

# Pembrolizumab-induced Polymyalgia Rheumatica

Jessica Thomas MD, Alexandra Thomson MD, Savannah Grunhard MD, Rohit Bishnoi MD

## Background

- Pembrolizumab is an immune checkpoint inhibitor that has a wide variety of adverse effects such as hepatitis, thyroiditis, pneumonitis, and colitis
- It specifically targets PD-1 and blocks an inhibitory pathway, causing increased T cell activation and greater immune response against tumors
- Rheumatologic immune-related adverse effects have been less commonly published in ongoing literature
- This patient that we are presenting developed an uncommon, severe rheumatologic response to pembrolizumab
- This unique medical case contributes to understanding a rare reaction to immunotherapy and highlights the risks vs. benefits of maintaining therapy

## Clinical Presentation

This case is a 72-year-old male who was diagnosed with stage IV renal clear cell carcinoma (pT3a N1 pM1). He underwent a right total nephrectomy and shortly after he began treatment with pembrolizumab and axitinib. A few days after receiving the first doses of each treatment, the patient had complaints of bothersome joint pains. He stated the pain was mostly in his shoulders, his thighs, and hips. Additionally, he developed painful swelling in his wrists, hands, and ankles. He required corticosteroid injections for his recurrent bilateral knee effusions. He was referred to a rheumatologist to assess his extensive condition. His labs revealed elevated sedimentation rate and CRP but normal CCP and rheumatoid factor. He was formally diagnosed with polymyalgia rheumatica. Given the severity of his arthralgia, a decision was made to discontinue the pembrolizumab and continue single agent axitinib. His symptoms remarkably improved after starting hydroxychloroquine and prednisone. Unfortunately, the patient now requires long-term prednisone therapy to control the painful joint swelling and is not on maximum therapy for his cancer. However, the patient continues to do well with no evidence of disease on repeat imaging with close monitoring of his symptoms.

## Mechanism of Action/Common Adverse Effects

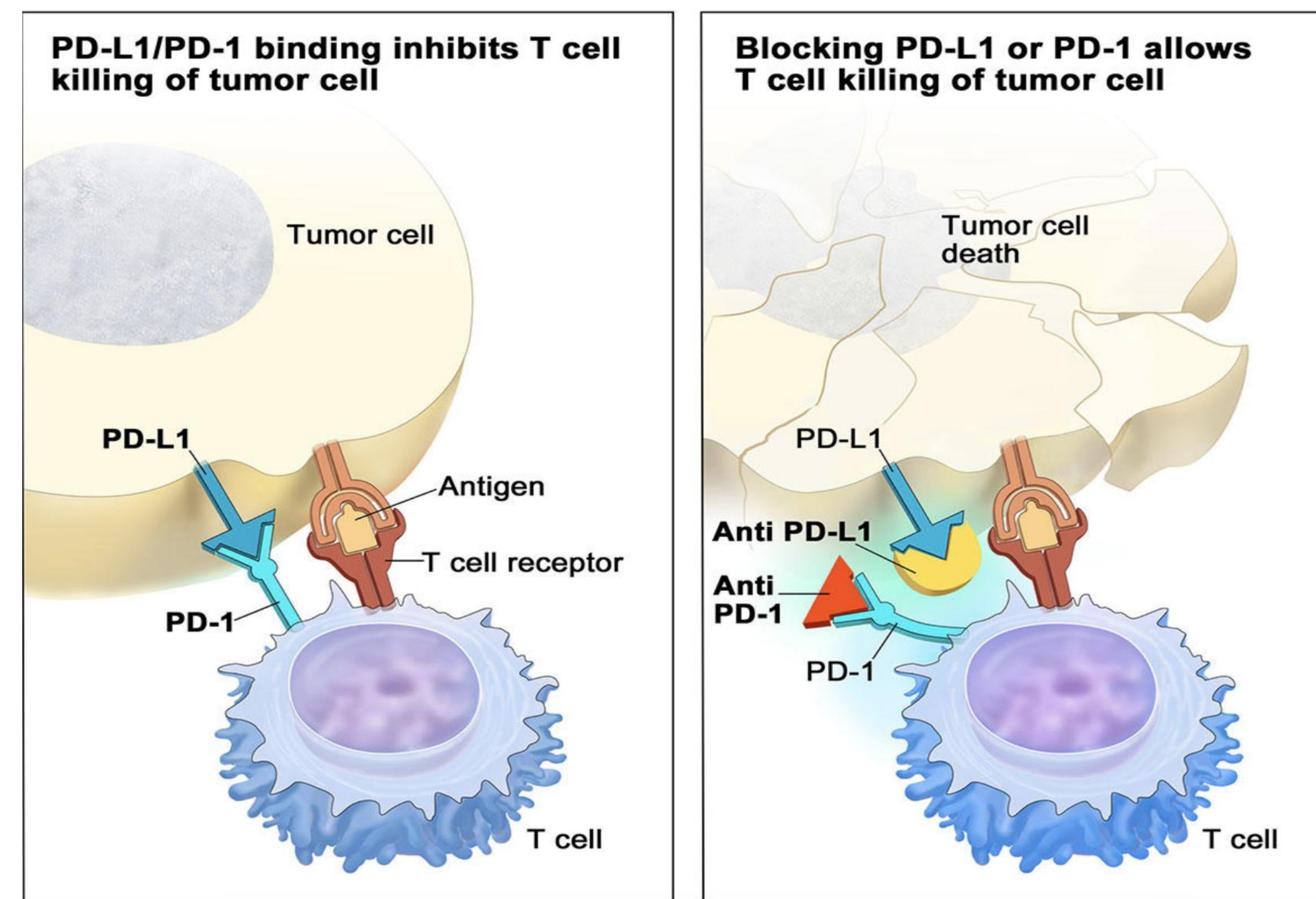


Figure 1. Mechanism of action.

<https://www.cancer.gov/news-events/cancer-currents-blog/2015/pembrolizumab-nscl>

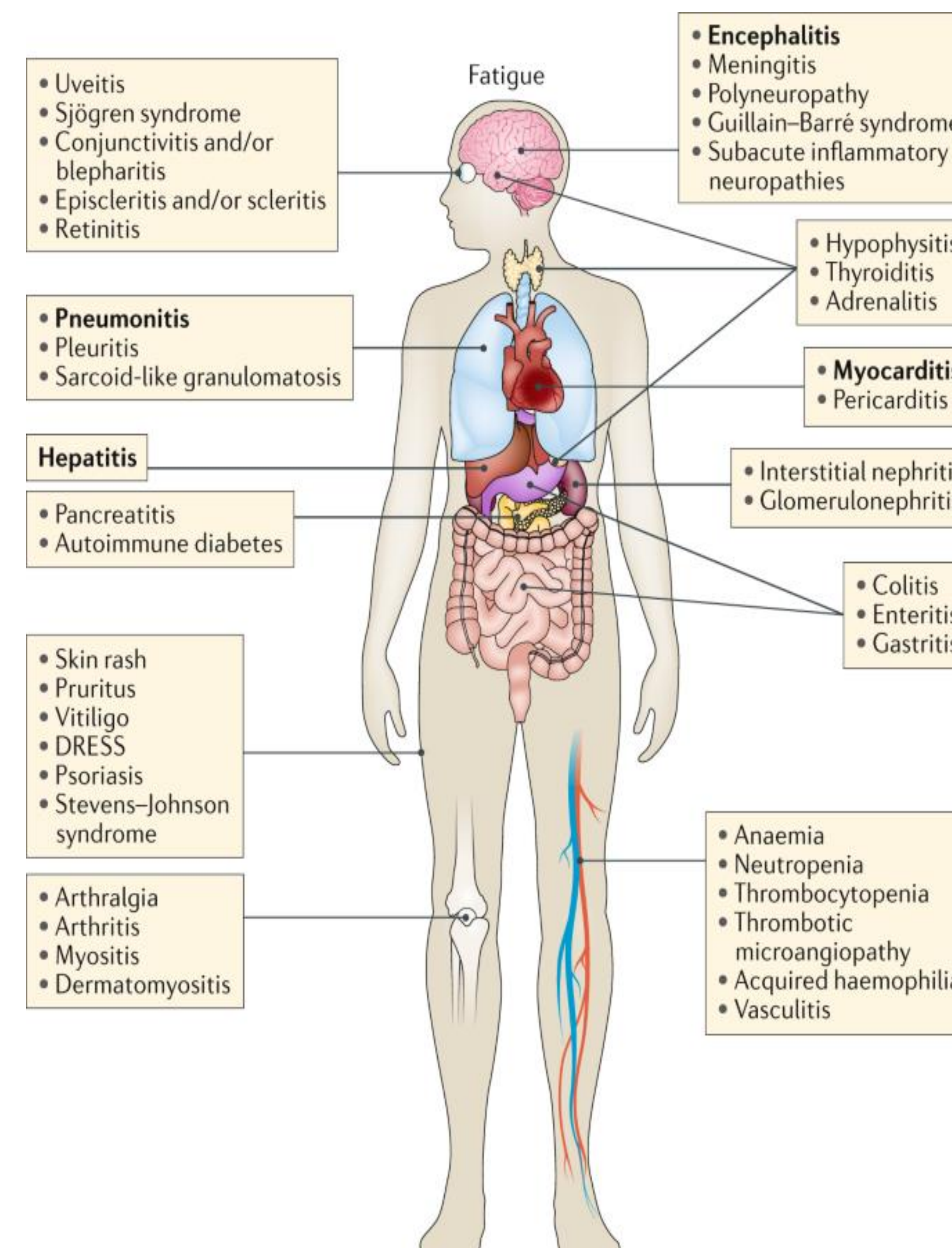


Figure 2. Common adverse effects.

<https://www.nature.com/articles/s41571-019-0218-0>

## Discussion

- The current treatment of inflammatory arthritis due to immune checkpoint inhibitors involves:
  - NSAIDs for mild inflammation
  - Low dose steroids for moderate inflammation
  - Moderate-high dose steroids when arthritis is severely refractory to these measures
- Polymyalgia rheumatica in this situation was treated as rheumatoid arthritis would be with the the use of low-risk disease-modifying antirheumatic drugs (DMARDs) such as hydroxychloroquine
- The decision if the patient can continue taking the immune checkpoint inhibitor therapy depends on how severe their reaction is, which can be a difficult choice to make when patients are dependent on immunotherapy for cancer
- In this scenario, pembrolizumab was not continued as the patient could not tolerate the extensive joint inflammation
- Although this was a risk to discontinue the maintenance therapy while being in remission, the patient now has controlled symptoms and remains cancer free

## Conclusion

- Adverse reactions from pembrolizumab can occur even after months of discontinuing the therapy and the effects can become chronic
- This case report increases the awareness of a rare autoimmune toxicity from pembrolizumab
- These side effects need to be thoroughly discussed with the patients before beginning treatment

## References

1. Iskandar A, Hwang A, Dasanu CA. Polymyalgia rheumatica due to pembrolizumab therapy. J Oncol Pharm Pract. 2019 Jul;25(5):1282-1284. doi: 10.1177/1078155218800386. Epub 2018 Sep 24. PMID: 30249155.
2. Kethireddy N, Thomas S, Bindal P, Shukla P, Hegde U. Multiple autoimmune side effects of immune checkpoint inhibitors in a patient with metastatic melanoma receiving pembrolizumab. Journal of Oncology Pharmacy Practice. 2021;27(1):207-211. doi:10.1177/1078155220921543
3. Manzo C, Isetta M, Natale M, Castagna A. Identification and Classification of Polymyalgia Rheumatica (PMR) and PMR-Like Syndromes Following Immune Checkpoint Inhibitors (ICIs) Therapy: Discussion Points and Grey Areas Emerging from a Systematic Review of Published Literature. Medicines (Basel). 2020 Nov 3;7(11):68. doi: 10.3390/medicines7110068. PMID: 33153016; PMCID: PMC7693468.
4. Martins, F., Sofiya, L., Sykiotis, G. P., Lamine, F., Maillard, M., Fraga, M., Shabafrouz, K., Ribi, C., Cairoli, A., Guex-Crosier, Y., Kuntzer, T., Michielin, O., Peters, S., Coukos, G., Spertini, F., Thompson, J. A., & Obeid, M. (2019, May 15). Adverse effects of immune-checkpoint inhibitors: Epidemiology, management and Surveillance. Nature News. Retrieved March 30, 2023, from <https://www.nature.com/articles/s41571-019-0218-0#Sec8>
5. February 23, 2023, January 20, 2023, & March 9, 2023. (2015, November 15). FDA approves pembrolizumab to treat non-small cell lung cancer. National Cancer Institute. Retrieved March 30, 2023, from <https://www.cancer.gov/news-events/cancer-currents-blog/2015/pembrolizumab-nscl>

*This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.*