Cutaneous Immune Related Adverse Effect in a Patient with Underlying Autoimmune Disorder

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LEARNING OBJECTIVES

1. Recognize common immune-related adverse reactions to checkpoint inhibitor therapy.
2. Patients with an underlying autoimmune disease receiving checkpoint inhibitor therapy may be at higher risk for adverse effects.

CASE INFORMATION

HPI

76-year-old male with multiple primary cutaneous squamous cell carcinomas of his extremities s/p resection developed new lesions at the site of his previous surgeries (Koebner phenomenon). He received radiation and a dose of pembrolizumab and presented one week later with lichenified reaction that progressed to hypertrophic plaques with erosion.

PMH/PSH

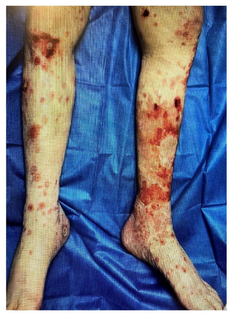
- Thymoma with thymectomy, recurrence and resection
- Left renal cell carcinoma with left nephrectomy
- Microscopic colitis for over 20 years
- Recurrent SCC treated with Mohs Micrographic Surgery (MMS)

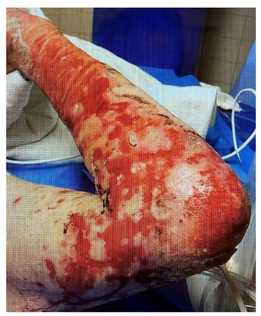
MEDS

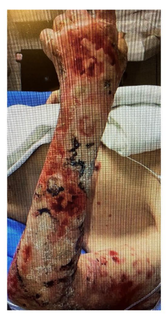
Apixaban for atrial fibrillation
Budesonide for microscopic colitis

PHYSICAL EXAM

Diffuse plaques/erosions on extremities, also with mucosal involvement (oral)





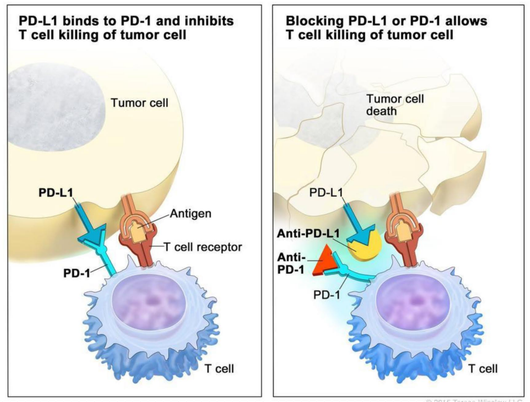


HOSPITAL COURSE

- Admitted to the burn unit and treated with wound care, steroids, and IVIG
- Biopsy showed erosive lichen planus thought to be immune related from the PD1 +/- radiation.
- Hospital course was complicated by:
  - Pancytopenia due to Bactrim used for prophylaxis
  - Progressive encephalopathy
  - Clostridium difficile infection
  - CMV esophagitis causing severe oropharyngeal dysphagia
  - CMV viremia
  - Acute GI bleeding in the setting of sterol colitis
  - Ongoing aspiration due to the severe oropharyngeal dysphagia
- Developed acute respiratory failure due to aspiration pneumonia.
- Family transitioned him to comfort measures only and he died a short while after.

WHAT ARE CHECKPOINT INHIBITORS

Immune checkpoint inhibitors work by blocking checkpoint proteins from binding with their partner proteins which allows T cells to kill the cancer cells.



Checkpoint inhibitors do not have the same toxic profile associated with traditional chemotherapies which significantly impacts treatment options for older adults with multiple co-morbid conditions.

Patients treated with checkpoint inhibitors can develop immune related adverse events (irAE), with younger people at risk of more severe toxicities and older people at higher risk for longer hospitalizations and death.

Most Common Immune Related Adverse Events (irAE)

Reaction	Median Onset (Weeks)	Frequency (%)*	Treatment*
Cutaneous	4 (2 – 150)	71.5	IVIG, rituximab
Gastrointestinal	6 (1-107.5)	8-27 Up to 54 for diarrhea	Loperamide/Lomotil Infliximab (anti-TNF) , vedolizumab (anti-integrin)
Hepatic	6-12 weeks	Monotherapy: 2-10 Combination: 25-30	Azathioprine, Mycophenolate
Endocrinopathies	14.5 (1.5 – 127)	10	Levothyroxine (for hypothyroidism) Hydrocortisone 20/10 mg or pred 7.5-10mg** +/- fludrocortisone (0.05-0.1 mg/day) Stress dose steroids
Pulmonary	34 (1.5 – 1.27)	0-10	Rule out infection/other causes Infliximab, mycophenolate mofetil IV, IVIG, cyclophosphamide

*Depends on drug(s) used, disease subtype, and grade
**Most reactions start with Prednisone 0.5-1 mg/kg/day or Methylprednisolone 1-2 mg/kg/day depending on grade, except endocrinopathies

IMPLICATIONS/DISCUSSION

Patients with autoimmune disorders
Excluded from trials
May be more likely to develop an adverse reaction and/or develop flares of underlying condition after exposure to checkpoint inhibitors. • 71% have autoimmune disease flare or other irAE • 41% exacerbation of preexisting condition (46% had active disease at drug initiation)
Radiation + Checkpoint inhibitors = may increase irAE
May be at higher risk for increased irAE --further studies are needed for safety and efficacy

TAKE HOME POINTS

ALL healthcare providers need to be aware that a patient has received checkpoint inhibitors because early recognition and treatment decreases life-threatening complications and may minimize treatment interruptions .

Checkpoint inhibitors can manifest adverse reactions in all organ systems at any time after even one dose of medication

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