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Oncology

Synchronous primary triple urogenital malignant tumors of kidney, prostate and bladder

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ABSTRACT

Synchronous occurrence of triple primary cancers of urinary tract is quite rare and represents a difficult treatment challenge. Here, we report a case of a 78-year-old man with synchronous renal cell carcinoma, urothelial carcinoma of urinary bladder and adenocarcinoma of prostate within a short period. To the best of our knowledge, this is the 20th reported of triple primary cancers of urinary tract and the first synchronous case with bone metastasis in the literature.

Introduction

Over the past a few decades, the techniques for cancer diagnostics and treatment, which have led to an increase in the multiple primary malignant tumors (MPMTs). MPMTs were first described in 1889 by Billroth. Since then, many cases of double or triple primary malignant neoplasms have been reported in the literature. However, synchronous occurrence of three different urological malignancies in the same patient is very rare.

Here, we report a case of synchronous renal cell carcinoma (RCC) with bone metastasis, bladder cancer and prostate cancer (PC). To our knowledge, this is the 20th case report in the literature.

Case presentation

A 78-year-old man was referred to our department for treatment of a right kidney tumor detected on follow-up US of his chronic pancreatitis. He had no history of malignancy and he was chronic smoker. His laboratory investigations were within normal limits, except for prostate specific antigen (6.31ng/mL). A CT revealed a 25 × 23 mm tumor in the lower pole of the right kidney, and hyperdensity in the early phase and wash out in the late phase were observed (Fig. 1). Bone scintigraphy revealed no bone metastasis. Based on these findings, we diagnosed RCC (cT1aN0M0), and robot-assisted partial nephrectomy was performed. Bladder tumor was discovered during the preoperative placement of a ureteral stent. Pathologic evaluation revealed a clear cell carcinoma and nuclear Fuhrman grade 3 (Fig. 2). Two months later, transurethral resection of bladder tumor (TURBT) and biopsy of prostate were performed. Pathologic evaluation revealed a non-papillary UC of bladder, pTa, low grade and adenocarcinoma of prostate with Gleason score of 3 + 4 = 7 (Fig. 2). Bone scintigraphy for staging of PC revealed bone metastasis in Th3, Th8 and L4 (Fig. 1). Bone biopsy of Th3 was performed, and pathological report showed clear cells with CD10(+), CK7 (−), CK20(−) and PSA(−) (Fig. 3). We diagnosed bone metastasis of RCC.

The patient underwent hormonal therapy for PC (cT1cN0M0), with Degarelix 240 mg administered once every three months. PSA decreased to 0.01 ng/mL after 6 months and there was no sign of bladder tumor recurrence. In addition, 4 sessions of chemotherapy were administered at 3-week intervals using Nivolumab and Ipilimumab, followed by treatment at 2-week intervals using Nivolumab, for RCC (pT1aN0M1). Denosumab therapy at 1-month intervals was performed for treatment of bone metastasis. At the 1-year follow up, the bone metastasis was stable, and there was no evidence of local recurrence or distant metastasis.

Discussion

Waren and Gate suggested diagnostic criteria of MPMTs consisting of 1) malignancy of any tumors should be confirmed through

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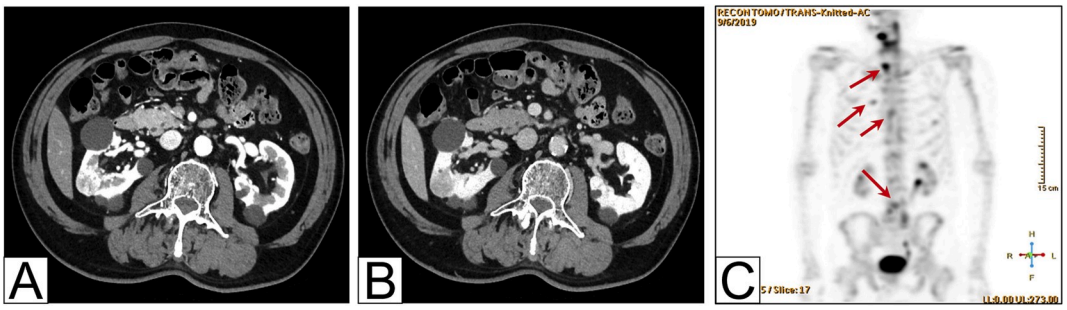

Fig. 1. A CT revealed a 25 × 23 mm tumor in the lower pole of the right kidney, and hyperdensity in the early phase (A) and wash out in the late phase (B). Bone scintigraphy revealed bone metastasis in Th3, Th8 and L4 (C).

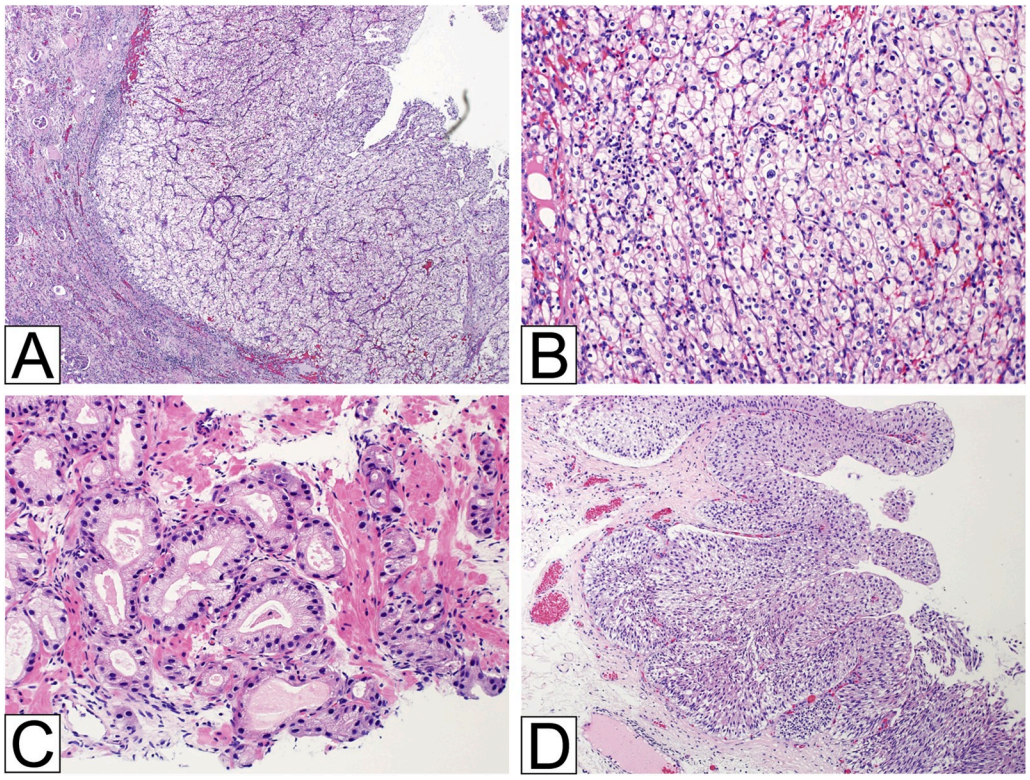

Fig. 2. Histopathological examination revealed clear cell renal cell carcinoma (A; H.E X40, B; H.E X200), adenocarcinoma of prostate with Gleason score of 3 + 4 = 7 (C; H.E X200) and a non-papillary UC of bladder, pTa, low grade (D; H.E X100).

histopathology. 2) Minimum distance with intact tissue between two tumors should be 2 cm and if both are located on the same site, the minimum interval should be 5 years. 3) The possibility of metastasis should be ruled out.[1] MPMTs are also categorized as metachronous and synchronous that mainly differ in terms of intervals of malignancy occurrence. Synchronous malignancy is defined as the occurrence of two tumors within a period of 6 months.[2] The histologic types of the carcinomas identified in the three organs of the present case report were all different and discovered over the course of approximately 2 months; thus, this is a representative example of a synchronous triple primary cancer.

The frequency of MPMTs has been reported to be 0.59–3.7% for double primary cancers and 0.029–2.0% for triple primary cancers, with an increase in occurrence observed in recent years.[3] Mikata et al. reported that 6.4% of all urinary system cancers presented as part of cases of MPMTs. The screening effect, where the diagnosis and treatment of a single cancer acts as an opportunity for the discovery of another asymptomatic cancer, has been cited for the high frequency of MPMTs in the urinary tract. The case outlined in this report was also due to the screening effect, as asymptomatic bladder and prostate cancer were discovered during the treatment of RCC. Reports of triple primary cancers all occurring in the urinary system are extremely rare, and our case is the 20th reported in the literature. Of these 20 patients, 17 were diagnosed with combinations of RCC, bladder cancer, and PC; 14 were synchronous. Our report documents the first synchronous case with bone metastasis, and the first case in which immune checkpoint inhibitors were used for the treatment of triple primary cancer of the urinary system. It is becoming apparent that the possibility of MPMTs must be considered, particularly when diagnosing and treating patients with urinary system cancers.

Campbell et al. reported that the frequency of a single cancer becoming a double primary cancer is lower than that of a double primary cancer becoming a triple primary cancer, and that individual carcinogenesis factors of the patient contribute more to this than simple probabilistic occurrence.[4] Carcinogenesis factors include genetic factors, environmental factors, radiation therapy for the primary cancer, and the occurrence of secondary cancers after chemotherapy.[5] Immunohistochemical staining for the tumor suppressor gene p53 and the

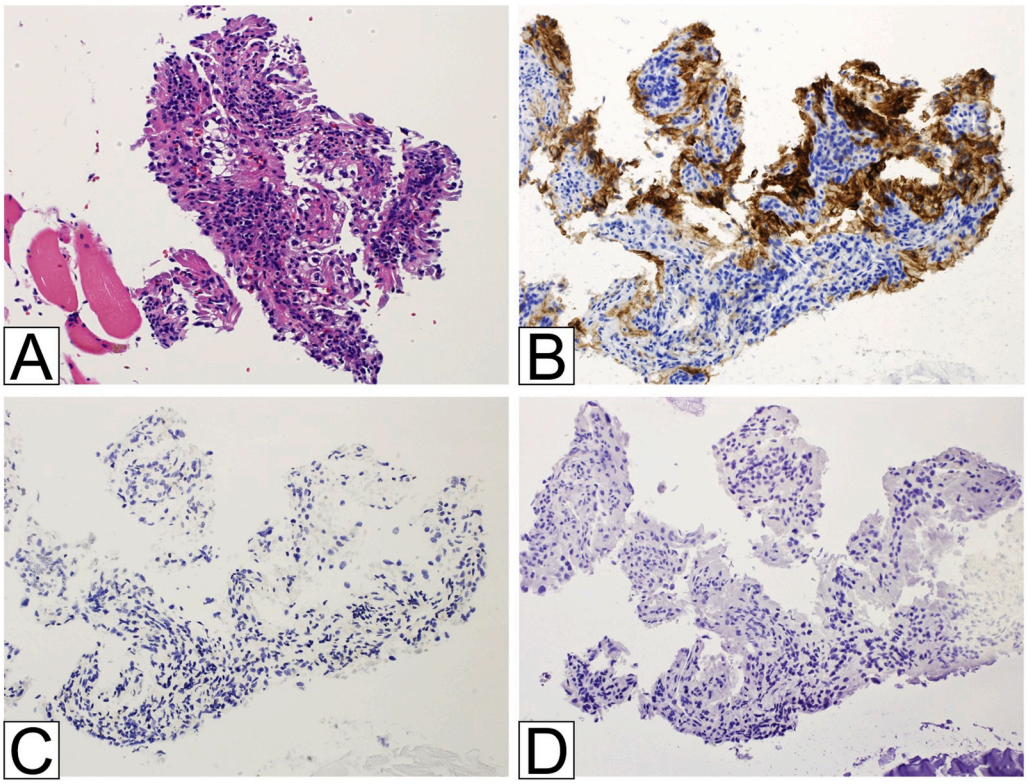

Fig. 3. Bone biopsy showing microscopic feature of RCC (A), positive staining CD10 (B), negative staining CK 7 (C) and negative staining PSA (D).

cancer gene HER-2 were conducted in the present case report as an investigation into genetic factors of carcinogenesis. HER-2 expression has been reported to contribute to increased nuclear grade and lymph node metastasis in prostate cancer. Mutant p53 expression has been correlated to decreased survival rate in RCC, increased grade in bladder cancer, and increased GS in PC. In this case, mutant p53 and HER-2 expression were negative in all tissues; thus, these genes were not thought to be involved in this triple primary cancer. In the treatment of synchronous MPMTs, the progress and prognosis of each individual cancer must be considered. RCC with metastasis is considered to have poor prognosis, and MPMT is considered to have poor prognosis relative to single cancers; therefore, increased follow-ups will need to be rigorously conducted.

Conclusion

Our case demonstrates a rare case of synchronous triple primary cancers all occurring in the urinary system. MPMTs frequently occurs in the urinary tract. Therefore, MPMTs should be taken into consideration when diagnosing and treating patients with urinary system cancers.

Consent for publication

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Declaration of competing interest

None declared.

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