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Case Report

A case report of renal pelvis carcinoma

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Abstract: Urothelial carcinoma (UC) is a common type of carcinoma worldwide, and it is rare to find it metastasize to the brain. Antibody-drug conjugates (ADCs) are an emerging treatment for patients. Our department treated a patient with Urothelial carcinoma (UC) that metastazied to the brain with Disitamab Vedotin. Therefore, the aim of this article is to review and share this rare carcinoma case treated in our department, and to have a deep understanding of Antibody-drug conjugates (ADCs) so that we can improve treatment for Urothelial carcinoma (UC). Informed consent was granted by the patient to share the case information.

Keywords: Urothelial carcinoma, antibody-drug conjugates (ADCs), disitamab vedotin

Introduction

Patients with advanced or metastatic Urothelial carcinoma (UC), which is generally incurable, have a 5-year overall survival rate that is about 15% [1-3]. The most common sites of metastasis are in the lymph, lung, bone, liver and peritoneum. Brain metastases from UC do occur but are pretty rare and associated with poor prognosis. For the majority of patients, especially the ones with metastatic or advanced UC, there is no approved therapy. Therefore, new treatments are urgently needed for patients with UC.

Case presentation

A 55-year-old man presented with paraphasia and disturbance of consciousness 3 months prior, the main issue was that he didn't realize that he was talking and his family couldn't understand what he was saying when the symptoms appeared. All these symptoms lasted for about 1 minute at a time. Therefore, he and his family came into our hospital to find the underlying problems. There was no other discomfort. Through further investigation of his case history, we found out that 1 year prior, he was diagnosed with renal pelvis carcinoma (**Figure 1**) and underwent a radical nephrectomy in our department. The intraoperative frozen section specimen showed that the mass on the right kidney was High grade urothelial carcinoma of the renal pelvis. Immunohistochemical staining of the tumor cells (**Figure 2**) revealed: CK20 (+), P63 (+), CK7 (+), Uroplakin III (+), P53 (-), AR (-), PSA (-), GATA3 (+), percentage of Ki67 positive cells were 60%, and C-erbB-2 (3+). Then he received chemotherapy with Gemcitabine and Cisplatin (GC) Regimen twice in June and November 2020, and Abdomen CT (**Figure 3**) revealed that there was no mass in the operation area on June 17th 2020.

Based on the symptoms of this patient, we arranged a brain MRI on August 19th for him, the images of the MRI showed that there was a mass in his brain (**Figure 4**). Combined with the patient's medical history, we diagnosed him with brain metastasis from the renal pelvis cancer. Considering that it is complicated to perform the operation and the Immunohistochemical staining of the tumor cells showed C-erbB-2 (3+), we decided to use Disitamab Vedotin for his treatment.

After 4 treatments with Disitamab Vedotin, approximately 3 weeks apart from mid August to mid October 2021, the symptoms of the patient disappeared. A brain MRI was performed again

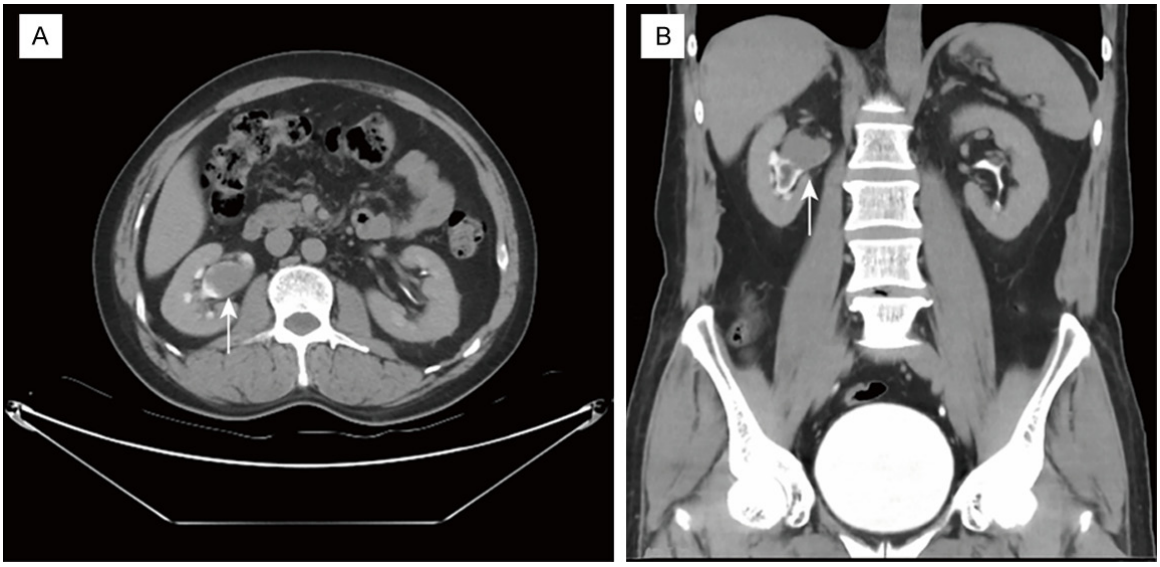

Figure 1. A: The transverse section of the CT, the tumor in the renal pelvis. B: The Coronal section of the CT, Hydronephrosis due to tumor compression.

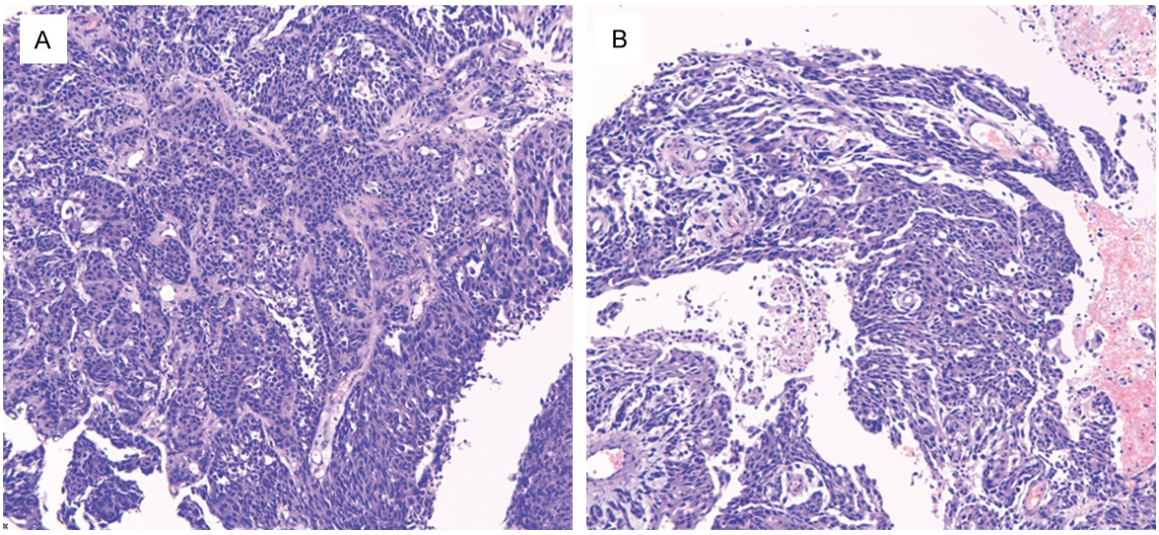

Figure 2. A: The urothelium is papillary hyperplasia, the cell arrangement is disordered and the size is inconsistent, the nuclear fission is easy to found. B: Intraoperative pathology image: CK20 (+), P63 (+), CK7 (+), Uroplakin III (+), P53 (-), AR (-), PSA (-), GATA3 (+), percentage of Ki67 positive cells were 60%, C-erbB-2 (3+).

on October 21st, and we found that the mass in his brain also disappeared (**Figure 5**). The patient is still currently under follow-up.

Discussion

Bladder cancer is one of the major health problems in the world. Urothelial Carcinoma (UC) is the most common histologic type of Bladder cancer (about 90%) [1]. The treatments of UC depend on the stage of the disease. Different stages of the disease have different five-year survival rates. The first line choice for patients with urothelial carcinoma is cisplatin-based combination therapy. However, because of a patient's poor kidney function, nearly half of patients do not tolerate the treatment well [2], Otherwise, death 1/programmed death ligand 1 (PD1/PD-L1) checkpoint inhibitors are also used in the treatmetn of UC. However, the average respond rate is only 10% and the me-

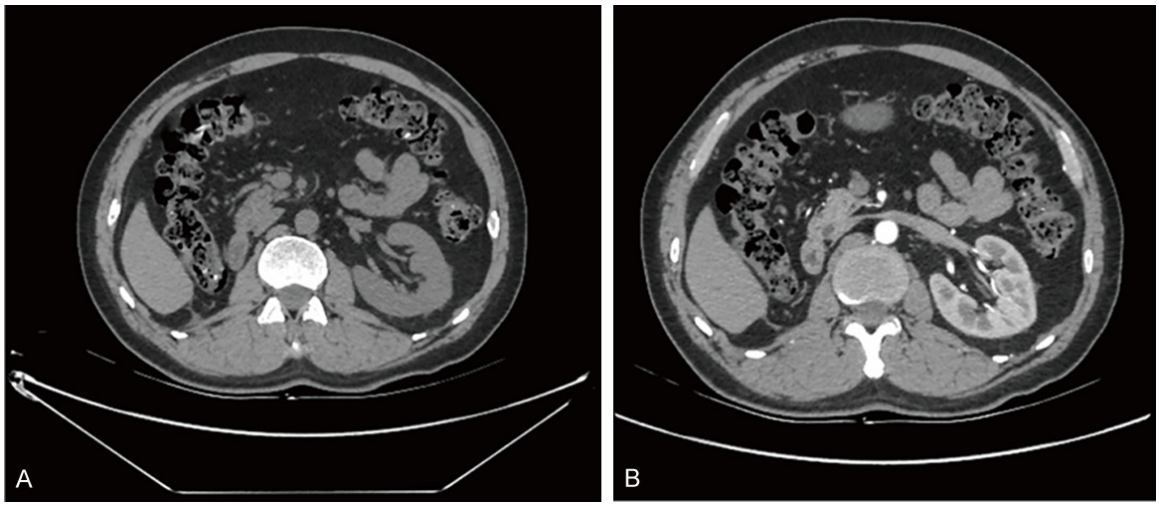

Figure 3. A: Postoperative CT, no obvious abnormality was found in CT. B: The postoperative enhanced CT also revealed that the right kidney was removed.

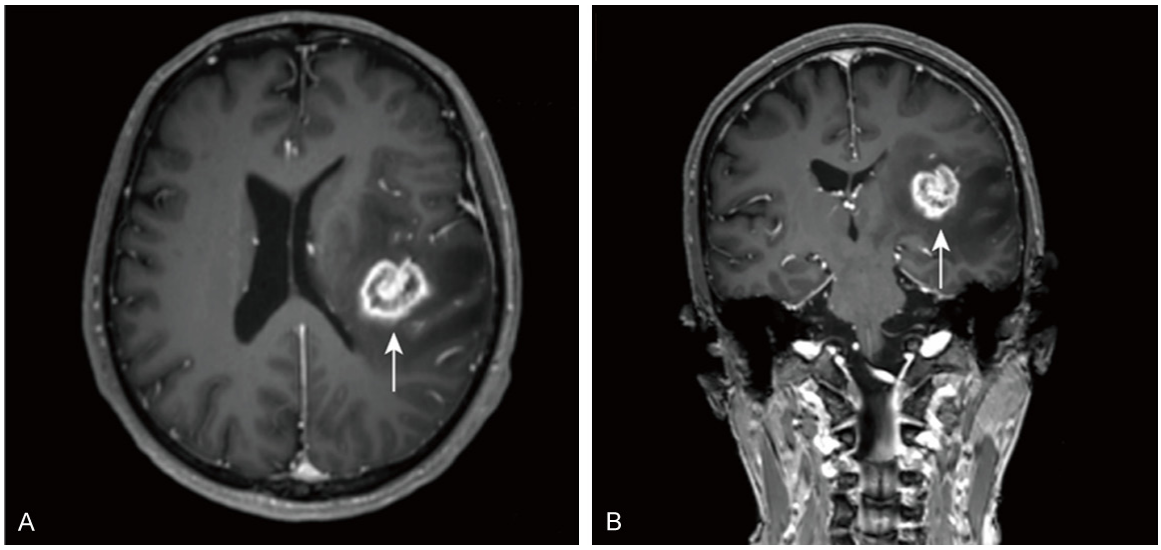

Figure 4. A: The MRI of the patient on August 19th, which shows the mass on his brain. B: The CT showed a nodular hyperdense shadow with a size of approximately 27×25×22 mm on the left brain frontotemporal lobar.

dian OS is 7.4 months with this treatment [3]. Patients with advanced or metastatic Urothelial carcinoma (UC) are generally considered to be non-treatable because the 5-year overall survival rate is only about 15% [4-6]. The most common sites of metastasis are in the lymph, lung, bone, liver and peritoneum. Brain metastases from UC do occur but they are rare and associated with a poor prognosis. For the majority of patients, especially the ones with metastatic or advanced UC, there are no approved therapies. Therefore, new treatments are urgently needed.

Antibody-drug conjugates (ADCs) are immunoconjugates, which are comprised of a monoclonal antibody tethered to a cytotoxic drug via a chemical linker [7, 8]. The ADCs are designed to selectively deliver the ultratoxic payload directly to the target cancer cells [9, 10]. Because of the poor oral bioavailability and also in order to avoid proteolytic degradation by digestive enzymes, the ADCs are administered intravenously. When bound to the antigen on the tumor cell surface, the ADCs and a linker degraded, are then released of the cytotoxic agent, which can lead to cell death [10-14].

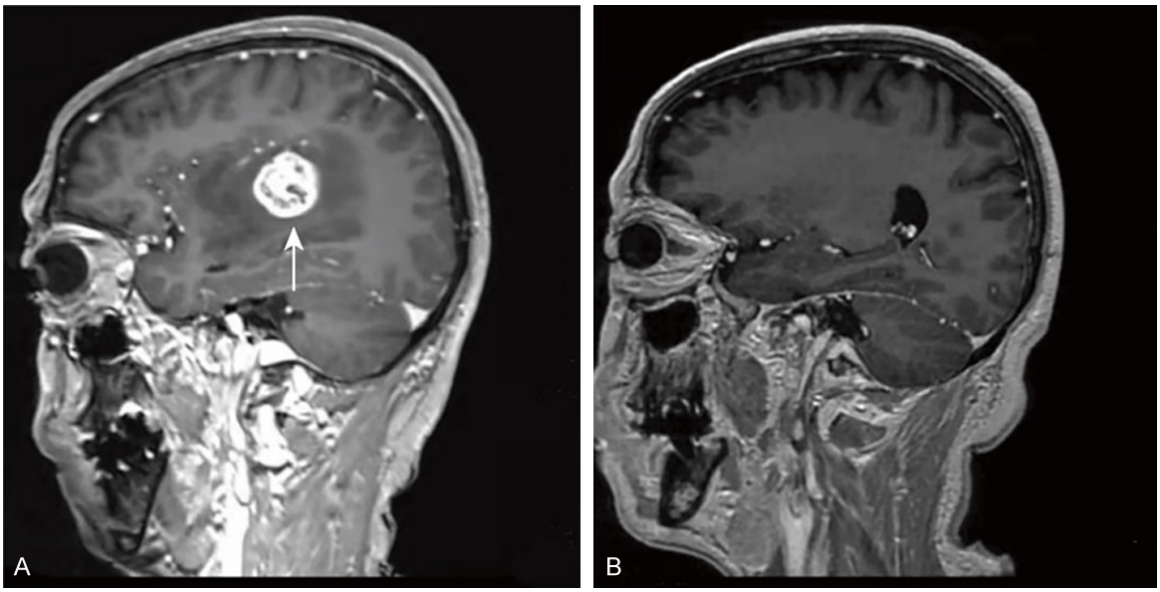

Figure 5. The (A) is the MRI on August 19th, which shows the mass in the patients' brain. (B) is the MRI on October 21st, after which the patient received 4 treatments. The size of the tumor was significantly reduced.

Disitamab Vedotin is one type of ADC, which is comprised of a monoclonal antibody against human epidermal growth factor receptor 2 (HER2) and was developed by RemeGen for treatment for solid tumors [13]. The effect of Disitamab Vedotin is through inhibition of HER2 receptor signaling, a small molecule toxin which is monomethyl auristatin E (MMAE), a synthetic antineoplastic agent to induce inhibition and apoptosis. Disitamab Vedotin showed good efficacy in urothelial cancer. In a phase II trial (NCT03809013; C009) [13] of distamab vedotin in patients with HER2-overexpression (IHC2+, 3+) who had failed platinum threapy, gemcitabine and taxane therapy, the duration of response (DOR) was 8.3 months, the median Progress Free Survival (PFS) was 4.3 months and the median Overall Survival (OS) was 14.8 months. Disitamab vedotin also showed good efficacy in a similarly designed phase II trial (NCT03507166; C005) [14] that enrolled patients with locally advanced or metastatic urothelial carcinoma (HER2 IHC2+, 3+). The DOR was 6.9 months, the median Progress Free Survival (PFS) was 6.9 months, the median Overall Survival (OS) was 13.9 months. In addition, a phase Ib/II trial which used distamab vedotin in combination with the anti-pro-grammed death receptor-1 agent toripalimab in patients with locally advanced or metastatic urothelial carcinoma (NCT04264936) [13] showed that 80% of patients had an objective response and 90% had disease control. As for side effects, the main adverse events of Disitamab Vedotin vary in accordance with patients' conditions, including: decreased white blood cell count, alopecia, decreased neutrophil count, increased aspartate aminotransferase, fatigue, increased alanine aminotransferase and hypoesthesia [14].

Because of the disease history and the MRI image, the patient was diagnosed with brain metastasis of renal pelvis cancer. After consulting neurosurgeons, we reached the conclusion that it is complicated and dangerous for us to perform a surgery to remove the mass. Combined with the earlier pathology report, which revealed the patient was HER2 positive. Therefore, after each treatment, we will monitor the patient's routine blood work and adverse reactions. After 4 applications of therapy, brain MRI was performed in the patient. According to the patient, his symptoms all disappeared and the main after-treatment discomfort was appetite suppression and rash, there were no other signs of discomfort, and the blood work revealed that (**Table 1**) the patient's white cell count was lower than normal, which may have been caused by drug-induced bone marrow suppression. These results indicate that the

Table 1. Laboratory data

variable	Reference Range	2021-8-19	2021-09-10	2021-09-27	2021-10-19
White-cell count	(4-10)*10^9/L	4.73	3.66	3.45	3.84
Differential count					
Neutrophils	0.5-0.70	0.76	0.48	0.30	0.30
Lymphocytes	0.2-0.4	0.17	0.42	0.56	0.60
Monocytes	0.03-0.08	0.05	0.07	0.12	0.09
Hemoglobin	120-160 g/L	121	125	118	113
Hematocrit	0.4-0.5	0.366	0.362	0.350	0.385
Platelet count	(100-300)*10^9/L	145	150	126	162
Sodium	135-145 mmol/L		140	141.5	139
Potassium	3.5-4.5 mmol/L		3.88	3.97	3.93
Chloride	96-106 mmol/L		107	108.6	106
Alanine aminotransferase	0-40 U		37	43	29
Aspartate aminotransferase	0-40 U		30	33	33
Alkaline phosphatase	45-125 U		106	94	92
Total protein	60-80 g/L		70.3	69.6	73.6
Globulin	20-35 g/L		33.9	32.3	34.5
Albumin	35-55 g/L		36.4	37.3	39.1

White cell count was lower than normal, no obvious abnormalities were observed on other indicators.

patient benefited a lot from the treatment of Disitamab Vedotin.

Conclusion

In summary, Disitamab Vedotin is an emerging therapeutic agent for patients with advanced UC or UC metastasis and especially for patients with HER2-overexpression. In this case, Disitamab Vedotin had good effect on our patient, and many clinical trials also suggest that the treatment of Disitamab Vedotin is remarkable. This information may help provide further imformation for UC treatment in clinical practice.

Disclosure of conflict of interest

None.

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