Dual checkpoint inhibitor-associated hypereosinophilic syndrome in renal cell carcinoma patient

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A 75-year-old man was referred to our oncologic clinic for incidentally discovered radiologic abnormalities. CT scans revealed a 7.9 cm kidney mass with a liver metastasis and multiple lung nodules. He was diagnosed as stage IV IMDC (International Metastatic renal cell carcinoma Database Consortium) poor risk group clear cell renal cell carcinoma after liver biopsy. The patient received first-line chemotherapy with dual immune checkpoint inhibitors (ICIs): 4 cycles of ipilimumab plus nivolumab, followed by nivolumab monotherapy. During the initial 5 cycles, numerous immune-related adverse events (irAEs) developed, including grade 1 pruritus, skin rash, and thyroiditis. After the 6th cycle, the patient experienced pubic pain and dysuria. Urinalysis revealed hematuria and pyuria without bacteriuria. Hypereosinophilia (absolute eosinophil count (AEC) 3304/μL) and grade 1 acute kidney injury (AKI) and cholestatic-pattern liver function test (LFT) elevation were detected. Eosinophilic infiltration of the bladder wall was confirmed by biopsy (Figure 1), and stool examination yielded negative results for parasites, suggesting immunotherapy-induced hypereosinophilic syndrome (HES). Treatment with intravenous methylprednisolone (1 mg/kg/day for 5 days) led to resolution of eosinophilia and improvement in AKI, LFT abnormalities, hematuria, and pyuria. However, the AEC increased again, and oral prednisolone was resumed, starting at a dose of 30 mg daily and then slowly tapered off over 12 weeks. After stopping steroids, the patient reported multiple arthralgia. As the condition worsened, we restarted low-dose oral prednisolone (10 mg daily) due to suspicion of inflammatory arthritis. Currently, the patient continues to receive nivolumab and a daily dose of 5 mg oral prednisolone, without eosinophilia, and maintains a partial response for 18 months. As ICIs enhance the immune system, they can trigger inflammation in various organs and the patient has developed several irAEs. In this report, we present a case of immunotherapy-related HES with multi-organ involvement, particularly biopsy proven-eosinophilic cystitis, that was successfully managed with corticosteroids.

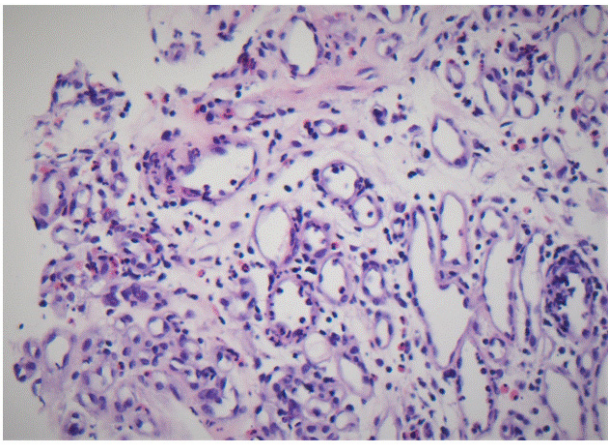

Figure 1. Histology of the bladder wall.