Oncology Case Reports Journal

Case Study
Published: 22 Jul, 2019

Ipilimumab and Nivolumab Associated Tenosynovitis in Metastatic Renal Cell Cancer (RCC)

Fatima Fayyaz, Karine Tawagi and Sarah Bonner*

Department of Oncology, St. Joseph Mercy Hospital, USA

Introduction

Immunotherapy relies on the body's immune system to fight disease. Immune checkpoint blockade increases antitumor immunity by blocking intrinsic down-regulators of immunity, such as Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4), Programmed cell Death 1 (PD-1) etc [1]. Owing to their non-specific mechanism of activating T cells, the main toxicities of Immune Checkpoint Inhibitors (ICI) are due to immunologically mediated and inflammatory damage of tissues, collectively referred to as Immune-Related Adverse Events (IRAEs) [2,3]. This report shows Tenosynovitis as a rare IRAE.

Clinical Vignette

A 67 year-old-male with RCC presented with severe enterocolitis causing diarrhea after his third cycle of Ipilimumab and Nivolumab. His past medical history included CHF, Paroxysmal Atrial Fibrillation, Coronary Artery Disease, Peripheral Vascular Disease and Gout. While patient was getting worked up for his enterocolitis, hospital course was complicated by bilateral ankle swelling and pain, left greater than right. Initially, this was thought to a be a flare up of Gout but patient kept insisting that this was different and that his flare-ups usually resolved within 1-2 days of steroids and were not bilateral. Patient was given steroids for a presumed gout flare up.

His ankle swelling did not respond well to 2 days of 40 mg prednisone. On physical exam, patient had Left > Right ankle swelling and warmth, No erythema and pain with active and passive movement at ankle joint. Patient had significant tenderness to palpation proximal to Achilles tendon as shown on a digital recreation in Figure 1. There was no swelling/tenderness/restriction in range of movement in bilateral MCP, wrist and knee joint. Patient's exam was consistent with tenosynovitis.

Pertinent blood work showed:

- ANA: Negative
- CRP: 5.0 mg/dL
- Anti- CCP: 22 Units
- Rheumatoid Factor: <15 IU/mL

Patient's ultrasound of Left ankle showed small tibiotalar joint effusion. Note was also made of mild soft tissue swelling and edema about the ankle within the overlying subcutaneous tissues.

Figure 1: Distribution of patient's swelling and tenderness.

OPEN ACCESS

Correspondence:
Fatima Fayyaz, Department of Oncology, St. Joseph Mercy Hospital, 3025 Whisperwood Dr Apt 249, Ann Arbor MI 48105, USA, Tel: 3472588266; E-mail: fatima.fayyaz@stjoeshealth.org

Received Date: *08 Jul 2019*
Accepted Date: *18 Jul 2019*
Published Date: *22 Jul 2019*

Citation:
Fayyaz F, Tawagi K, Bonner S. Ipilimumab and Nivolumab Associated Tenosynovitis in Metastatic Renal Cell Cancer (RCC). Oncol Case Report J. 2019; 2(2): 1013.

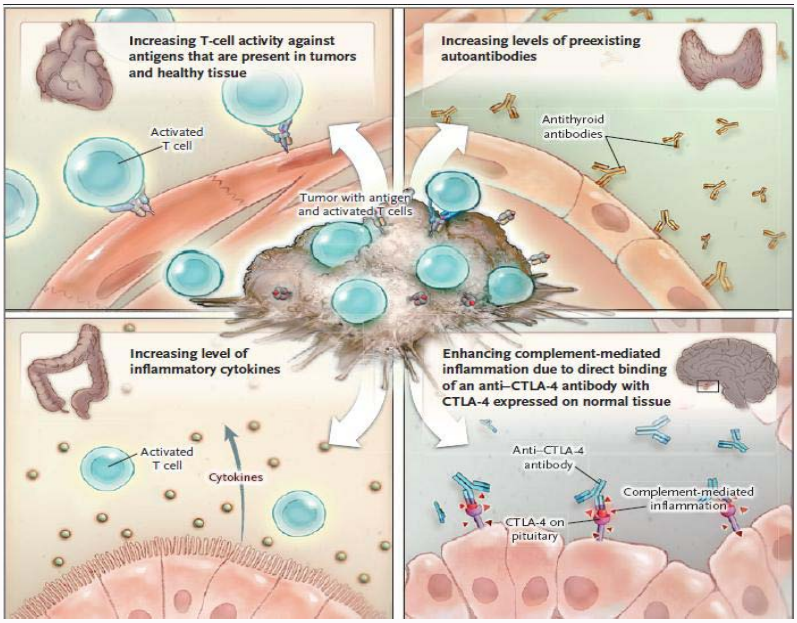

Figure 2: Possible mechanisms underlying immune-related adverse events [1].
The mechanisms that result in a immune-related adverse events are still being elucidated. Some potential mechanisms include increasing T-cell activity against antigens that are present in tumors and healthy issue, increasing levels of preexisting autoantibodies, an increase in the level of inflammatory cytokines, and enhanced complement-mediated inflammation due to direct binding of an antibody against cytotoxic T-lymphocyte antigen 4 (CTLA-4) with CTLA-4 expressed on normal tissue, such as the pituitary gland.

Eventually, patient was started on a 1 month long high dose steroid taper (1/mg/kg) and symptoms resolved. Patient has still not been able to resume immunotherapy.

Discussion

Musculoskeletal IRAEs are rare, and the pathophysiology is still unclear. Recently, the New England Journal of Medicine published a comprehensive review of IRAEs and the pathophysiology is summarized in Figure 2. No defined guidelines currently exist for grading severity and treatment of rheumatic IRAEs; however most have been reported to be steroid-sensitive, and resolved within 6-12 weeks with prolonged courses of high-dose steroids [4]. Physicians should be aware of IRAEs and how to treat them. It is still unclear if patients can re-start immunotherapy after developing IRAEs.

Conclusion

As the use of immunotherapy grows, internists will be encountering more cases of IRAEs. It is important that we learn to distinguish IRAEs from common disorders. {For instance, this patient also had gout but instead of the usual 7-10 days of treatment with anti-inflammatories for gout, he needed almost a month of treatment with high dose steroids} Prompt recognition of IRAEs will lead to appropriate and timely treatment.

References

1. Michael AP, Robert S, Matthew DH. Immune-related adverse events associated with immune checkpoint blockade. N Engl J Med. 2018;378:158-68.
2. Cappelli LC, Shah AA, Bingham CO. Cancer immunotherapy induced rheumatic diseases emerge as new clinical entities. RMD Open. 2016;2(2):e000321.
3. Weber JS, Kähler KC, Hauschild A. Management of immune-related adverse events and kinetics of response with ipilimumab. J Clin Oncol. 2012;30(21):2691-7.
4. Calabrese C, Kirchner E, Kontzias A, Velcheti V, Calabrese LH. Rheumatic immune-related adverse events of checkpoint therapy for cancer: case series of a new nosological entity. RMD Open. 2017;3(1):e000412.