ISSN: 2476-2377

Case Report

International Journal of Cancer Research & Therapy

Pembrolizumab-Induced Acute Interstitial Nephritis: Case Report of a Colorectal Cancer Patient

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Submitted: 2024, Jul 07; **Accepted**: 2024, Aug 09; **Published**: 2024, Aug 19

Citation: Peshin, S., Sonar, N., Sadiq, Z., Kaur, G. (2024). Pembrolizumab-Induced Acute Interstitial Nephritis: Case Report of a Colorectal Cancer Patient. *Int J Cancer Rest Ther, 9*(2), 01-02.

Abstract

The emergence of immune checkpoint inhibitors (ICIs) has revolutionized cancer treatment, offering new hope to patients with advanced malignancies. Pembrolizumab (Keytruda), a PD-1-targeting ICI, is integral in treating various cancers, such as melanoma, non-small cell lung cancer, renal cell carcinoma, and Hodgkin lymphoma, by enhancing T-cell activity against cancer cells. Despite its efficacy, pembrolizumab is associated with immune-related adverse events (irAEs), including renal complications like acute tubulointerstitial nephritis (ATIN). This case report presents a 58-year-old female with stage IIa colorectal cancer on pembrolizumab therapy, who developed acute kidney injury (AKI) manifesting as worsening fatigue, decreased urine output, and malaise. Laboratory findings indicated elevated serum creatinine and the presence of white blood cell casts in the urine. Renal biopsy confirmed lymphocytic and eosinophilic infiltration of the interstitial tissues, consistent with pembrolizumab-induced nephritis. Following treatment with prednisone and supportive measures, her renal function improved, allowing continued pembrolizumab therapy. This case highlights the necessity of vigilant monitoring and early intervention for renal irAEs in patients on ICIs to optimize outcomes and minimize long-term renal damage.

1. Introduction

The advent of immune checkpoint inhibitors (ICIs) has heralded a new era in cancer therapy, instilling renewed hope in patients battling advanced malignancies. Pembrolizumab (Keytruda), a PD-1-targeting ICI, has become a cornerstone in the treatment of various cancers, including melanoma, non-small cell lung cancer, renal cell carcinoma, and Hodgkin lymphoma. By inhibiting the PD-1 pathway, pembrolizumab revitalizes T-cells, thereby augmenting the immune system's capability to recognize and eradicate cancer cells. Despite its remarkable efficacy, pembrolizumab is associated with immune-related adverse events (irAEs), including renal complications. Although less prevalent, pembrolizumab-induced nephrotoxicity, especially acute tubulointerstitial nephritis (ATIN), presents significant clinical challenges. A comprehensive understanding of the incidence, risk factors, and management strategies for these renal adverse effects is imperative for optimizing patient outcomes in cancer therapy.

2. Case Presentation

The patient is a 58-year-old female diagnosed with stage IIa colorectal cancer with lymph node involvement, for which she began pembrolizumab therapy three months ago. Over the past two weeks, she has experienced worsening fatigue, decreased urine output, and generalized malaise. Notably, she reported no accompanying symptoms such as fever, hematuria, or flank pain. There have been no changes to her medication regimen, nor has she experienced any recent illnesses, fevers, or contact with sick individuals.

2.1 Past Medical History

The patient's medical history includes stage IIa colorectal cancer with lymph node involvement, arthritis managed with topical diclofenac gel, and gastroesophageal reflux disease (GERD) managed with famotidine as needed. She has a history of smoking for the past ten years but quit following her cancer diagnosis. She has no significant allergies.

2.2 Family History

There is no significant family history of renal or autoimmune diseases.

2.3 Social History
The patient is a former smoker, having quit after her cancer diagnosis. She does not consume alcohol or use recreational drugs.

2.4 Physical Examination
On examination, her vital signs were stable, and she had no fever. She appeared fatigued. Cardiovascular examination revealed normal S1 and S2 heart sounds with no murmurs. Respiratory examination showed clear lung fields bilaterally. Her abdomen was soft and non-tender with no organomegaly. Mild tenderness was noted on deep palpation of the flanks. There was no edema in the extremities, and the neurological examination was unremarkable, with the patient being alert and oriented and exhibiting no focal deficits.

2.5 Laboratory Investigations
Laboratory tests showed a hemoglobin level of 13 g/dL, white blood cell count of 13 x10^9/L, and platelet count of 353 x10^9/L. Her sodium level was 138 mmol/L, potassium 4.4 mmol/L, and serum creatinine was elevated at 1.7 mg/dL from a baseline of 0.9 mg/dL. Blood urea nitrogen was 28 mg/dL, glucose 104 mg/dL, and bicarbonate 18 mmol/L. Urinalysis showed 10-24 white blood cells (WBCs), 0-5 red blood cells (RBCs), with no proteinuria, hematuria, or casts.

2.6 Clinical Course
Upon her initial clinic visit, the patient was advised to increase oral fluid intake, and a renal ultrasound, urine sodium, and urine osmolality tests were ordered. Her medications were reviewed with no offending agents identified. Repeat urinalysis and chemistries were planned for one week later. A week later, her serum creatinine had increased to 1.9 mg/dL, and BUN was 33 mg/dL, with urinalysis showing no changes except for the addition of WBC casts. Renal ultrasound showed no medical renal disease, urine sodium was 55 mmol/L, and urine osmolality was normal. Given the worsening AKI and suspicion of intrinsic renal disease, she was referred to nephrology.

At the nephrology office, 17 days from the original clinic visit, her serum creatinine was 2.0 mg/dL, and BUN was 47 mg/dL. She remained non-oliguric. Autoimmune serologies, including ANA, c-ANCA, p-ANCA, C3, and C4, were within normal limits. The patient was given the option of observation or a renal biopsy and chose the latter. The biopsy revealed lymphocytic and eosinophilic infiltration of the interstitial tissues without glomerular injury, consistent with AIN, likely due to pembrolizumab.

Following discussions with her hematology-oncology team, the patient was advised to maintain supportive measures, including oral hydration and bicarbonate supplements. Subsequent visits to the hematology-oncology office showed a serum creatinine level of 2.2 mg/dL and BUN of 48 mg/dL. She was started on prednisone 40 mg daily for five days, with a repeat BMP afterward showing stable creatinine at 2.2 mg/dL. She continued on prednisone along with pembrolizumab, with a follow-up BMP scheduled two weeks later revealing a creatinine level of 1.5 mg/dL. With the resolution of AKI, the patient, who remained non-oliguric, was slowly tapered off steroids while continuing follow-up with her specialists.

3. Conclusion
This case underscores the importance of vigilant monitoring for renal complications in patients undergoing pembrolizumab therapy. The prompt recognition and management of pembrolizumab-induced nephrotoxicity are vital for preventing long-term renal damage while allowing the continuation of life-saving cancer therapy. A collaborative approach involving oncologists, nephrologists, and other specialists is essential to optimize patient outcomes and manage the delicate balance between therapeutic efficacy and adverse event management.

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