Journal of Community Hospital Internal Medicine Perspectives

Volume 14 | Issue 4 Article 13

2024

A Recurring Theme: A Rare Case of Pembrolizumab-Induced Acute Interstitial Nephritis

Jonathan London
Internal Medicine Resident at Long Island Community Hospital, jonathan.london@nyulangone.org

Sabrina Bulancea
Internal Medicine Resident at Long Island Community Hospital, sabrina.bulancea@nyulangone.org

Inaas Shirazi
Internal Medicine Resident at Long Island Community Hospital, Inaas.Shirazi@nyulangone.org

Victoria Oriuwa
Internal Medicine Resident at Long Island Community Hospital, victoria.oriuwa@nyulangone.org

Olena Bolotova
Nephrologist at Long Island Community Hospital, olena.bolotova@nyulangone.org

See next page for additional authors

Recommended Citation

London, Jonathan; Bulancea, Sabrina; Shirazi, Inaas; Oriuwa, Victoria; Bolotova, Olena; and Tharayil, Zubin (2024) "A Recurring Theme: A Rare Case of Pembrolizumab-Induced Acute Interstitial Nephritis," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 14: Iss. 4, Article 13.
DOI: 10.55729/2000-9666.1362
Available at: https://scholarlycommons.gbmc.org/jchimp/vol14/iss4/13

A Recurring Theme: A Rare Case of Pembrolizumab-Induced Acute Interstitial Nephritis

Authors

Jonathan London, Sabrina Bulancea, Inaas Shirazi, Victoria Oriuwa, Olena Bolotova, and Zubin Tharayil

CASE REPORT

A Recurring Theme: A Rare Case of Pembrolizumab-induced Acute Interstitial Nephritis

Jonathan London [a,*], Sabrina Bulancea [a], Inaas Shirazi [a], Victoria Oriuwa [a], Olena Bolotova [b], Zubin Tharayil [a]

[a] Department of Internal Medicine, Long Island Community Hospital, USA
[b] Department of Nephrology, Long Island Community Hospital, USA

Abstract

Pembrolizumab is utilized in the treatment of multiple different malignancies, including non-small cell lung cancer, head and neck squamous cell carcinoma, melanoma, renal cell carcinoma, endometrial cancer, and more. Pembrolizumab is an immune checkpoint inhibitor that inhibits the programmed cell death-1 (PD-1) signaling pathway. Despite its benefits in treating multiple cancers, there are many reported adverse effects of Pembrolizumab affecting various organ systems; rarely it can cause acute interstitial nephritis (AIN). We present the case of a 79-year-old male with metastatic retroperitoneal squamous cell carcinoma who was found to have recurrent acute interstitial nephritis after pembrolizumab therapy.

Keywords: Pembrolizumab, Acute interstitial nephritis

1. Introduction

Pembrolizumab is an immunotherapy used for a wide variety of malignancies, including non-small cell lung cancer, head and neck squamous cell carcinoma, melanoma, and renal cell carcinoma.[1] The mechanism of action of pembrolizumab is inhibition of the programmed cell death-1 (PD-1) signaling pathway.[1,2] Certain tumors express programmed death receptor ligand-1 (PD-L1), which binds to PD-1 receptors on T-cells, thereby inhibiting T-cell mediated killing. Pembrolizumab inhibits the formation of the PD-1 and PD-L1 interaction, which allows for T-cell mediated killing to occur.[1,2] Although pembrolizumab has had a ground-breaking impact on treatment of various cancers, there are many adverse effects associated with its use. Pembrolizumab-induced acute interstitial nephritis (AIN) is a rarely documented adverse effect despite its frequent use as an immunotherapy agent.[2–4]

2. Case description

A 79-year-old male with history of metastatic retroperitoneal squamous cell carcinoma secondary to head and neck, GERD, Barrett's esophagus, CKD stage 3B, and HTN presented to the emergency department after ambulatory laboratory studies showed a sudden increase of creatinine (Cr) from his baseline of 1.9 mg/dl to 4.6 mg/dl. The patient had been receiving pembrolizumab maintenance therapy since completing four rounds of carboplatin and paclitaxel therapy alongside pembrolizumab. The aforementioned lab studies were collected four days after receiving his maintenance pembrolizumab therapy. He reported having an intermittent chest rash that would occur a few days after receiving pembrolizumab. He also reported months-long weight loss and poor oral intake. He denied having any fever, dysuria, hematuria, nausea, vomiting, fatigue, or decreased urinary output. On examination, vitals were T: 97.9 °F, BP: 114/82, HR: 84, RR 15, SpO2: 98% in room air. The patient's physical exam was unremarkable. Labs revealed a hemoglobin of 10.7 g/dl (consistent with his baseline), BUN: 46 mg/dl, Cr: 4.6 mg/dl, and ESR elevated at 72 mm/h. No eosinophilia was present. Urinalysis revealed white blood cells, white blood cell casts, trace proteinuria, no bacteria, and no eosinophiluria (Table 1). Urine culture was negative.

Received 24 February 2024; accepted 23 April 2024.
Available online 2 July 2024

* Corresponding author.
E-mail addresses: Jonathan.London@nyulangone.org (J. London), Sabrina.Bulancea@nyulangone.org (S. Bulancea), Inaas.Shirazi@nyulangone.org (I. Shirazi), Victoria.Oriuwa@nyulangone.org (V. Oriuwa), Olena.Bolotova@nyulangone.org (O. Bolotova), Zubin.Tharayil@nyulangone.org (Z. Tharayil).

https://doi.org/10.55729/2000-9666.1362

Table 1. Urinalysis on arrival following Pembrolizumab maintenance dose.

Urinalysis	Normal range	Patient results
Urine specific gravity	1.001–1.030 NM	1.012 NM
Urine pH	5.0–8.5 NM	6.0 NM
Urine protein	Negative	Trace
Urine glucose	Negative	Negative
Urine ketone	Negative	Negative
Urine bilirubin	Negative	Negative
Urine blood	Negative	Negative
Urine urobilinogen	Negative	Negative
Urine leukocyte esterase	Negative	Small amount
Urine nitrite	Negative	Negative
Urine white blood cells	0–5 HPF	10–25 HPF
Urine epithelial	0–5 HPF	0–5 HPF
Urine bacteria	Negative	Negative
Urine casts	Negative	WBC Casts

Renal ultrasound was negative for calculi, focal lesion, and hydronephrosis.

The patient's decline in renal function and intermittent chest rash following pembrolizumab treatment, and sterile pyuria was consistent with acute interstitial nephritis. Pembrolizumab was discontinued, and he was subsequently started on prednisone 80 mg daily. His renal function improved on prednisone, and he was discharged on a prednisone taper. While on the prednisone therapy at the hospital, his Cr improved from 4.6 mg/dl to 3.4 mg/dl. A kidney biopsy was not performed because the clinical picture was consistent with AIN and he improved after initiating steroids. As an outpatient, his Cr returned to his baseline after approximately two weeks of treatment.

Shortly after his renal function returned to baseline, the patient's maintenance pembrolizumab was restarted approximately two months after prednisone therapy was complete. After being restarted on pembrolizumab, his creatinine increased to 4.4 mg/dl again three days after receiving his maintenance dose. A urinalysis demonstrated white blood cells and white blood cell casts without bacteria. Repeat renal ultrasound did not show any acute findings. He was diagnosed with AIN and treated again with prednisone and a subsequent steroid taper. Following prednisone treatment, his renal function returned to baseline after three weeks of treatment. Due to re-occurrence of AIN following pembrolizumab therapy, the decision was made to discontinue its use for maintenance therapy.

3. Discussion

Acute interstitial nephritis is characterized by inflammatory infiltrates and edema in the kidney interstitium leading to decreased kidney function.[5] It is most commonly caused by medication therapy; however it can also be caused by infections, autoimmune disorders, and systemic diseases such as lupus.[5] Common medications that are associated with AIN include penicillin, cephalosporins, ciprofloxacin, NSAIDs, furosemide, and omeprazole.[5] Drug-induced AIN represents over two-thirds of all cases, and infection-related AIN represents roughly 15% of all cases.[5] The pathogenesis of AIN involves an immunologic reaction against endogenous antigens or exogenous antigens that are processed by tubular cells.[5]

Clinical manifestations may present as fever, skin rash, and arthralgias.[5,6] Lab findings for AIN may reveal acute renal failure, eosinophilia, presence of white cells and white cell casts in the urine, non-nephrotic proteinuria, and microhematuria.[5,6] Eosinophilia is generally only found in approximately 35 percent of patients with AIN.[5] Our patient was found to have an elevated Cr level, sterile pyuria, and mildly elevated proteinuria (Table 1). The patient did not have eosinophilia. The classic triad of rash, fever, and eosinophilia is only found in 10% of AIN cases. The diagnosis for drug induced AIN should be suspected when you have the initiation of a drug that commonly causes the disease, characteristic laboratory findings, and improvement once stopping the medication.[7] Our patient's laboratory findings of elevated Cr from baseline, sterile pyuria, and improvement following steroid therapy matched the characteristic presentation of AIN. A definitive diagnosis of AIN can be made with biopsy, however it is often considered unnecessary based off of clinical history and laboratory findings.[7] A biopsy for our patient was deferred due to his clinical improvement following prednisone therapy.

AIN is a rarely reported adverse effect of pembrolizumab. The incidence of acute kidney injury caused by pembrolizumab was found to be 1.77% out of 676 patients.[8] Approximately twelve case reports have been published with patients who developed acute interstitial nephritis following pembrolizumab use. Our patient is the first reported case with recurrent AIN following pembrolizumab use. Treatment for drug-induced AIN involves discontinuing the offending drug and starting corticosteroids.[8,9] There is no mainstay dose and duration of corticosteroid therapy following pembrolizumab-induced AIN.[8] Restarting pembrolizumab therapy following resolution of AIN has been found to be a reasonable decision.[8] If pembrolizumab is restarted, serum creatinine levels should be monitored regularly; if an acute kidney injury occurs with no other etiology, then pembrolizumab should be discontinued.[8] If a patient has severe AIN, hemodialysis may be a

necessary treatment.[5,9] Untreated AIN has the potential to progress to permanent renal insufficiency.[9] The prognosis of AIN is favorable when diagnosed promptly and the offending medication is discontinued early.[9] Prognostic data is limited for patients who develop pembrolizumab-induced AIN. AIN persisting for three weeks or longer is associated with worse outcomes.[9]

4. Conclusion

Physicians should consider acute interstitial nephritis in patients treated with pembrolizumab who present with renal failure.

Ethics information

Identifying information for the patient was not included in the manuscript.

Sources of support

The authors of this manuscript do not have financial support or competing interests to disclose.

Disclaimers

The article has not been submitted to other places.

Conflict of interest

There are no conflict of interests to report.

References

1. Flynn JP, Gerriets V. Pembrolizumab. In: *StatPearls. Treasure Island (FL): StatPearls Publishing; June 26*. 2023.
2. Basnet S, Dhital R, Tharu B. Acute tubulointerstitial nephritis: a case report on rare adverse effect of pembrolizumab. *Medicina (Kaunas)*. 2019;55(5):176. https://doi.org/10.3390/medicina55050176. Published 2019 May 21.
3. Mukherjee A, Ghosh R. Pembrolizumab induced acute tubulointerstitial nephritis. *Am J Therapeut*. 2022;29(6):e722–e724. https://doi.org/10.1097/MJT.0000000000001248.
4. Escandon J, Peacock S, Trabolsi A, Thomas DB, Layka A, Lutzky J. Interstitial nephritis in melanoma patients secondary to PD-1 checkpoint inhibitor. *J Immunother Cancer*. 2017;5:3. https://doi.org/10.1186/s40425-016-0205-2. Published 2017 Jan 17.
5. Praga M, González E. Acute interstitial nephritis. *Kidney Int*. 2010;77(11):956–961. https://doi.org/10.1038/ki.2010.89.
6. Kodner CM, Kudrimoti A. Diagnosis and management of acute interstitial nephritis. *Am Fam Physician*. 2003;67(12):2527–2534.
7. Perazella MA. Diagnosing drug-induced AIN in the hospitalized patient: a challenge for the clinician. *Clin Nephrol*. 2014;81(6):381–388. https://doi.org/10.5414/CN108301.
8. Izzedine H, Mateus C, Boutros C, et al. Renal effects of immune checkpoint inhibitors. *Nephrol Dial Transpl*. 2017;32(6):936–942. https://doi.org/10.1093/ndt/gfw382.
9. Finnigan NA, Rout P, Leslie SW, Bashir K. Allergic and drug-induced interstitial nephritis. In: *StatPearls. Treasure Island (FL): StatPearls Publishing; September 12*. 2023.