported [4]. In our case, two courses of palliative chemotherapy with gemcitabine and carboplatin were highly effective, with complete radiological disappearance of all tumor-suspected retroperitoneal lymph nodes. However, during follow-up our patient developed rapid progression in her retroperitoneal lymphatic metastases followed by osseous and cerebral metastases,

highlighting the aggressive biology and poor clinical course of patients with this rare tumor variant.

Cellular appearance is characterized by a plasmacytoid aspect owing to medium-sized cells, eosinophilic cytoplasm, and eccentric nuclei [4]. Other neoplasias like lymphoma or multiple myeloma must be excluded in the differential diagnosis. Expression of epithelial markers such as CK7, CK20, PAN-CK, and CAM5.2 are characteristic of PUC [3, 5]. Our case showed negative staining for CK20, CD138, and E-cadherin, whereas staining for PAN-CK and CK7 were positive. The World Health Organization (WHO) classification states that, for a correct diagnosis, the PUC must be accompanied by conventional UC or carcinoma in situ [6]. Diagnostically important is the negative staining for E-cadherin, which is indicative of this particular UC variant, and which may be causally related to its highly aggressive nature [3, 7]. Loss of E-cadherin expression has also been described in other epithelial tumors, e.g. in breast carcinomas where loss of E-cadherin is a specific sign of lobular breast carcinoma and is associated with a reduced response to chemotherapy [8].

Conclusions

Our knowledge of this particular variant of UC is limited and must be improved in order to develop better future therapeutic strategies. For this purpose, a joint collection of clinical data and tumor materials is warranted with the goal of encouraging more molecular studies, and increasing our understanding of the pathogenesis of this tumor. This may lead to the development of new therapeutic approaches, which might be more effective than the current ones.

Disclosure Statement

The authors confirm that they have no conflicts of interest.

Consent

Written informed consent was obtained from the patient to collect tumor tissue, blood or urine samples for molecular analysis, and to extract all the clinical data needed for research purposes and publication.

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