Cutaneous Side Effects of Targeted Cancer Therapies: Diagnosis and Management

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Disclosures

• Regeneron: Principal investigator, Consultant, Speaker
• Merck: Principal investigator
• Iderra: Principal investigator
• Adgero: Consultant
• Amgen: Consultant, Speaker

• I will be discussing off-label use of medications
Case 1: “I am so embarrassed to go outside”

- 40 year old female patient with metastatic colon cancer
- Medical oncology started her on empirically on doxycycline 100 mg PO BID and hydrocortisone 2.5 % cream applied BID

EGFR acneiform reaction

- Gentle soap and water
- Topical antimicrobials (mupirocin, gentamicin, ketoconazole)
- Triamcinolone ointment 0.1% BID
- Transition to good emollient moisturizer

One week after starting combination of topical steroids and antibiotics
Apply under occlusion (shower cap) on scalp x 3 nights then shampoo in AM

Pseudomonas super-infection

• Important to culture, many drug resistant cases
• Patients can get septic due to concomitant cytotoxic chemotherapy and neutropenia
• Stop DCN/MCN and switch to appropriate antibiotic
• Monitor closely for C. difficile colitis
Case 2: “I am miserable but I really need to finish my chemotherapy cycles”

- 50 year old female patient with high risk breast cancer
- Patient and medical oncologist with strong determination to complete 4 additional cycles of chemotherapy
- No evidence of SADR (fever, LFTs, systemic symptoms, pain, blistering, mucosal lesions)

Toxic erythema of chemotherapy

- Careful review of risks and benefits
- Discuss signs and symptoms of SADR
- Triamcinolone ointment 0.1% BID, occlusion as tolerated
- Clobetasol ointment 0.05% to worst areas BID (dispense 120 grams)
- Cool packs, fans (no more warm blankets!)
Case 3: “I am itching like crazy. I can’t sleep!”

- 50 year old female patient with lung cancer on Nivolumab
- Excoriations but otherwise normal appearing skin
- No prior history of skin disease

Immunotherapy-related pruritus

- **Anti-PD1 and anti-PDL1**
  - Pembrolizumab
  - Nivolumab
  - Atezolizumab
  - Durvalumab
  - Avelumab
  - Cemiplimab

- **Prolonged therapy (years) and responses**
- **Expanding indications for adjuvant and combination therapy**
Immunotherapy related pruritus

- 14-47% of patients on immunotherapy
- Majority present within 1st 6 cycles
- Commonly with no primary lesions
- Unclear etiology
- Mean ItchyQOL 2.29
  - vs 2.0 for patients on hemodialysis
- 49% of patients with grade 2 or 3

Counselling (dry skin care, good emollients)
Topical menthol creams
Triamcinolone ointment 0.1% bid (454 gram jar)
Topical doxepin ($$)
NBUVB

Systemic medications:
- Oral antihistamines (H1 and H2)
- Gabapentin, Pregabalin
- Doxepin
- Aprepitant
- Oral steroids (short course)
- Dupilumab
Case 4: “I’ve had a rash for over a year”

- 50 year old female patient with melanoma
- Ipilimumab plus Nivolumab
- Discontinued therapy due to rash “all over”, itching
- Treated with oral steroids for over 1 year without improvement
- Presented with Cushingoid features

Immunotherapy induced psoriasis

- Can have unusual morphologies and many sub-types reported including guttate, hand-foot, hyperkeratotic, periungual
- Can be intensely pruritic
- Personal and family history are predictive of flares but de novo cases are common

Management:
- Topical steroids
- NBUVB
- Acitretin
- Methotrexate
- TNF inhibitors
  - Relatively contraindicated, careful review of risks and benefits
- Other immunomodulatory agents (PDE4, IL23, IL12, IL17, IL17A)
  - Considered less immunosuppressive but no data
Completely resolved with MTX 15 mg x 3 months, discontinued without recurrence

Patient refused acitretin due to cost ($300/month)

Case 5: Referred for “disseminated zoster”

• 60 year old male patient with lung cancer on Nivolumab
• 3 month history of rash, initially treated with oral antibiotics, then topical antifungals, then oral antifungals
• Referred for “disseminated zoster” refractory to antivirals

Also with penile erosions (not photographed)
Near complete resolution after topical triamcinolone, mupirocin, gentamicin x 2 weeks

Case 4: “No one will even look at my rash!”

Triamcinolone ointment x 1 weeks
Case 5: “I can’t eat anything”

Complete resolution after high dose oral steroid taper, chlorhexidine rinse, and topical steroids

One area of persistent erosion is due to recurrent trauma from loose tooth, extraction is scheduled
Case 6: “I’ve tried steroids and they don’t work”

Progression after 2 more cycles of Nivolumab and conservative topical therapy
After high dose steroids, weekly fluconazole, chlorhexadine rinse, topical ultra-potent steroids

After 2 months of acitretin (25 mg)
After 3 months of acitretin (25 mg)

Case 7: “I think my husband is having a seizure”
Metastatic squamous cell carcinoma

• Initially seen by both ENT and ophthalmology
• Treated with multiple courses of oral steroids for Bell’s Palsy
• MRI:
  • Perineural spread of metastatic squamous cell carcinoma within the right Meckel’s cave, right cavernous sinus, with inferior extension to the Pterygopalatine fossa and masticator space

Two days after 1st cycle of pembrolizumab

• Non-responsive for 10 min with memory loss
• In ED:
  • No pain but slightly confused
  • Troponin 9.5
  • BNP 1850
• Cath Lab:
  • No coronary artery disease
  • Pacemaker placed for “unrecognizable rhythm”
What do you do next?

- A) Stop pembrolizumab
- B) Start high dose steroids
- C) Give IVIG
- D) Both A and B
- E) Both A and C

“Cardiology: These are the cleanest vessels I have seen in a 77 year old!”

Immunotherapy induced cardiomyopathy

- Rare complication (<1%)
- Possible mechanisms:
  - Autoimmune myocarditis
  - Conductive disease (role of circulating anti-conductive tissue autoantibodies)
  - Coronary vasculitis
- Treatment algorithm similar to other immune toxicities
  - Oral steroids 0.5-2 mg/kg
  - Consider infliximab

Heinzerling, et al., JITC 2016
Lyon et al., Lancet Oncol 2018
Thank you!

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