Concomitant Use of IL-17 Inhibitor and PD-1 Inhibitor for Pembrolizumab-Aggravated Psoriasis in the Context of Metastatic Non-Small Cell Lung Cancer

Adina Greene BA[1,2]; Scott Penner BS[1]; Jiaxin Niu MD PhD[3]; Jordan Abbott MD[3]

1- University of Arizona College of Medicine-Phoenix 2- Mayo Clinic AZ Department of Dermatology

3- Banner MD Cancer Center- Gilbert

Background / Introduction

- Programmed death-1 (PD-1) inhibitors are immune checkpoint inhibitors (ICI) which are used in the treatment of numerous malignancies[1] and often cause nonspecific immune activation termed immune-related adverse events (irAEs)
- Psoriasiform dermatitis is a well-documeted cutaneous irAE (ircAE) of PD-1 inhibitors[2]
- ircAEs are classified according to body surface area (BSA) involvement
  - Grade 1 or 2 eruptions (BSA <30%): topical steroids recommended
  - Grade 3 or 4 eruptions (BSA 30-100%): ICI therapy held and systemic steroid treatment administered 3
- Prolonged systemic steroid use may cause side effects and hinder ICI antitumor activity[4]
- We present a case of an ICI-induced psoriasiform dermatitis eruption which demonstrated complete skin response to IL-17 inhibition with ixekizumab and safety in the setting of lung malignancy without progression of the malignancy

Clinical Presentation

- Patient is a 68 y/o male with a remote history of psoriasis which was well-controlled with topical steroids for thirty years
- Patient presented with metastatic non-small cell lung cancer and was started on carboplatin, paclitaxel, and pembrolizumab (PD-1 inhibitor)
- One month into treatment, patient presented to dermatology with 80% BSA involvement with bright red scaly plaques (Figure 1)
- Diagnosis of psoriasiform dermatitis secondary to pembrolizumab was made and treatment was paused
- Triamcinolone 0.1% cream was applied twice daily for two weeks
- Due to lack of improvement with topical steroids, (Figure 2) patient was then started on 80 mg subQ ixekizumab, an IL-17 inhibitor, every two weeks for five doses
- At 12 week follow up visit, patient presented with total skin clearance
- Ixekizumab was continued as maintenance therapy at 80 mg every four weeks and was rechallenged with pembrolizumab due to progression of his pulmonary malignancy
- Following three cycles of pembrolizumab, repeat PET/CT demonstrated an excellent tumor response

Clinical Images

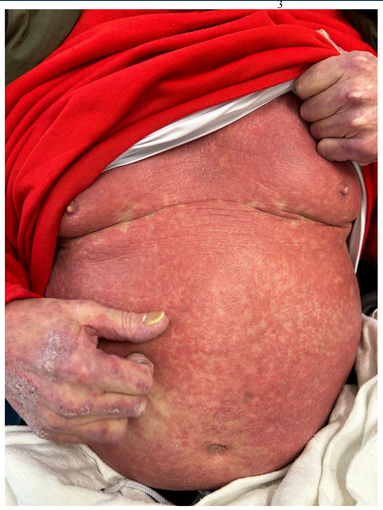

Figure 1: Psoriasiform dermatitis secondary to pembrolizumab on torso initial presentation

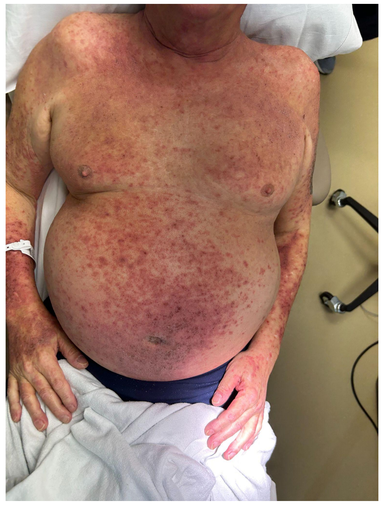

Figure 2: Psoriasiform dermatitis secondary to pembrolizumab on torso after triamcinolone treatment

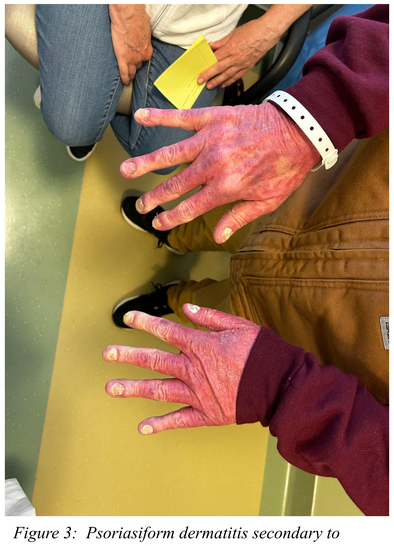

Figure 3: Psoriasiform dermatitis secondary to pembrolizumab on hands

Case Discussion & Literature

- PD-1 inhibitor was re-initiated after the psoriasiform skin eruption was well controlled with IL-17 inhibition and patient demonstrated both an excellent pulmonary tumor response and the skin toxicity remained controlled at 12-week follow-up
- Treatment of ircAEs with extensive BSA involvement includes systemic steroids. However, psoriasis typically flares in the setting of systemic steroid withdrawal and alternative systemic treatment strategies are needed[4]
- A literature search was conducted which found five cases of IL-17 inhibitors with all cases showing improvement of psoriasiform dermatitis [5-9]
  - In three cases, the patients showed progression free survival after rechallenging with ICI, while remaining on an IL-17 inhibitor.
  - In two cases, the patients had progression of malignancy
- Mouse models have shown potential benefit of concurrent IL-17 and PD-1 blockade[10-11]

Conclusion and Implications

- This case supports the efficacy and safety of IL-17 inhibitor use for ICI-induced psoriasiform dermatitis
- Other case reports have also demonstrated safety of IL-17 inhibitor use in the setting of malignancy
- Mouse models have suggested that IL-17 inhibitor use may potentiate anti PD-1 response

References

1. Kwok G, Yau TC, Chiu JW, Tse E, Kwong YL. Pembrolizumab (Keytruda). Hum Vaccin Immunother. 2016 Nov;12(11):2777-2789. doi: 10.1080/21645515.2016.1199310. Epub 2016 Jul 11. PMID: 27398650; PMCID: PMC5137544.
2. Bhardwaj M, Chiu MN, Pilkhwal Sah S. Adverse cutaneous toxicities by PD-1/PD-L1 immune checkpoint inhibitors: pathogenesis, treatment, and surveillance. Cutan Ocul Toxicol. 2022 Mar;41(1):73-90. doi: 10.1080/15569527.2022.2034842. Epub 2022 Feb 20. PMID: 35107396.
3. Muntyanu A, Netchiporouk E, Gerstein W, Gniadecki R, Litvinov IV. Cutaneous Immune-Related Adverse Events (irAEs) to Immune Checkpoint Inhibitors: A Dermatology Perspective on Management [Formula: see text]. J Cutan Med Surg. 2021 Jan-Feb;25(1):59-76. doi: 10.1177/1203475420943260. Epub 2020 Aug 3. PMID: 32746624.
4. Geisler AN, Phillips GS, Barrios DM, Wu J, Leung DYM, Moy AP, Kern JA, Lacouture ME. Immune checkpoint inhibitor-related dermatologic adverse events. J Am Acad Dermatol. 2020 Nov;83(5):1255-1268. doi: 10.1016/j.jaad.2020.03.132. Epub 2020 May 23. PMID: 32454097; PMCID: PMC7572894.
5. Gleason L, Hunter E, Cohen A, Suriano J, Nikbakht N. Atezolizumab-induced psoriasiform drug eruption successfully treated with ixekizumab: a case report and literature review. Dermatol Online J. 2023 Feb 15;29(1). doi: 10.5070/D329160215. PMID: 37040912..
6. Kost Y, Mattis D, Muskat A, Amin B, McLellan B. Immune Checkpoint Inhibitor-Induced Psoriasiform, Spongiotic, and Lichenoid Dermatitis: A Novel Clinicopathological Pattern. Cureus. 2022 Aug 14;14(8):e28010. doi: 10.7759/cureus.28010. PMID: 36134105; PMCID: PMC9470384.
7. Johnson D, Patel AB, Uemura MI, Trinh VA, Jackson N, Zobniw CM, Tetzlaff MT, Hwu P, Curry JL, Diab A. IL17A Blockade Successfully Treated Psoriasiform Dermatologic Toxicity from Immunotherapy. Cancer Immunol Res. 2019 Jun;7(6):860-865. doi: 10.1158/2326-6066.CIR-18-0682. Epub 2019 Apr 17. PMID: 30996018.
8. Monsour EP, Pothen J, Balaraman R. A Novel Approach to the Treatment of Pembrolizumab-induced Psoriasis Exacerbation: A Case Report. Cureus. 2019 Oct 2;11(10):e5824. doi: 10.7759/cureus.5824. PMID: 31754559; PMCID: PMC6827694.
9. Esfahani K, Miller WH Jr. Reversal of Autoimmune Toxicity and Loss of Tumor Response by Interleukin-17 Blockade. N Engl J Med. 2017 May 18;376(20):1989-91. doi: 10.1056/NEJMc1703047. PMID: 28514612.
10. Liu C, Liu R, Wang B, Lian J, Yao Y, Sun H, Zhang C, Fang L, Guan X, Shi J, Han S, Zhan F, Luo S, Yao Y, Zheng T, Zhang Y. Blocking IL-17A enhances tumor response to anti-PD-1 immunotherapy in microsatellite stable colorectal cancer. J Immunother Cancer. 2021 Jan;9(1):e001895. doi: 10.1136/jitc-2020-001895. Erratum in: J Immunother Cancer. 2021 Oct;9(10): PMID: 33462141; PMCID: PMC7813395.
11. Zhang Y, Chandra V, Riquelme Sanchez E, Dutta P, Quesada PR, Rakoski A, Zoltan M, Arora N, Baydogan S, Horne W, Burks J, Xu H, Hussain P, Wang H, Gupta S, Maitra A, Bailey JM, Moghaddam SJ, Banerjee S, Sahin I, Bhattacharya P, McAllister F. Interleukin-17-induced neutrophil extracellular traps mediate resistance to checkpoint blockade in pancreatic cancer. J Exp Med. 2020 Dec 7;217(12):e20190354. doi: 10.1084/jem.20190354. PMID: 32860704; PMCID: PMC7953739.