DERMATOLOGIC TOXICITIES ASSOCIATED WITH IMMUNOTHERAPIES AND MANAGEMENT STRATEGIES

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June 30, 2018
DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

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DISCLOSURES
Biotest AG: Consultant – Honoraria
Bayer: Speaker – Honoraria
Incyte: Principal Investigator – Research
Veloce Pharmaceuticals: Principal Investigator – Research
Spectrum of immune-related Adverse Events (irAEs)
Cutaneous: 30-40%

Neurologic & Ophthalmologic:
- Autoimmune neuropathy
- Demyelination
- Uveitis
- CN VI & VII paresis
- Motor dysfunction
- Guillain-Barré syndrome
- Myasthenic syndrome

Endocrine: 1-8%

Renal:
- Nephritis

GI: 6-16%

Pulmonary:
- Pneumonitis
- Sarcoidosis

irAEs from Checkpoint Inhibitors

# Dermatologic Adverse Events to Anti-PD-1 Therapies

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J Clin Oncol 2015; 33  
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J Clin Oncol 2015; 33  

### Nivolumab + Ipilimumab

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<td>44-65% (6-7%)</td>
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<tr>
<td>Pruritus</td>
<td>17-65% (0%)</td>
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Rash

Median time to onset = 4-6 weeks

Eczema

- Interface, perivascular and periadnexal lymphocytic dermatitis
- Few plasma cells and eosinophils

Lichenoid dermatitis

- Band-like lymphocytic infiltrate along DEJ
- Vacuolar interface
- Coexisting spongiosis

References:
Eczematous/spongiotic dermatitis

Eczematous
• Generalized
• Localized
Eczematous
- Generalized
- Localized
Eczematous
• Generalized
• Localized
Clinical Patterns of Lichenoid Dermatitis

- Discrete
- Localized
- Inverse
- Generalized
- Palmoplantar
- Mucosal
Lichenoid: Discrete
Lichenoid: Discrete
Lichenoid: Localized

[Images showing various dermatological conditions]

Lichenoid: Localized
- Inverse

Lichenoid: Generalized
Lichenoid: Palmoplantar
Lichenoid: Mucosal
- 20 patients
- Time to onset: **3 days to 13 months**
- 16/20 (80%): erythematous papules with scale
  - 11/20 (55%): Localized on trunk or extremities
  - 9/20 (45%): Generalized distribution
- 16/17 (94%): lichenoid histology
- 8/16 (50%): lichenoid + spongiotic histology
- 4/20 (20%): peripheral eosinophilia
- 16/20 (80%) on concurrent medications previously reported to cause lichenoid drug eruptions
Association of Dermatitis after PD-1/PD-L1 Inhibitor Therapy and Progression Free Survival and Overall Survival

Lee CK et al. JAAD May 2018
NCCN Guidelines Version 1.2018
Management of Immunotherapy-Related Toxicities

DESKTOPLOGIC
ADVERSE
EVENT(S)

ASSESSMENT/GRADING

MANAGEMENT

Mild (G1)

• Continue immunotherapy
• Treatment with moderate potency topical steroids
• Oral antihistamine
• Topical emollient

Moderate (G2)

• Consider holding immunotherapy
• Treatment with high potency topical steroids AND/OR
• Prednisone 0.5–1 mg/kg/day
• Oral antihistamine
• Topical emollient

Severe (G3–4)

• Hold immunotherapy
• Treatment with high potency topical steroids
• Prednisone 0.5–1 mg/kg/day (increase dose if no improvement)
• Urgent dermatology consultation

Maculopapular rash

• Total body skin exam, including mucosa
• Assess for history of prior inflammatory cutaneous diseases
• Consider biopsy if unusual features

Pruritus

IMMUNO-2

Blistering disorder

IMMUNO-3

aCharacterized by the presence of macules (flat) and papules (elevated). Also known as morbilliform rash, it is one of the most common cutaneous adverse events, frequently affecting the upper trunk, spreading centripetally and may be associated with pruritus.
bCharacterized by an intense itching sensation.
cCharacterized by inflammation of the skin and the presence of bullae, which are filled with fluid.
dMacules/papules covering <10% body surface area (BSA) with or without symptoms (e.g., pruritus, burning, tightness).
eMacules/papules covering 10%–30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental activities of daily living (ADLs).
fMacules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADLs.
gPrednisone 0.5–1 mg/kg/day.
hSee Principles of Immunosuppression (IMMUNO-A).
iSee Principles of Immunotherapy Rechallenge (IMMUNO-C).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Management of Rash by Immune Checkpoint Blockade


Grade

1
Macules/papules covering <10% BSA*
*Asymptomatic or with symptoms

2
Macules/papules covering 10-30% BSA*
*Asymptomatic or with symptoms
*Limiting self-care ADLs

3-4
Macules/papules covering >30% BSA*
*Asymptomatic or with symptoms
*Severe/life-threatening symptoms
*Generalized exfoliative/ulcerated/bullous rash

Investigations

• Mucocutaneous clinical exam
• Serum testing for liver, kidney function
• Consider dermatology consult
• Consider skin biopsy

Management

• Continue immunotherapy
• Topical corticosteroids (intermediate to high potency)
• Oral antihistamines for pruritus

• Oral prednisone 1 mg/kg/day or equivalent
• Oral antihistamines for pruritus

• Hold immunotherapy
• Oral prednisone 1mg/kg/day or equivalent
• Oral antihistamines for pruritus

• Repeat skin exam
• If develops symptoms, treat as higher grade

Follow-Up

• If improves to ≤Grade 1, resume immunotherapy
• After symptoms improve, taper steroids over ≥1 month

• If improves to ≤Grade 1, taper steroids over ≥1 month
• If worsens in 48 hours, consider additional immunosuppression (infliximab, cyclophosphamide, MMF) or supportive measures
• If no improvement ≥12 weeks from last dose of therapy, discontinue immunotherapy

• If improves to ≤Grade 1, taper steroids over ≥1 month
• If worsens in 48 hours, consider additional immunosuppression (infliximab, cyclophosphamide, MMF) or supportive measures
• If no improvement ≥12 weeks from last dose of therapy, discontinue immunotherapy

• If improves to ≤Grade 1, taper steroids over ≥1 month
• If worsens in 48 hours, consider additional immunosuppression (infliximab, cyclophosphamide, MMF) or supportive measures
• If no improvement ≥12 weeks from last dose of therapy, discontinue immunotherapy
### Treatment of Severe and Steroid-Refractory Immune-Related Adverse Events

<table>
<thead>
<tr>
<th>Type and Severity of irAE</th>
<th>Initial Management</th>
<th>Additional Immunosuppression</th>
<th>Immunosuppression Tapering Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colitis and/or diarrhea</strong>&lt;br&gt;Grade 3-4&lt;br&gt;- Increase of ≥7 stools per day over baseline&lt;br&gt;- Abdominal pain, fever, and change in bowel habits</td>
<td>- Admit to hospital for intravenous corticosteroid therapy (methylprednisolone 1-2 mg/kg daily dose)&lt;br&gt;- Supportive care including intravenous fluids, supplemental oxygen, and antibiotics as needed&lt;br&gt;- Withhold hepatotoxic drugs&lt;br&gt;- Consider further diagnostic imaging or procedures</td>
<td>- If no improvement after 3 days, give infliximab 5 mg/kg&lt;br&gt;- Can redose infliximab after 2 weeks if needed</td>
<td>- Rapidly tapering course of steroids as tolerated over 4-6 weeks&lt;br&gt;- Increase steroids if diarrhea flares and then restart tapering</td>
</tr>
<tr>
<td><strong>Hepatitis</strong>&lt;br&gt;Grade 3-4&lt;br&gt;- Aspartate transaminase and/or alanine transaminase levels &gt;5 times ULN&lt;br&gt;- Total bilirubin level &gt;3 times ULN</td>
<td></td>
<td>- If no improvement after 3 days, start mycophenolate mofetil 500-1000 mg every 12 hours</td>
<td>- Rapidly tapering course of steroids as tolerated; discontinue mycophenolate mofetil once tapered to prednisone 10 mg daily</td>
</tr>
<tr>
<td><strong>Pneumonitis</strong>&lt;br&gt;Grade 3-4&lt;br&gt;- Severe, life-threatening symptoms&lt;br&gt;- Worsening hypoxia</td>
<td></td>
<td>- If no improvement after 48 hours, start additional agent as above or cyclophosphamide</td>
<td>- Taper steroids slowly over 6 weeks&lt;br&gt;- Mycophenolate mofetil management as above if needed</td>
</tr>
</tbody>
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Patient Course

• Started on prednisone 80 mg daily with 3-4 week taper
• Clobetasol ointment BID x 2 weeks to genital area and oral ulceration; resolved and did not recur
• After prednisone dose reached 10 mg QD, rash and pruritus always recurred.
• Started narrowband ultraviolet B phototherapy 2-3 times a week – treated for 3 months
• Able to stop phototherapy and was maintained on prednisone 4 mg daily, then discontinued prednisone completely 2 months later.
• Still on pembrolizumab with stable disease.
• No recurrence of rash or pruritus for past 12 months.
Anti-PD-1 Cutaneous Eruptions
Severe/life-threatening

TEN-like reaction associated with nivolumab following ipilimumab

J Immunother 2016, 39(3):149-152

TEN due to nivolumab

J Cutan Pathol 2017; 00:1–4

- Diffuse morbilliform eruption -> slow progression over weeks to months
- Marked increase in PD-L1 staining expression in epidermis

- Pembrolizumab: 8 SJS, 2 TEN
• 50 yo woman, metastatic melanoma
• 3 months prior to admission, started ipilimumab + nivolumab x 1 cycle -> diffuse morbilliform, grade 2.
• Ipilimumab stopped.
• 2 more cycles of nivolumab -> slow progression. Short course of systemic steroids after each dose with some improvement. After 3rd dose nivolumab, treatment held. Started prednisone 1 mg/kg.
• Biopsy: mild interface dermatitis with rare necrotic keratinocytes. **PD-L1 staining in few scattered keratinocytes and weak expression along epidermis.**
• On admission, 90% BSA with 10% Nikolsky sign. Extensive conjunctival, oral, and genital desquamation. Immunohistochemical analysis demonstrated CD8+ cells aggregated at the dermal-epidermal junction and epidermal exocytosis of CD8+ cells. **PD-L1 expression was markedly increased in the epidermis.** Direct immunofluorescence was negative. Dx: **TEN.**
• Infliximab, prednisone 1 mg/kg. 2 days later, started IVIG x 3 doses. Developed septic shock and multiorgan failure. Died on hospital day 6.

*Ability of anti-PD-1 antibodies to induce TEN without the classic clinical morphology or time course of the disease.*
Immunotherapy-Induced Pruritus

- Approximately 30% of patients
- Associated with rash and xerosis
- Enhanced immune system activation in the skin

- Adversely affects quality of life
NCCN Guidelines Version 1.2018
Management of Immunotherapy-Related Toxicities

<table>
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<th>Dermatologic Adverse Event(s)</th>
<th>Assessment/Grading</th>
<th>Management</th>
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| Pruritus<sup>b</sup>            | Mild (G1)<sup>l</sup> | Continue immunotherapy  
|                                |                    | Treatment with high potency topical steroids |
|                               | Moderate (G2)<sup>k</sup> | Consider holding immunotherapy until ≤ G1<sup>l</sup>  
|                                |                    | Treatment with high potency topical steroids  
|                                |                    | Oral antihistamines (cetirizine, hydroxyzine)  
|                                |                    | Dermatology consultation |
|                               | Severe (G3–4)<sup>j</sup> | Hold immunotherapy<sup>i</sup>  
|                                |                    | Prednisone/methylprednisolone 0.5–1 mg/kg/day<sup>g</sup>  
|                                |                    | GABA agonists (gabapentin, pregabalin)  
|                                |                    | Consider aripiprazole  
|                                |                    | Consider omalizumab  
|                                |                    | Urgent dermatology consultation |

<sup>b</sup>Characterized by an intense itching sensation.

<sup>i</sup>Treat until symptoms improve to Grade ≤ 1 then taper over 4–6 weeks.

<sup>g</sup>See Principles of Immunosuppression (IMMUNO-A).

<sup>h</sup>See Principles of Immunotherapy Rechallenge (IMMUNO-C).

<sup>i</sup>Mild or localized.

<sup>j</sup>Intense or widespread; intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification, oozing/crusts); limiting instrumental ADLs.

<sup>k</sup>Intense or widespread; constant; limiting self-care ADLs or sleep. Assess serum IgE and histamine; consider oral antihistamines for increased histamine and omalizumab for increased IgE.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
76-year-old Japanese woman
Advanced NSCLC with nivolumab
Severe rash with mucosal involvement → SJS
Oral prednisolone 1 mg/kg
Rash resolved, but pruritus unremitting with emollients, antihistamines, steroids
Aprepitant 80 mg QD x 5 days
Vitiligo

- 8-25% vitiligo
- 52 to 453 days to onset


Association of Cutaneous AE and Vitiligo With Tumor Response in Patients With Metastatic Melanoma Treated With Pembrolizumab

OR (complete or partial) associated with a higher occurrence of vitiligo: 71% vs 28%

JAMA Dermatol. 2015 Nov;151(11):1206-12
Vitiligo in non-melanoma cancer patients

75 year old woman
Stage IV NSCLC
Carboplatin + pemetrexed
4 months later, started on nivolumab
8 months after nivolumab initiation:
Patch of depigmentation on right hand
Vitiligo in non-melanoma cancer patients

- 75 yo man with stage 4 NSCLC, treated with docetaxel. Started nivolumab 3 months later due to progressive disease.
- 6 days later, vitiligo appeared on back, chest, abdomen, and extremities
- 66 yo man with AML in remission after chemotherapy and NSCLC previously treated with chemotherapy and local radiation
- On nivolumab as part of phase II clinical trial for prevention of AML recurrence
- Depigmentation starting 4 months after nivolumab initiation: arms, chest, face, neck

Lung Cancer. 2017 Jul;109:42-44
JAAD Case Reports 2017;3:90-2
Vitiligo in non-melanoma cancer patients

• Cross-reaction with melanocyte differentiation antigens: gp100, MelanA/MART-1, tyrosinase?

• Another shared antigen between NSCLC and melanocytes?
Hair Repigmentation During Immunotherapy Treatment With an Anti-Programmed Cell Death 1 and Anti-Programmed Cell Death Ligand 1 Agent for Lung Cancer

Noelia Rivera, MD; Aram Boada, MD; M. Isabel Bielsa, MD, PhD; M. Teresa Fernández- Figueras, MD, PhD; Enric Carcereny, MD; M Teresa Moran, MD; Carlos Ferrándiz, MD, PhD

• 13/14 patients with lung cancer
• 4 = squamous cell lung cancer
• 10 = lung adenocarcinoma
• 13/14 complete hair repigmentation to baseline hair color
• Nivolumab (n=11)
• Pembrolizumab (n=1)
• Atezolizumab (n=2)
• 13/14 partial response or stable disease

8 patients on anti-PD1 therapy vs 30 vitiligo controls
Photoexposed areas with specific depigmentation pattern consisting of multiple flecked lesions
No personal or family history of vitiligo, thyroiditis, or other autoimmune d/o
Blood and skin samples:
- Increased CXC motif ligand 10 levels in serum
- Skin infiltration of CD8 T cells expressing CXC motif receptor 3 and producing elevated levels of IFN-γ and TNF-α
- Mean BSA 4.25% (1-9%)
Repigmentation of Vitiligo Associated with Melanoma Relapse

Figure 2. Clinical Appearance of Treatment-Related Vitiligo and Repigmentation of Vitiligo in Association With Brain Metastases

A, Multiple vitiligo areas appeared on the right dorsal hand during nivolumab therapy. B, Eight months after cessation of nivolumab treatment, repigmentation of vitiligo was observed.

Nakamura Y et al. JAMA Dermatol. 2017 Sep 1;153(9):942-944
Case

• 83 year old Caucasian woman with metastatic melanoma to lung and spine
• Pembrolizumab 2 mg/kg IV every 3 weeks
• 2 month history of worsening vaginal and intergluteal eruption
• Onset between cycles 2 and 3
• Empiric systemic anti-fungal and antibacterial therapy with minimal response
• Consulted after admission to hospital for rash
Anti-PD-1 Cutaneous Eruptions

- Exacerbation of psoriasis
- Psoriasiform eruptions

J Eur Acad Dermatol Venereol. 2015 Sep 21
Acta Derm Venereol. 2015 Aug 13
JAMA Dermatol. 2015 Jul;151(7):797-9
Curr Opin Oncol 2016, 28:25-263
JAMA Dermatol. 2016 May 1;152(5):590-2
Current Prob Cancer. 2017;41:407-412
Anti-PD-1 Induced Psoriasis

- 21 patients
- 86% male
- 71% with history of psoriasis
- Mean time of onset between anti-PD1 initiation and psoriasis flare: 50 days
  - De novo psoriasis: 90 days
  - Preexisting psoriasis: 33 days
- 95% developed plaque psoriasis
  - + guttate: n=6
  - + palmoplantar: n=4
  - + pustular palmoplantar: n=1

- 81% topical treatment
- 10% systemic steroids
- 5% acitretin (5/17 patients required acitretin as second-line tx)
- 5% phototherapy
- 91% controlled by treatment; 9% worsened
• If known history of psoriasis, make sure patients are followed carefully during immunotherapy.
• Initiate topical steroid treatment early on with a maintenance regimen:
  E.g. Topical steroids BID x 2 weeks, then topical calcipotriene cream/ointment QD-BID during on weekdays and topical steroids QD-BID on weekends
• Low threshold to add on phototherapy while on immunotherapy.
• Can consider additional therapy: acitretin, low-dose methotrexate
Anti-PD-1 Cutaneous Eruptions

- Autoimmune bullous skin disorders
  - Bullous pemphigoid

• At least 21 cases reported: pembro, nivo, durvalumab, atezolizumab
• Pruritus: prominent feature, preceding or concurrent
• Mean time to pruritus: 17 weeks
• Time to development of bullae: 6 to 80 weeks (median 24 weeks)
• Metastatic melanoma, head/neck SCC, lung adenocarcinoma, lung SCC, NSCLC, renal cell carcinoma, urothelial carcinoma
• Mean age: 71 years
• 6/21 patients = 29% had oral mucosal involvement
- Topical steroid monotherapy
- Oral steroids + topical steroids
- Doxycycline + niacinamide: n=1; + oral and topical steroids: n=3
- Rituximab: n=1
- Omalizumab: n=1
- 3/21 patients: prolonged courses of BP for 3-12 months after discontinuation of checkpoint inhibitor
- Discontinuation necessary in 16/21 cases = 76%
- 7/19 patients = 37% had cancer progression or patient death shortly after BP diagnosis and checkpoint inhibitor discontinuation
• 2 theories:
  • Altered regulation of T-cells targeting collagen XVII/BP180
  • Increased autoantibody production against BP180
• In patients with persistent or unusual pruritus, consider subclinical BP.
• Can take months to resolve due to autoimmune activation
**NCCN Guidelines Version 1.2018**

**Management of Immunotherapy-Related Toxicities**

**DERMATOLOGIC ADVERSE EVENT(S)**

- **Bullous dermatitis**
  - Urgent dermatology consult for skin biopsy
  - **Mild (G1)**
    - Hold immunotherapy
    - High potency topical steroids
  - **Moderate (G2)**
    - Hold immunotherapy until <G1
    - Prednisone/methylprednisolone 0.5–1 mg/kg/day
  - **Severe (G3)**
    - Permanently discontinue immunotherapy
    - Prednisone/methylprednisolone 1–2 mg/kg/day
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
  - **Life-threatening (G4)**
    - Permanently discontinue immunotherapy
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
    - Methylprednisolone/prednisolone 1–2 mg/kg/day

- **Stevens-Johnson syndrome (SJS)**
  - Urgent dermatology consult for skin biopsy
  - **Mild (G1)**
    - Hold immunotherapy
    - High potency topical steroids
  - **Moderate (G2)**
    - Hold immunotherapy until <G1
    - Prednisone/methylprednisolone 0.5–1 mg/kg/day
  - **Severe (G3)**
    - Permanently discontinue immunotherapy
    - Prednisone/methylprednisolone 1–2 mg/kg/day
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
  - **Life-threatening (G4)**
    - Permanently discontinue immunotherapy
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
    - Methylprednisolone/prednisolone 1–2 mg/kg/day

- **Toxic epidermal necrolysis (TEN)**
  - Urgent dermatology consult for skin biopsy
  - **Mild (G1)**
    - Hold immunotherapy
    - High potency topical steroids
  - **Moderate (G2)**
    - Hold immunotherapy until <G1
    - Prednisone/methylprednisolone 0.5–1 mg/kg/day
  - **Severe (G3)**
    - Permanently discontinue immunotherapy
    - Prednisone/methylprednisolone 1–2 mg/kg/day
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
  - **Life-threatening (G4)**
    - Permanently discontinue immunotherapy
    - Inpatient care required
    - Urgent dermatology and ophthalmology consultation
    - Methylprednisolone/prednisolone 1–2 mg/kg/day

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**Note:** All recommendations are category 2A unless otherwise indicated.

**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Other reported cutaneous side effects to checkpoint inhibitors

- Acneiform eruption
- Actinic keratosis
- Acute generalized exanthematous pustulosis (AGEP)
- Annular granuloma
- Alopecia areata, universalis
- Basal cell carcinoma
- Dermal hypersensitivity reaction (DHR)
- Dermatitis herpetiformis
- Dermatomyositis
- Drug rash with eosinophilia and systemic symptoms (DRESS)
- Eruptive keratoacanthoma
- Erythema
- Erythema-nodosum-like panniculitis
- Exfoliative reaction
- Grover’s disease
- Hyperhidrosis
- Nail changes
- Necrotizing vasculitis
- Papulopustular rosacea
- Peritumoral inflammatory cellulitis
- Photosensitivity reaction
- Pityriasis lichenoides-like reaction
- Prurigo nodularis
- Pyoderma gangrenosum-like ulcerations
- Radiation-associated dermatitis
- Regression of melanocytic nevi
- Sarcoidosis
- Sclerodermoid reaction
- Seborrheic keratosis
- Sjögren’s syndrome
- Squamous cell carcinoma
- Sweet’s syndrome
- Tumoral melanosis
- Urticaria
- Xerosis
Eruptive keratoacanthomas

Cutaneous SCCs
5/82 patients = 6.1%
Face, chest, arms
Older patients (73 yo vs 60 yo)

Eruptive keratoacanthomas

- 3 patients on pembrolizumab
- Sudden onset of multiple lesions on sun-exposed areas of extremities
- Median 13 months (4-18 mos)
- Pathology:
  - Multiloculated, crateriform, keratin-filled lesions
  - Squamous cells w/ glassy appearing cytoplasm and minimal cytologic atypia
  - Distinct lichenoid infiltrate in underlying dermis w/ CD3+ T cells
- IL + topical steroids +/- cryotherapy
Autoimmune fasciitis

- 43-year-old woman with metastatic melanoma
- Started on nivolumab
- 14 months later: developed progressive fatigue, widespread myalgia of bilateral upper and lower limbs, progressive dysphagia
- Skin-muscle biopsy: focused fascial and perifascicular inflammatory infiltrate

Parker M et al. BMJ Case Rep 2018;Jan8
Pembrolizumab-induced scleroderma

- 66-year-old man with metastatic melanoma. Started on pembrolizumab. After cycle 13, developed fatigue and swelling of joints and ankles. Progression to burning and muscle weakness. Developed diffuse skin thickening over bilateral extremities and face.
- Treated with IVIG 5 days weekly per month and mycophenolate mofetil 1000 mg BID. Symptom improvement, then 14 weeks later, began to decline and died 2 months later.

- 79-year-old man with metastatic melanoma. Started on pembrolizumab. After cycle 5, severe stiffness of hands and feet. Pembrolizumab was discontinued.
- Treated with hydroxychloroquine 200 mg BID and oral prednisone. Improvement in symptoms.

Checkpoint inhibitor-induced dermatomyositis

- Ipilimumab: n=1
- Nivolumab: n=1
- 42-year-old man with stage IV lung adenocarcinoma. Treated with 4 cycles of cisplatin, pemetrexed, and bevacizumab -> 7 cycles of pemetrexed and bevacizumab -> 4 cycles of docetaxel. Started on nivolumab (3 mg/kg Q2 weeks).
- A few days after cycle 1: general fatigue and minor proximal limb muscle weakness
- 6 weeks later: clear proximal muscle weakness and skin findings
- MRI legs: abnormally high intensity areas in bilateral adductor and obturator muscles; EMG showed myogenic conversion.
- Treated with prednisolone 0.6 mg/kg QD -> slight temporary improvement
- Then diagnosed with spinal cord and meningeal dissemination 10 days later -> death
Erythema nodosum-like panniculitis
Sarcoidosis
Immunotherapy-induced alopecia areata

- 1-1.6% of patients on immunotherapy
- Anti-CTLA-4, PD-1, and PD-L1 inhibitors
- Scalp, face, eyebrows, eyelashes, trunk
- Areata and universalis
- Treatment with intralesional steroids (triamcinolone) and topical steroids (clobetasol)
- Resultant regrowth with poliosis

Thank You

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