Hyperprogressive disease after avelumab maintenance therapy in a patient with advanced ureter cancer: A case report

Keita Ogasawara a,*, Daiki Ikarashi a, b, Shinji Tamada a, Takashi Tsuyukubo a, Hiromitsu Fujisawa a, Wataru Obara b

a Department of Urology, Iwate Prefectural Central Hospital 4-1, Ueda, Morioka-shi, Iwate, 020-0066, Japan
b Department of Urology, Iwate Medical University School of Medicine, 2-1-1, Yahaba, Shiwa-gun, Iwate, 028-3695, Japan

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ABSTRACT

In the early stages of immunocheckpoint inhibitor administration, we should be aware of rapid cancer progression, known as hyperprogressive disease, in real-world clinical practice. We report a case of a 73-year-old man who presented with right abdominal pain and was diagnosed with advanced right ureteral cancer involving the duodenum. He received four cycles of chemotherapy with gemcitabine plus cisplatin, followed by maintenance with avelumab. After two cycles of avelumab within a month, his primary cancer dramatically progressed and he died.

This is the first report of a case in which unresectable ureteral cancer caused hyperprogressive disease after avelumab maintenance therapy.

1. Introduction

The efficacy of avelumab maintenance therapy was demonstrated in the JAVELIN bladder 100 trial for unresectable or metastatic urothelial carcinoma (UC) that has not progressed with platinum-based chemotherapy as the PFS and OS were prolonged compared to those of the best supportive care group. Similarly, the Japanese subgroup analysis showed a favorable benefit-risk balance, which supports maintenance avelumab as the new standard of care. Thus, immune checkpoint inhibitors (ICIs) have been associated with long-term survival in several cancers. However, there is a small group of patients with rapid disease progression during the initiation of ICIs, known as hyperprogressive disease (HPD), which severely compromises the quality of life and prognosis of patients.

Herein, we report a case of HPD after avelumab maintenance therapy in a patient with advanced ureteral cancer despite achieving partial response (PR) with prior chemotherapy.

2. Case presentation

A 73-year-old hypertensive man presented with primary complaints of right abdominal pain and frequent vomiting. Abdominal computed tomography (CT) demonstrated a tumor surrounding his right upper ureter with hydronephrosis and duodenal invasion causing ileus (Fig. 1).

On admission, his Karnofsky performance status (KPS) score was 90, and his laboratory parameters showed renal dysfunction, high inflammatory marker (such as neutrophils and CRP) levels. Urine cytology was unremarkable at this time.

The clinical diagnosis of a primary tumor was unchanged. Gastrointestinal endoscopic findings showed no abnormalities in the mucosa and duodenal stenosis due to compression by the tumor. Thereafter, we performed retrograde pyelography with a right ureteral filling defect, which revealed the tumor was in the right ureter. Moreover, divided urine cytology suggested UC. We diagnosed the patient with unresectable advanced ureteral cancer (cT4N0M0) and considered starting systematic chemotherapy as soon as possible.

To ameliorate renal dysfunction, a ureteral stent was implanted, which resulted in an improvement in renal dysfunction and hydronephrosis. However, we thought that it was first necessary to improve the patient’s general condition which was worsened by anorexia secondary to severe duodenal stenosis. In fact, he experienced frequent vomiting because of ileus. Since endoscopic duodenal stent insertion was difficult due to the risk of gastrointestinal perforation, palliative gastrojejunostomy was performed. His postoperative course was uneventful, and he could start...
eating and improve his general condition. One month after surgery, we started chemotherapy with gemcitabine and cisplatin. After four cycles of chemotherapy with achieving PR (Fig. 2a and b), we switched to maintenance therapy using avelumab. However, after two doses of avelumab, he experienced severe fatigue, anorexia, and frequent vomiting, and his KPS was 60. CT scanning revealed the rapid re-growth of an aggressive tumor invading the abdominal wall, along with the appearance of cancerous ascites and suspected intestinal tract compression causing ileus (Fig. 2c and d). We considered that these findings met the criteria for HPD. Thereafter, his general condition rapidly worsened, and he died of the disease 49 days after avelumab therapy was initiated.

3. Discussion

There still has been no consensus on the definition of HPD because HPD is evaluated by several methods. At present, the tumor growth rate is ≥ twofold, which is the most widely used method of evaluating HPD treated with ICIs in comparison with the pretreatment duration. Moreover, a time-to-treatment failure of less than 2 months was also considered an alternative assessment method for HPD. In the present case, we determined our patient had experienced HPD because all of these criteria were met.

Hwang et al. reported that HPD occurred in up to 11.9% of UC patients treated with ICIs, a rate that was higher than that in RCC patients (0.9%). Multivariate analyses showed that UC and creatinine levels above 1.2 mg/dL were independent predictive factors for HPD in this study. In our case, laboratory data such as creatinine levels during avelumab treatment, which were predictive of HPD as reported in a previous report, had not been changed. Only one case of HPD after maintenance anti-PD-1 therapy following chemotherapy with proper disease control has been reported. On the other hand, in this case, pembrolizumab was used as maintenance therapy after third-line chemotherapy with platinum-doublet regimen re-challenge. To our knowledge, this is the first report of a patient having advanced ureteral cancer with HPD after maintenance anti-PD-L1 therapy following chemotherapy with PR.

4. Conclusion

In this report, we demonstrated HPD after avelumab maintenance therapy for advanced UC. We should be aware of the possibility of HPD at the start of ICI therapy, regardless of the good response of prior chemotherapy.
Consent

Written informed consent to publish was obtained from the patient for the publication of this case report and any accompanying images.

Author contributions

KO and DI drafted the report and cared for the patient. ST, TT, and HF cared for the patient. DI and WO supervised the work and critically reviewed the report.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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