

Case Report

Invasive urothelial carcinoma with chordoid features of the ureter: a rare entity and review of literature

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Abstract: Invasive urothelial carcinoma (UC) is characterized by some histologic variants that can sometimes lead to diagnostic difficulty. In addition to those described by the World Health Organization. Recently invasive urothelial carcinoma with chordoid features (UCC) has been described as a distinct entity and there are relatively few reported cases in the English-language literature. To date 13 cases of UCC have been reported in 2 case series, respectively in 2009 and 2015. We report the 14th case in an 80-year-old female, and to the best of our knowledge this is the second case report of UCC in the ureter. She was admitted to our hospital with macroscopic haematuria and unspecific left lower abdominal pain. Computed tomography scan revealed a soft tissue nodule in the middle of the left ureter. The left nephroureterectomy was performed. Morphologically, 85% areas had acellular myxoid stroma was associated with the neoplastic cells. The neoplastic cells had scant eosinophilic cytoplasm and were arranged into cords closely mimicking chordoma or extraskeletal myxoid chondrosarcoma. 15% areas was typical invasive urothelial carcinoma, and focal areas had transition phenomenon between them. Immunohistochemically, the tumor cells were positive for CK, 34 β E12 and p63, but were negative for S100, AFP, CD34, Syn and CgA. The final histopathological diagnosis was UCC of the ureter.

Keywords: Urothelial carcinoma, ureter, chordoid, myxoid

Introduction

Invasive urothelial carcinoma (UC) has a broad morphologic spectrum. According to the World Health Organization classification of UC, it mainly including divergent differentiation (squamous, glandular, sarcomatoid and trophoblastic), unusual growth patterns (micropapillary, nested, microcystic and lymphoepithelioma-like), even unusual cytologic features (plasmacytoid, clear cell, lipid rich, rhabdoid, giant cell and lymphoma-like). Invasive urothelial carcinoma with chordoid features (UCC) is recently recognized as a distinct entity and there are relatively few reported cases in the English-language literature [1-3]. Since it was reported by Cox and his colleagues in 2009 [1], only 13 known prior cases reported to date, and to the best of our knowledge this is the second case report of UCC in the ureter. Herein we report a

rare case of UCC in the ureter in an 80-year-old woman and present a brief review of the literature.

Case report

An 80-year-old Chinese female was admitted to our hospital because she presented with no apparent cause of left lower abdominal pain and macroscopic haematuria for 3 days. Ultrasonography revealed an occupying lesion in the left ureter. Computed tomography scan revealed a soft tissue nodule measuring 19 mm×16 mm in the middle of the left ureter, the boundary was slightly lobulated (**Figure 1A**), dynamic enhanced scanning the mass with an obvious enhancement (**Figure 1B**), and the effect was most obvious in the venous phase (**Figure 1C**). The left renal pelvis and ureter were expanded in the reconstruction period

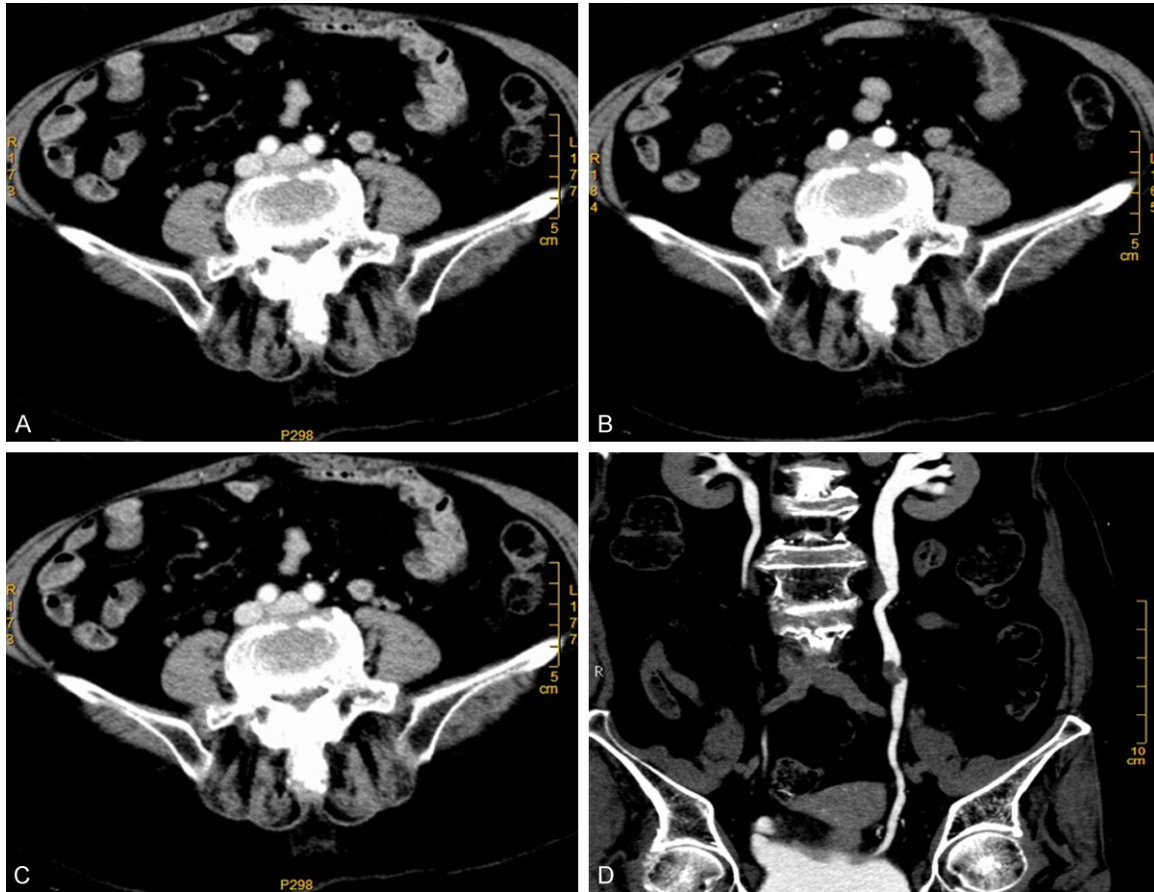


Figure 1. CT findings revealed a nodule measuring 19 mm×16 mm in the middle of the left ureter (A), dynamic-enhanced scanning the mass with an obvious enhancement (B), and the effect was most obvious in the venous phase (C); the left renal pelvis and ureter were expanded in the reconstruction period (D).

(Figure 1D). Bilateral kidney and bladder were normal. The patient underwent the left nephro-ureterectomy. Our patient was not given any treatment after operation. And the patient has been free from tumor recurrence and metastasis in the 6 months since surgery.

Pathological examination

Macroscopic examination the surgical specimen consisting of a left kidney which measuring 13.0 cm×9.0 cm×6.0 cm, no abnormal was found in the left kidney; the length of the ureter was 17.0 cm, the diameter was between 0.5 cm and 2.0 cm, in the 6.5 cm distance from the lower cut edge, there was a nodule in the sub-mucosa, mucosal surface erosion, cross-sections revealed a gray white and hard texture mass, infiltrated the ureteral full thickness and measured 2.0 cm×1.7 cm×1.0 cm. Morphologically, 85% areas had acellular and basophilic myxoid stroma and was associated with the

neoplastic cells (Figure 2A). The neoplastic cells had scant eosinophilic cytoplasm and were arranged into cords closely mimicking chordoma or extraskeletal myxoid chondrosarcoma (Figure 2B), and infiltrated into fat tissue of the serous membrane (Figure 2C). 15% areas was typical urothelial carcinoma, and focal areas had transition phenomenon between them (Figure 2D). Focal areas with glandular formation (Figure 2E) and squamous differentiation (Figure 2F).

Immunohistochemically, in the typical urothelial carcinoma areas and chordoid areas, the tumor cells were diffusely and strongly positive for CKpan, p63 (Figure 3A) and 34βE12 (Figure 3B), but was negative for S100, GFAP, SMA, calponin, AFP, CD34, Syn and CgA. CK7 (Figure 3C) and CK20 (Figure 3D) were positive in the typical urothelial carcinoma areas, but were negative in the chordoid areas. Histochemical stains for Alcian blue with and without hyal-

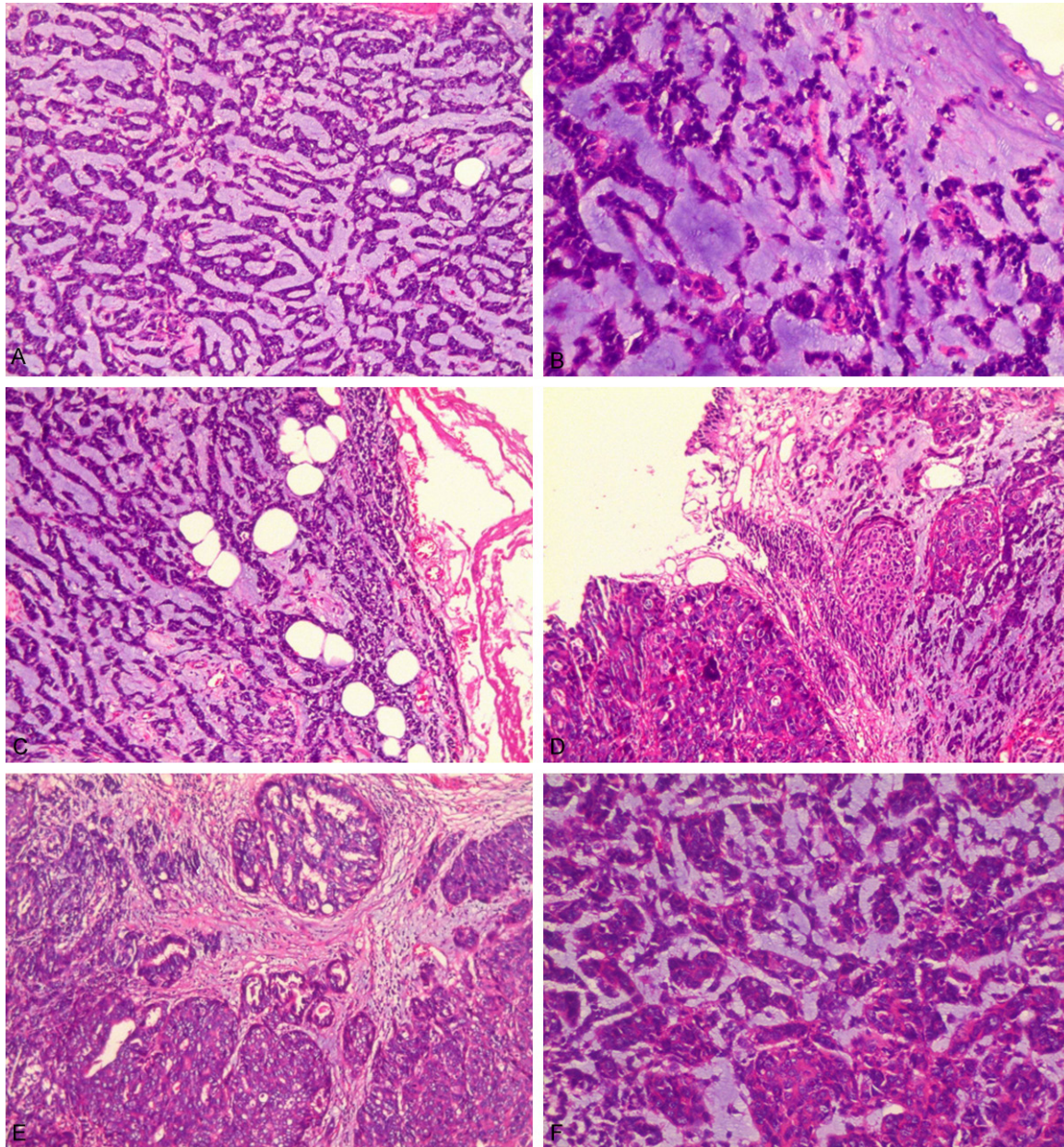


Figure 2. The tumor contained abundant myxoid stroma, the neoplastic cells had scant eosinophilic cytoplasm and were arranged into cords closely mimicking chordoma or extraskeletal myxoid chondrosarcoma (A and B), and infiltrated into fat tissue of the serous membrane (C); focal areas had transition phenomenon between the typical urothelial carcinoma and chordoid areas (D); focal areas with glandular formation (E) and squamous differentiation (F).

uronidase was positivity in extracellular myxoid stroma at pH 4.0 (**Figure 4**).

Discussion

Invasive urothelial carcinoma with chordoid features (UCC) is a rare variant of urothelial carcinoma (UC) [2]. The 14 cases of UCC (including our cases) demonstrated similar demographic and clinical features as conventional UC. Patient age ranged from 50 to 85 years (mean age

70.4, median age 74.5), and most commonly arise in middle aged and elderly people (usually older than 50 years) with a male preponderance. Nine of the patients were male and 5 were female, the male: female ratio was 2:1. Twelve cases were located in bladder, 2 cases were located in ureter. The most common symptoms were gross hematuria, individual patients had an initial complaint of abdominal pain or weight loss, but no specific features [1, 3]. Our patient presented with no apparent

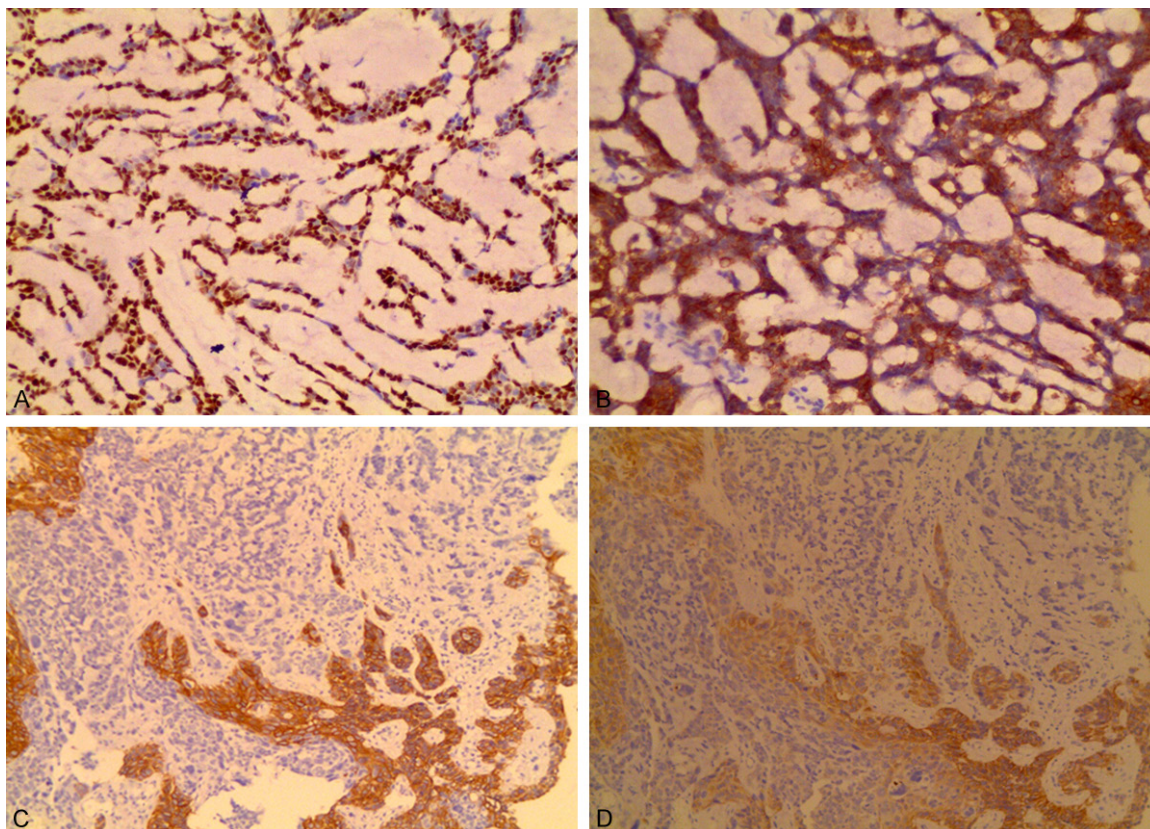


Figure 3. Immunohistochemically, tumor cells were strongly reactive for p63 (A) and 34βE12 (B); CK7 (C) and CK20 (D) were positive in the typical urothelial carcinoma areas, but were negative in the chordoid areas.

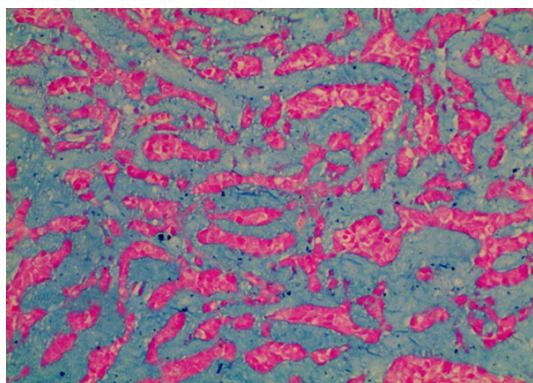


Figure 4. Histochemical special stains for Alcian blue was positivity in extracellular myxoid stroma at pH 4.0.

cause of left lower abdominal pain and macroscopic haematuria for 3 days.

UCC was first reported by Cox et al. in 2009 [1]. And the International Consultation on Urological Diseases (ICUD) reached consensus in 2015, they thought UCC with a special morphology

reminiscent of extraskeletal myxoid chondrosarcoma, chordoma, yolk sac tumor, or myoepithelioma of soft tissue [2]. The most typical morphology of UCC was that the striking pattern of cellular cording was present within an abundant basophilic myxoid matrix, neoplastic cells with scant eosinophilic cytoplasm and small, typically round to elongated nuclei. The myxoid stroma may be prominent in conventional UC and has been described as 'UC with abundant myxoid stroma', suggests that tumors reported as 'with chordoid features', or 'associated with abundant myxoid stroma' are within a similar spectrum of histopathology [2]. Although at least focal identifiable conventional UC was seen in almost all UCC [1-3], but there were no chordoid morphologic pattern in conventional UC with abundant myxoid stroma [4-8].

There are no tumor markers or imaging characteristics that allow a preoperative diagnosis, and all cases have been diagnosed after surgical resection, the diagnosis is based entirely

on histopathological and immunohistochemical assessment. Morphologically, UCC had at least focal areas had abundant, acellular, faintly basophilic myxoid stroma and was associated with the neoplastic cells. In areas with well-developed chordoid morphology, the neoplastic cells had scant eosinophilic cytoplasm arranged in cords, closely mimicking chordoma, extraskeletal myxoid chondrosarcoma, mixed tumor/myoepithelioma of soft tissue, or yolk sac tumor. In the reported literature, all cases had at least focal areas with more typical invasive high grade urothelial carcinoma. In addition to the typical invasive UC areas, focal areas with glandular formation and squamous differentiation in our case. Immunohistochemically, UCC show expression of urothelial-associated markers such as p63 and high molecular weight cytokeratin 34 β E12, but CK7 and CK20 were negative in chordoid areas, which may be useful to confirm the diagnosis.

The differential diagnosis included other carcinomas with significant extracellular myxoid or mucinous components, such as primary ureter adenocarcinomas, colonic or prostatic mucinous adenocarcinomas that have secondarily involved the ureter, and nonneoplastic glandular proliferations such as ureteritis with mucin extravagation [9], or myxoid ureteritis with "chordoid" lymphocytes [10]. The ureter or intestinal mucinous adenocarcinomas usually have mucinous pools lined by neoplastic glandular epithelium with varying degrees of cytological atypia. Mucinous adenocarcinoma of the prostate usually contains individual or cribriform glands floating within mucin, and can be relatively cytologically bland. Moreover, Mixed UC and adenocarcinoma, where the adenocarcinoma component contains abundant extracellular mucin, is similarly characterized by neoplastic glandular epithelium typically of enteric morphology. Also UC with abundant myxoid stroma or sarcomatoid carcinomas with myxoid changes should be in the differential diagnosis, the former do not have chordoid morphologic pattern, the latter spindle neoplastic cells have cellular atypia and many abnormal mitotic figures [11, 12].

Another important differential diagnosis of UCC is fibromyxoid nephrogenic adenoma that is characterized by compressed epithelial or spindle cells separated by abundant fibromyxoid stroma, it also express nuclear PAX-2 and PAX-

8 by immunohistochemistry, which is not typical of UCC [13]. Other potential mimics include myxoid leiomyosarcoma, inflammatory myofibroblastic tumor [14], myxoid malignant fibrous histiocytoma [15] and myxoid melanomas [16]. Although some of the closest morphologic mimics, such as extraskeletal myxoid chondrosarcoma or myoepithelioma/mixed tumor of soft tissue, but they have not been reported in the ureter.

The phenomenon of urothelial carcinoma with chordoid features is not described in numerous contemporary general surgical pathologies or urologic pathology textbooks. The histogenesis of UCC is still controversial. When these cases were presented at the 2011 Vienna and Austria ICUD, divergent opinions were expressed by various experts in the field [2]. Some experts given the absence of overt glandular epithelium, felt strongly that by convention, this tumor should be designated as UCC, however, other experts favored that the myxoid matrix represented mucinous secretions from UC, based on morphology they should be designated as "chordoid UC", because it can appear mucin in normal urothelium and UC [17, 18].

There is no consensus on standardized treatment strategy for UCC, radical surgical resection and chemotherapy is considered to be the most effective treatment. Although the patients of UCC may have a better prognosis than conventional UC, because the presence of mucin in normal urothelium and some UC is believed to have a protective role [18], but given a limited number of cases reported to date and to the short follow-up periods, the clinical outcomes of the reported 13 patients with UCC were quite variable. Of the 13 cases in reported literature, 10 patients had available clinical follow-up. Four of the 10 patients were alive with disease (5 to 8 mo), and 4 patients were alive with no evidence of disease (2 to 120 mo), only two patients were dead of disease (respectively in 1 and 10 mo). Our patient didn't accept any treatment after the surgery, with a follow-up period of 5 months, no recurrence and metastasis was found.

In conclusion, we describe a morphologic pattern of UC of the ureter with prominent myxoid stroma and cellular cording that imparts a distinct chordoid appearance, and UCC maintains an immunophenotype characteristic of UC and usually present with high stage disease.

Disclosure of conflict of interest

None.

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