Dermatology Week

May 14–16, 2025
October 22–25, 2025

Dermatology Week

Rash Decisions: Managing Dermatological Toxicities Associated with EGFR Inhibitor Treatment to Improve Patient Outcomes

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Disclosures

- **Silvina Pugliese, MD, FAAD** has nothing to disclose.

Learning Objectives

- Describe the role of EGFR in tumorigenesis
- Assess current data on the dermatological AE profiles of available EGFR inhibitors
- Evaluate the most recent guidelines and expert recommendations for identifying, preventing, and managing skin AEs in patients receiving EGFR inhibitor therapy
- Outline strategies for interdisciplinary and personalized care in patients receiving EGFR inhibitors for the optimal management of dermatologic toxicities

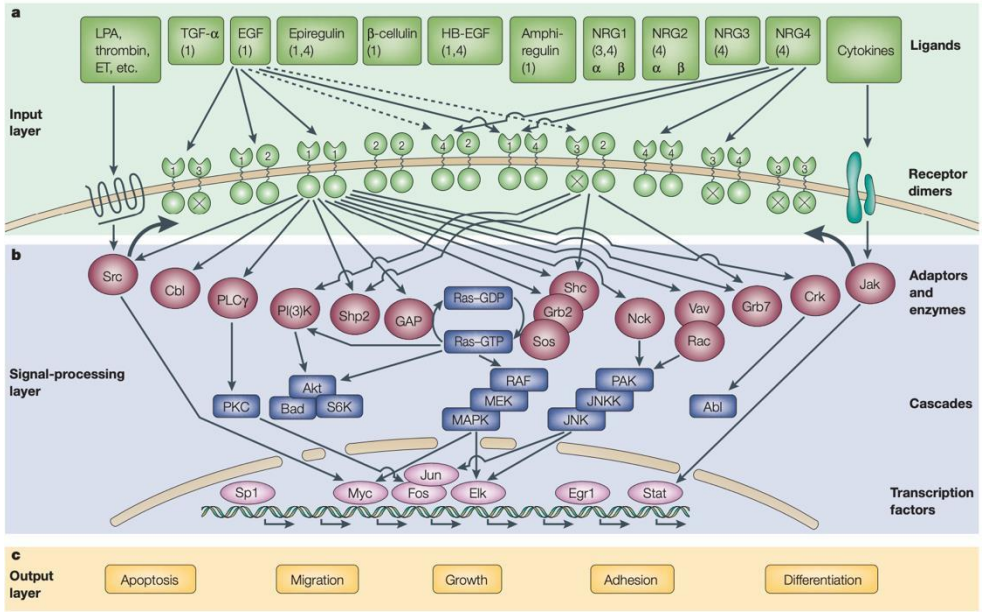
EGFR = epidermal growth factor receptor; AE = adverse event.

Dermatology Week

EGFR and Its Role in Cancer

Epidermal Growth Factor Receptor

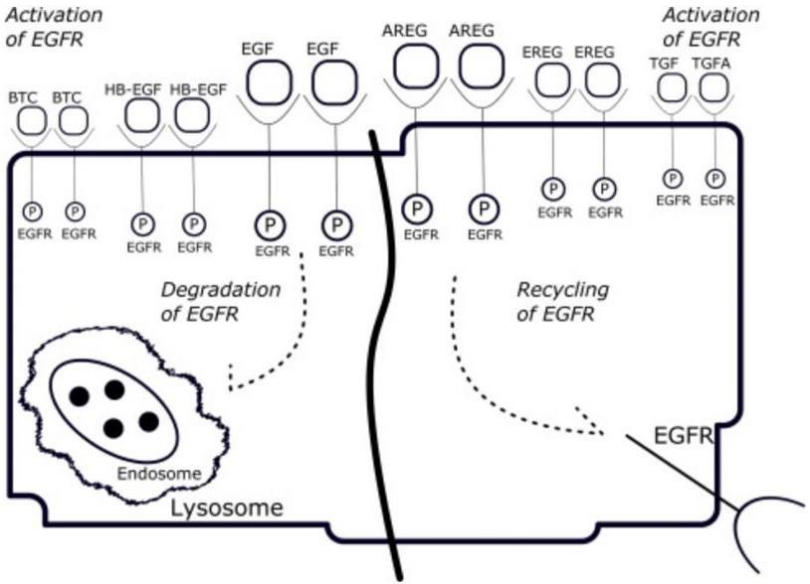
- ErbB family of tyrosine kinase receptors
- Critical to epithelial cell physiology
- Activation → proliferation, differentiation, survival, migration



Yarden Y, Sliwkowski MX. *Nat Rev Mol Cell Biol*. 2001;2(2):127-137.

EGFR and Carcinogenesis

- Cancer cells can utilize the EGFR pathway for uncontrolled growth via
  - Constitutive activation of receptors
  - Overexpression of receptors
  - Inhibition of apoptosis
  - Disruption of normal endocytosis (“recycling”) → sustained activation



Sigismund S, et al. *Mol Oncol*. 2018;12(1):3-20. Williams CB, et al. *Adv Cancer Res*. 2015;127:253-81.

EGFR and Carcinogenesis

EGFR (Epidermal growth factor receptor)	Epidermal growth factor receptor, a member of receptor tyrosine kinase. When dysregulated due to mutations or overexpression, its tyrosine kinase activity can drive oncogenic processes, especially nonsmall cell lung cancer	Yarden (2001); Paez et al. (2004)
HER2 (Human EGFR 2)	Growth factor receptor tyrosine kinase. Amplification or overexpression of *HER2* has been associated with aggressive growth in breast and other cancers	Yarden and Sliwkowski (2001); Ménard et al. (2003); Moasser (2007)

Heo Y, et al. *Genes Genomics*. 2025;47(4):399-416.

EGFR and Cancer Therapy

- Advanced or metastatic non-small cell lung cancer (NSCLC)
  - Molecular testing for EGFR mutations is standard of care
- Invasive breast cancer
  - Systemic adjuvant treatment for HER2 positive cancer
- Metastatic colorectal cancer
  - KRAS wild type
- Head and neck cancer
- Pancreatic cancer

Lilenbaum RA, Horn LA. *J Natl Compr Canc Netw*. 2016;14(5 Suppl):672-674. Owen DH, et al. *JCO*. 2025;43:e2-e16.

Commonly Used EGFR Inhibitors

Monoclonal antibodies
Cetuximab
Panitumumab
Necitumumab
Trastuzumab
Pertuzumab

EGFR Inhibitors: Monoclonal Antibodies

Monoclonal Antibodies				
Drug	**Tumor Type**	**Therapeutic Indication**	**Molecular Target**	**Molecular Markers of Efficiency**
Cetuximab	Advanced or metastatic SCCHN, metastatic CRC	With radiation therapy: treatment of locally or regionally advanced SCCHN With platinum-based therapy with fluorouracil: metastatic SCCHN Metastatic SCCHN progressing after platinum-based therapy With FOLFIRI: first-line treatment of KRASwt EGFR-overexpressing mCRC With irinotecan in patients who are refractory to irinotecan-based chemotherapy: treatment of KRASwt EGFR-overexpressing mCRC; as a single-agent in patients who have failed oxaliplatin-and irinotecan-based chemotherapy or who are intolerant to irinotecan	The binding site in domain III of EGFR	KRAS wild-type status of EGFR-overexpressing tumor
Panitumumab	Metastatic CRC	Single agent treatment of metastatic CRC with disease progression on or following fluoropyrimidine, oxaliplatin, and irinotecan chemotherapy regimens	The binding site in domain III of EGFR	RAS wild-type status of EGFR-overexpressing tumor
Necitumumab	Metastatic NSCLC	With gemcitabine and cisplatin: first-line treatment of patients with metastatic NSCLC	The binding site in domain III of EGFR	EGFR-overexpressing status of tumor

SCCHN = squamous cell carcinoma of head and neck; CRC = colorectal cancer; FOLFIRI = folinic acid, fluorouracil, irinotecan.
Shaban N, et al. *Cells*. 2023;13(1):47.

EGFR Inhibitors: Monoclonal Antibodies

Drug	Target	Tumor	Indication
Trastuzumab	Extracellular domain of human epidermal growth factor receptor 2 (HER2)	HER2+ invasive or metastatic breast cancer	Preoperative systemic therapy for HR+ or HR- and HER2+ disease Adjuvant systemic therapy for HR-positive, HER2+ disease, paired with chemotherapy, endocrine therapy, and/or pertuzumab Adjuvant systemic therapy for HR-negative, HER2+ disease, paired with chemotherapy and/or pertuzumab
Pertuzumab	Extracellular domain of human epidermal growth factor receptor 2 (HER2)	HER2+ metastatic breast cancer	Adjuvant systemic therapy for HR-positive, HER2+ disease, paired with trastuzumab and endocrine therapy Adjuvant systemic therapy for HR-negative, HER2+ disease, paired with chemotherapy and/or trastuzumab

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines. Accessed May 8, 2025. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.

Commonly Used EGFR Inhibitors

Monoclonal antibodies	Bispecific antibodies
Cetuximab	Amivantamab
Panitumumab	
Necitumumab	
Trastuzumab (HER2)	
Pertuzumab (HER2)	

EGFR Inhibitors: Bispecific Antibodies

Drug	Target	Tumor	Indication
Amivantamab	Extracellular domain of EGFR and MET receptors	Advanced or metastatic NSCLC	NSCLC with EGFR exon 19 deletion or exon 21 L858R mutations discovered prior to or during 1st-line systemic therapy; used in conjunction with lazertinib NSCLC with progression of disease on osimertinib with multiple systemic foci of metastatic disease NSCLC with EGFR exon 20 insertion mutation

NCCN Clinical Practice Guidelines. Accessed May 8, 2025. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.

Commonly Used EGFR Inhibitors

Monoclonal antibodies	Bispecific antibodies	Tyrosine kinase inhibitors
Cetuximab	Amivantamab	Erlotinib
Panitumumab		Gefitinib
Necitumumab		Lapatinib
Trastuzumab (HER2)		Afatinib
Pertuzumab (HER2)		Osimertinib
		Lazertinib

EGFR Inhibitors: 1st Generation TKIs

Tyrosine Kinase Inhibitors					
Drug	**Tumor Type**	**Therapeutic Indication**	**Molecular Target**	**Inhibitor Type**	**Molecular Markers of Efficiency**
•	*First Generation*				
Gefitinib	Advanced or metastatic NSCLC	First-line therapy for NSCLC carrying EGFR-activating mutations	EGFR: ATP-binding site	I	Activating mutations of *EGFR*: Exon 19 deletions; *L858R*
Erlotinib	Advanced or metastatic NSCLC, pancreatic cancer	First-line therapy for NSCLC carrying EGFR-activating mutations With gemcitabine: first-line treatment option for patients with locally advanced and metastatic pancreatic carcinoma	EGFR: ATP-binding site	I	Activating mutations of *EGFR*: Exon 19 deletions; *L858R*
Lapatinib	Metastatic breast cancer	With capecitabine: the treatment of HER2-positive MBC in patients who have previously received therapy (anthracycline, a taxane, trastuzumab) With letrozole: the treatment of postmenopausal women with hormone receptor positive MBC that overexpresses the HER2 receptor for whom hormonal therapy is indicated	ATP-binding site of EGFR and HER2	I½	HER2-positive status of tumor

TKI = tyrosine kinase inhibitor.
Shaban N, et al. *Cells*. 2023;13(1):47.

EGFR Inhibitors: 2nd & 3rd Generation TKIs

Drug	Tumor Type	Therapeutic Indication	Molecular Target	Molecular Markers of Efficiency
Afatinib (2nd gen TKI)	Metastatic NSCLC	First-line therapy for metastatic NSCLC carrying EGFR-activating mutations	ATP-binding site of EGFR, HER2, and HER4	Activating mutations of EGFR: Exon 19 deletions; L858R
Osimertinib (3rd gen TKI)	Advanced or metastatic NSCLC	Adjuvant and first-line therapy for metastatic NSCLC carrying EGFR-activating mutations The treatment of adult patients with metastatic EGFR T790M mutation-positive NSCLC, whose disease has progressed on or after EGFR TKI therapy	ATP-binding site of the EGFR	Activating mutations of EGFR: Exon 19 deletions; L858R The secondary T790M resistance mutation
Lazertinib (3rd gen TKI)	Advanced NSCLC	Treatment of locally advanced or metastatic NSCLC carrying EGFR T790M mutation	ATP-binding site of the EGFR	Activating mutations of EGFR: Exon 19 deletions; L858R The secondary T790M resistance mutation

Shaban N, et al. *Cells*. 2023;13(1):47.

Key Takeaways

- Epidermal growth factor receptor is a tyrosine kinase receptor that is crucial to epithelial cell physiology
- EGFR mutations increase receptor activation, inhibit apoptosis, and disrupt normal endocytosis to contribute to tumorigenesis/carcinogenesis

- EGFR inhibitors are used to treat a variety of cancers and are available as monoclonal antibodies, bispecific antibodies, and tyrosine kinase inhibitors

Dermatology Week

Dermatological Events Associated with EGFR Inhibitor Treatment

Your Dermatology Expertise Is Needed

- EGFR inhibitors cause significant cutaneous adverse events
- Given the expanding indications for EGFR inhibitors across a variety of cancer types, you **will** see these patients in clinic
- Road map
  - Review role of EGFR in the skin (and consequences of inhibition)
  - Review clinical trial data reporting skin AEs
  - Review classic presentations of acneiform rash, xerosis, paronychia, and mucositis

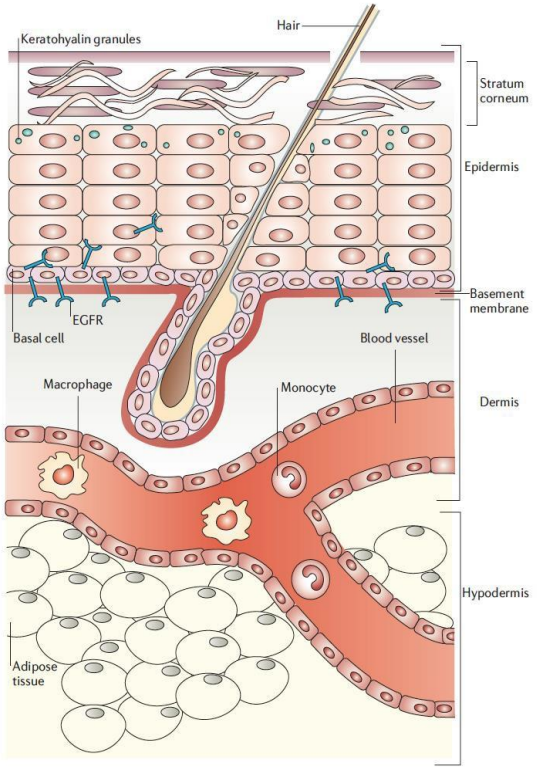
EGFR and the Skin

- Epidermal growth factor receptor is critical to epithelial cell physiology

Box 1 | Roles of EGFR in skin physiology

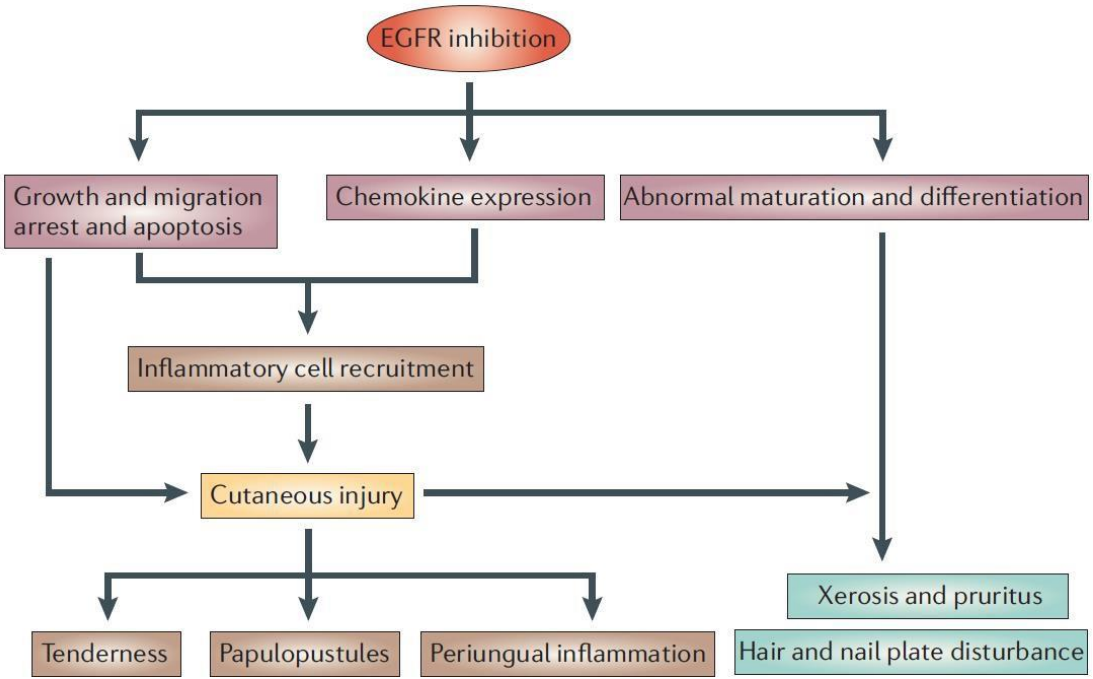
- Stimulation of epidermal growth
- Inhibition of differentiation
- Acceleration of wound healing
- Stimulation of keratinocyte migration through α2 integrins
- Activation of phosphatidylinositol turnover
- Activation of phospholipase A2 and, subsequently, arachidonic acid and prostaglandin E2
- Stimulation of vasoconstriction
- Diacylglycerol formation

EGFR, epidermal growth factor receptor.



Lacouture ME. *Nat Rev Cancer*. 2006;6(10):803-12.

EGFR Inhibition and the Skin



Lacouture ME. *Nat Rev Cancer*. 2006;6(10):803-12.

Skin AEs to Monoclonal Antibodies

- 2009 phase II study of cetuximab monotherapy in metastatic colorectal cancer patients: 85.9% of patients reported **acneiform rash** (7.1% reported at least grade 3 rash)
- Cetuximab package insert: 82% of patients across clinical trials developed **acneiform rash** (10% reported at least grade 3 rash)
- 2015-2023 phase III clinical trial of panitumumab vs bevacizumab in addition to first-line chemotherapy in patients with *RAS* wild-type, left-sided metastatic colon cancer: 74.8% of patients receiving panitumumab reported **acneiform rash**, 61.6% of patients receiving panitumumab reported **stomatitis**

Wierzbicki R, et al. *Invest New Drugs*. 2011;29(1):167-74. Watanabe J, et al. *JAMA*. 2023;329(15):1271-1282. Drugs@FDA: FDA-Approved Drugs. Accessed May 8, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s279lbl.pdf.

Skin AEs to Bispecific Antibodies

	Amivantamab-chemo (N=151)		Chemotherapy (N=155)	
Cutaneous AE	**All Grades**	**Grade ≥ 3**	**All Grades**	**Grade ≥ 3**
Paronychia	85 (56%)	10 (7%)	0	0
Rash	81 (54%)	17 (11%)	12 (8%)	0
Dermatitis acneiform	47 (31%)	6 (4%)	5 (3%)	0
Stomatitis	38 (25%)	2 (1%)	9 (6%)	0

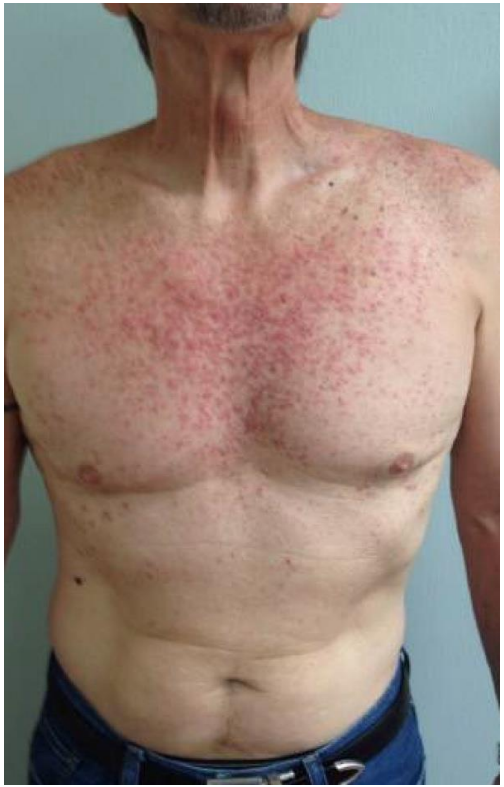
Zhou C, et al. *N Engl J Med*. 2023;389(22):2039-2051.

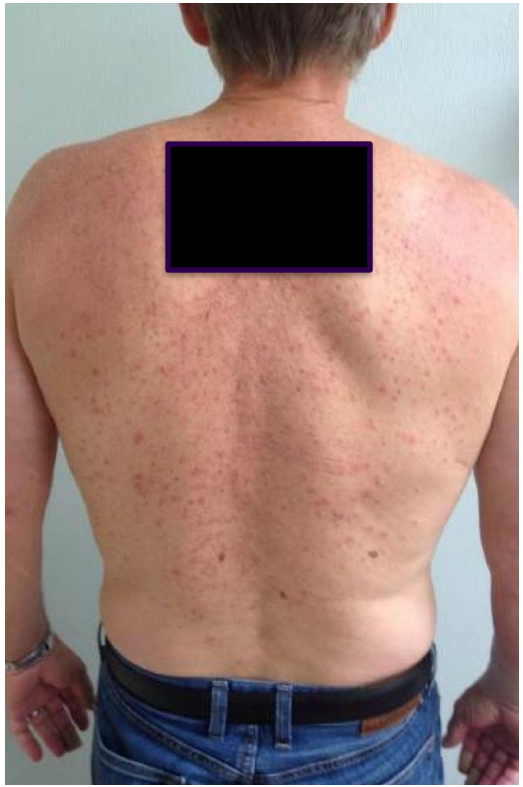
Skin AEs to TKIs

		Gefitinib			
		250 mg/d (n = 103)		500 mg/d (n = 106)	
Adverse Event	CTC Grade*	No.	%	No.	%
Skin					
Rash	1	27	26.2	31	29.2
	2	20	19.4	35	33.0
	3	1	1.0	6	5.7
	4	0	0	1	0.9
Pruritus	1	26	25.2	34	32.1
	2	5	4.9	3	2.8
	3	0	0	1	0.9
Dry skin	1	25	24.3	23	21.7
	2	3	2.9	8	7.5
Acne	1	10	9.7	5	4.7
	2	3	2.9	8	7.5
	3	0	0	2	1.9

CTC = common terminology criteria.
Fukuoka M, et al. *J Clin Oncol*. 2003;21(12):2237-2246.

Acneiform Rash



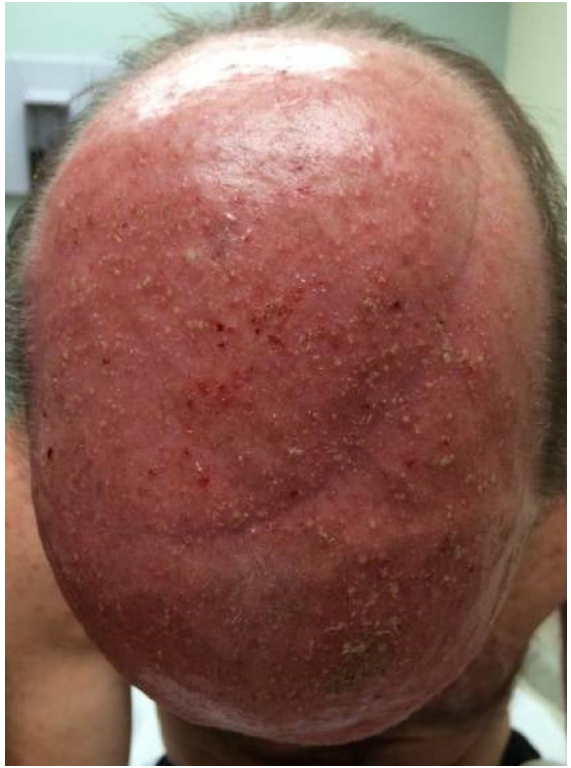


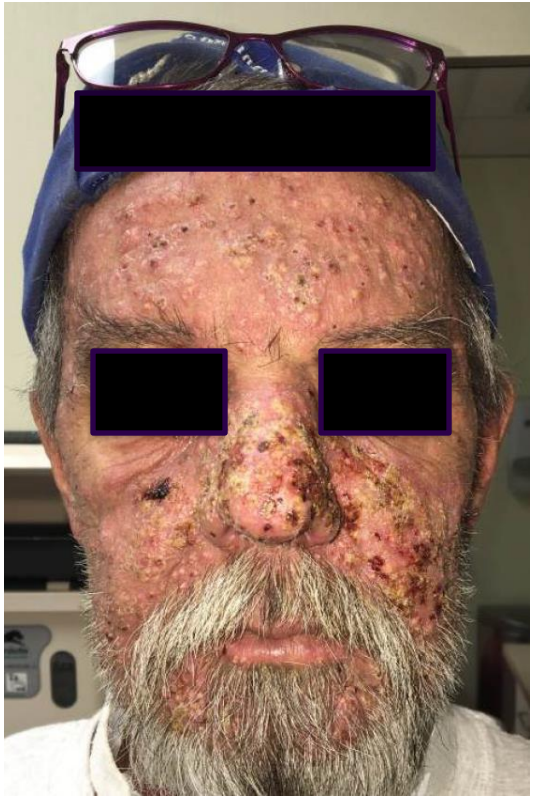
Acneiform Rash

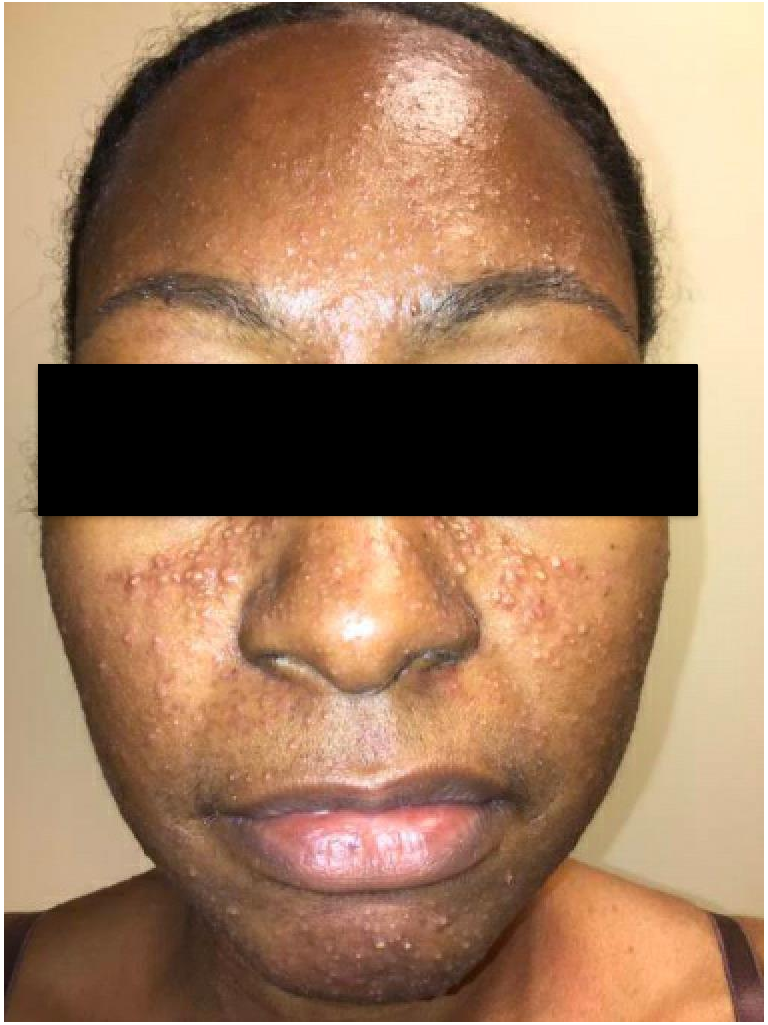
- *Acneiform drug eruption, papulopustular eruption*
- **Most common (incidence: 50-100%)**
- Seborrheic distribution (face, scalp, upper chest, upper back)
- Pruritic papules and pustules
- Develops 1-2 wks into treatment, peaks at ~4-6 wks
- Sterile but at risk for secondary infection

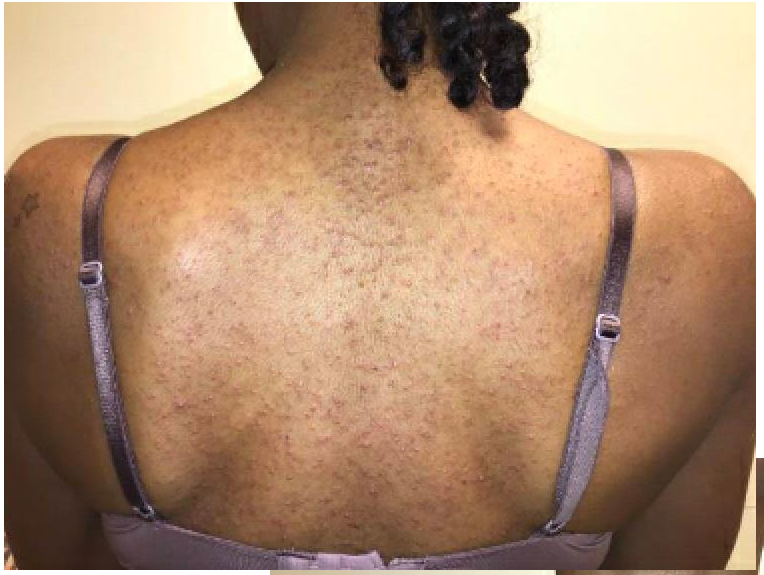
Macdonald JB, et al. *J Am Acad Dermatol*. 2015;72(2):203-218. Fabbrocini G, et al. *Skin Appendage Disord*. 2015;1(1):31-37.

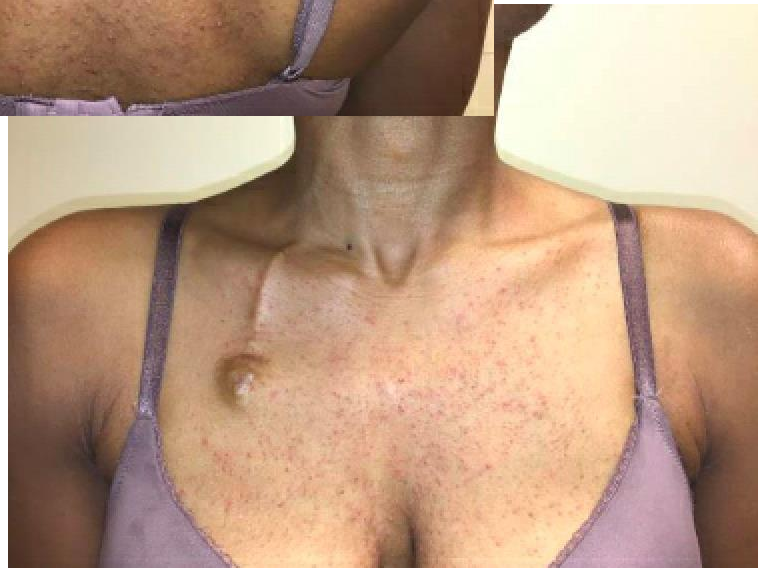
Acneiform Rash

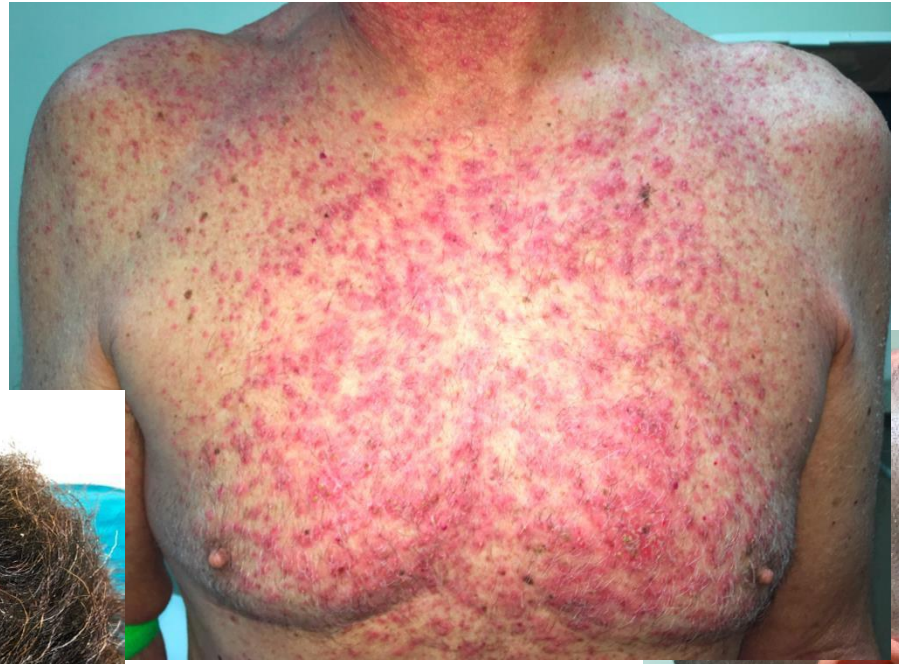


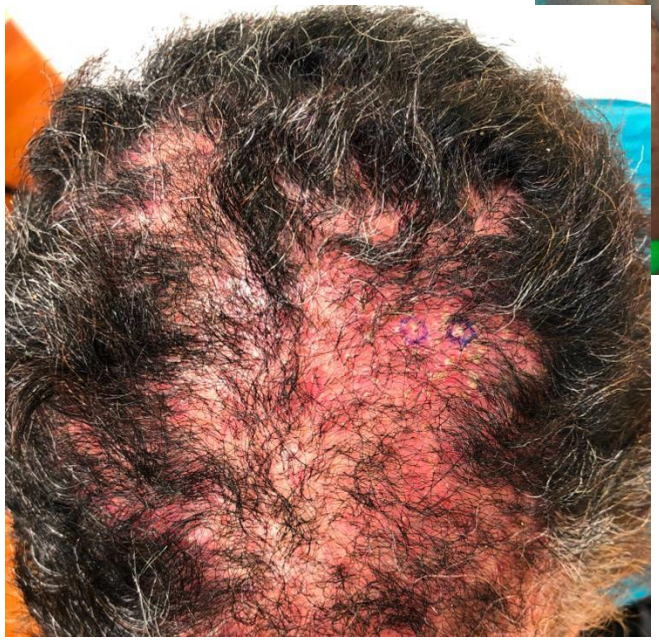


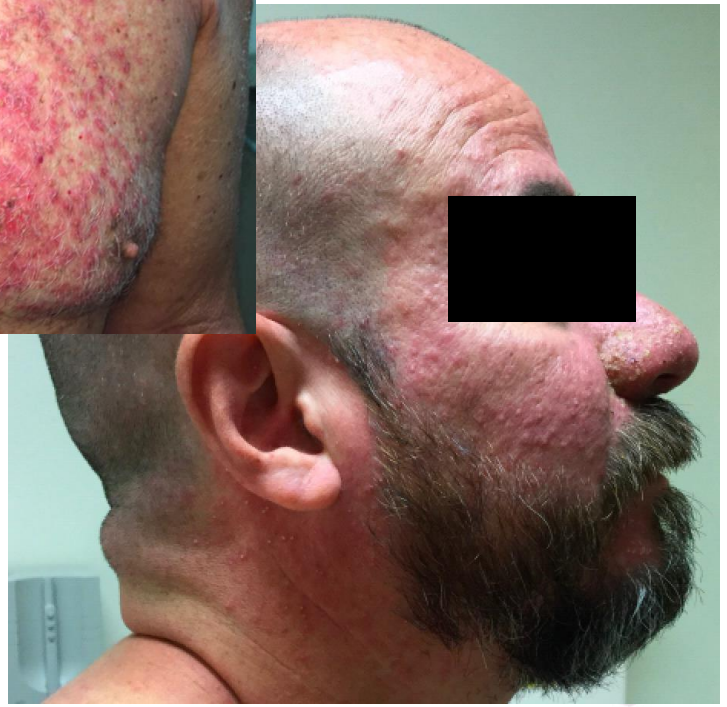




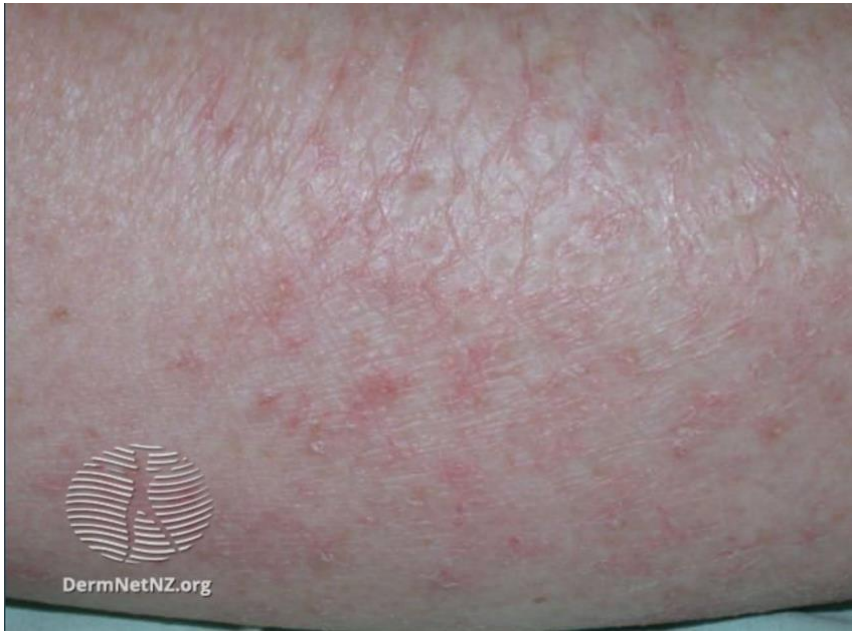


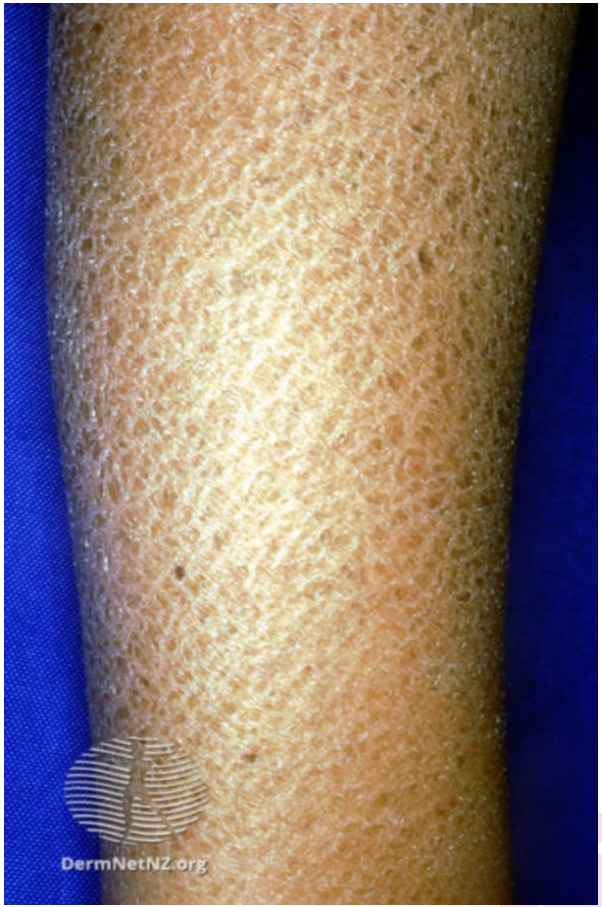






Xerosis





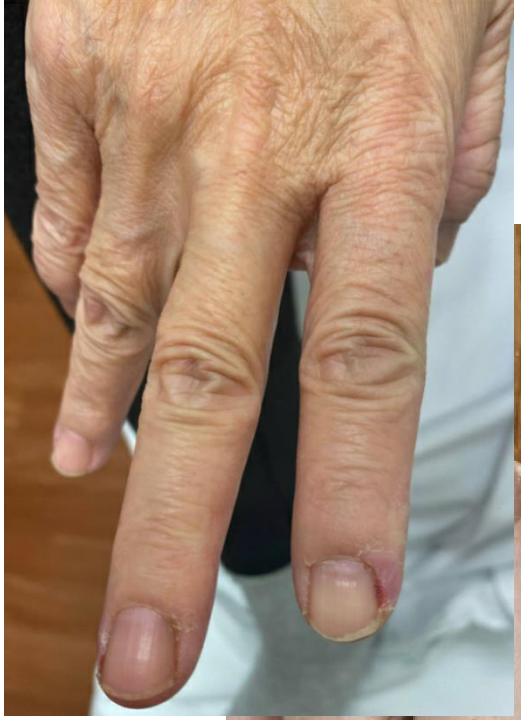
DermnetNZ. Accessed April 28, 2025. https://dermnetnz.org/topics/asteatotic-eczema; https://dermnetnz.org/topics/dry-skin.

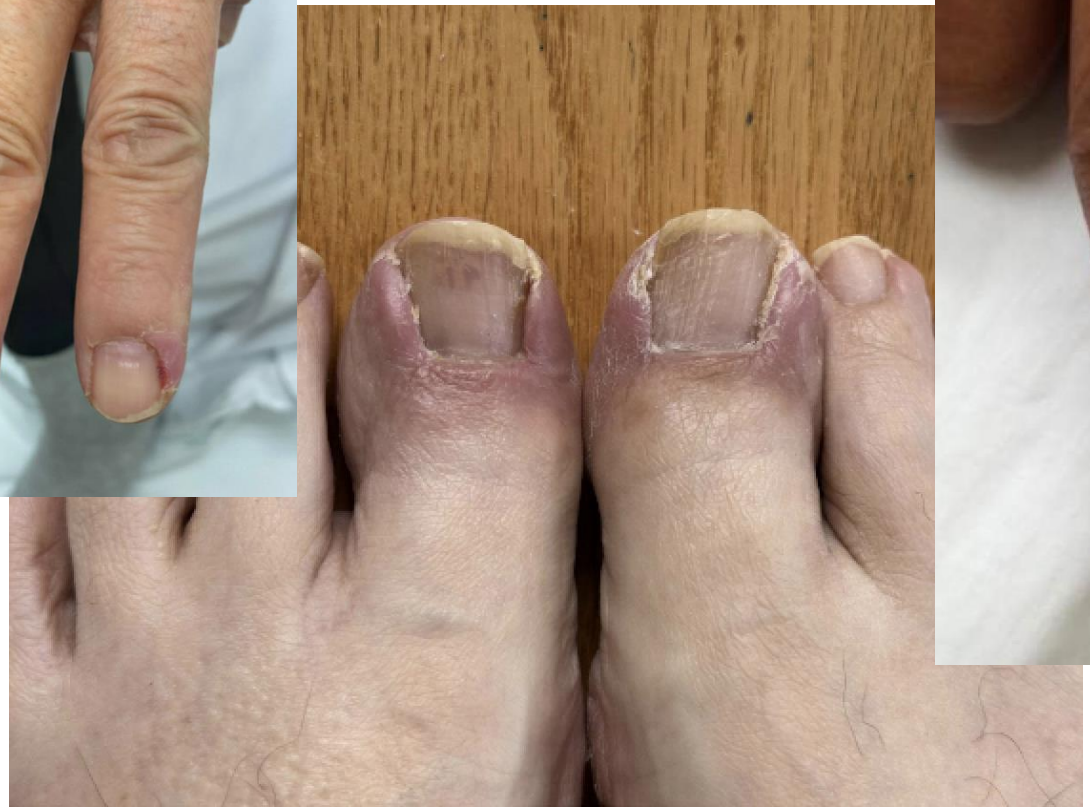
Xerosis

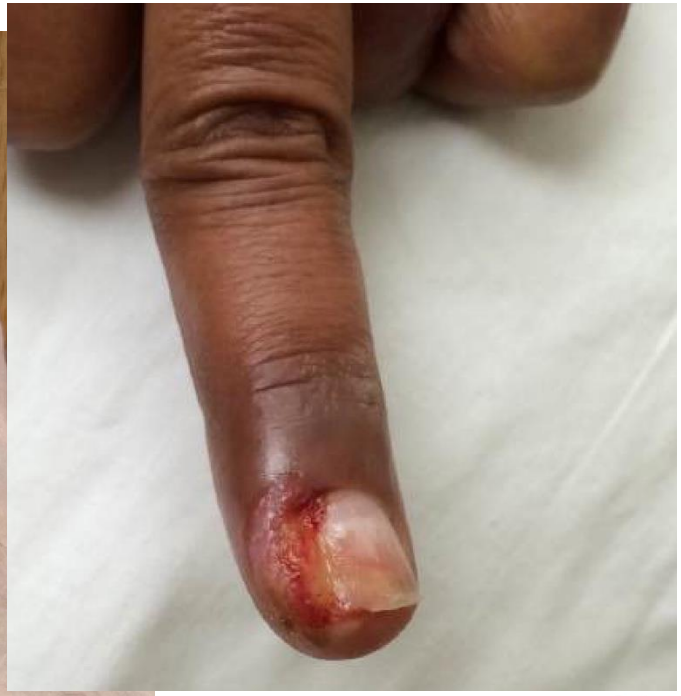
- Dry, cracked skin
- Incidence: 30-50%
- Later onset (1-3 months)
- Dose-dependent
- Increased skin fragility
- Can be associated with pruritus

Macdonald JB, et al. *J Am Acad Dermatol*. 2015;72(2):203-218. Clabbers JMK, et al. *Support Care Cancer*. 2016;24(2):513-521.

Paronychia





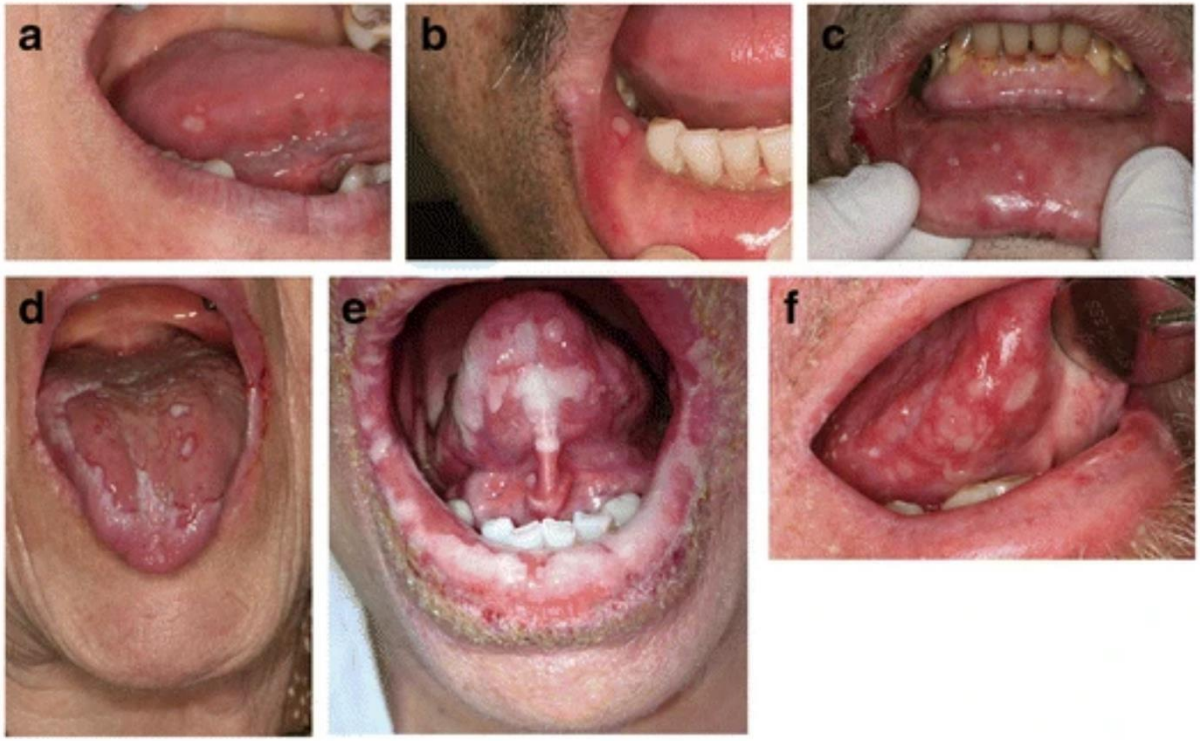


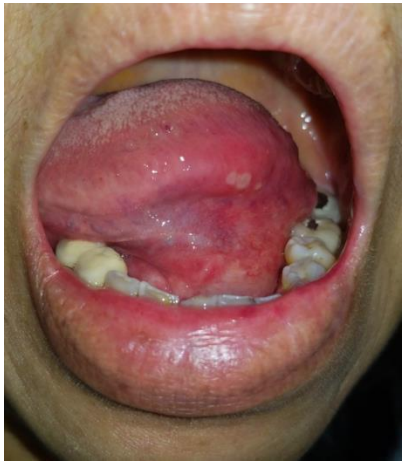
Paronychia

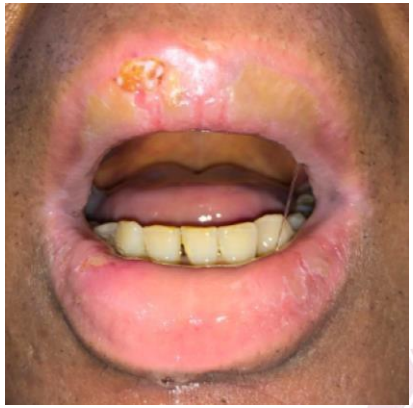
- Toxicity of the nail fold characterized by swelling, redness
- Incidence: 7-46.9% of patients
- Onset 4-8 weeks after treatment initiation
- Can see pyogenic granuloma-like changes
- Patients can develop infection

Gupta MK, Lipner SR. *Int J Dermatol*. 2022;61(4):410-415. Liu TH, et al. *Medicine (Baltimore)*. 2022;101(42):e31208. Macdonald JB, et al. *J Am Acad Dermatol*. 2015;72(2):203-218.

Oral Mucositis







Vigarios E, et al. *Support Care Cancer*. 2017;25(5):1713-1739.

Oral Mucositis

- Incidence: 5% panitumumab, 7% cetuximab, 8-20% erlotinib, 17-24% gefitinib, 25-72.1% afatinib
- Erythema, ulcerations, aphthous-like appearance, nonkeratinized oral mucosa
- Lips commonly involved: Erythema, erosions, fissures, angular cheilitis

Vigarios E, et al. *Support Care Cancer*. 2017;25(5):1713-1739.

Differential Diagnosis

Acneiform Rash	Xerosis	Paronychia	Mucositis
Demodex acne Rosacea Steroid-induced acne Perioral dermatitis drug-induced acne Pityrosporum folliculitis Eosinophilic pustular folliculitis	Itchthyosis Atopic dermatitis Irritant contact dermatitis Allergic contact dermatitis	Bacterial paronychia Herpetic whitlow Syphilitic chancre Onychocryptosis	Herpes simplex Paraneoplastic pemphigus Mucous membrane pemphigoid Aphthous stomatitis Oral lichen planus Nutritional deficiency

Key Takeaways

- EGFR plays an important role in normal skin physiology and inhibition leads to significant cutaneous toxicity
- The most common dermatologic side effect of EGFR inhibitors is acneiform rash, which presents with pruritic papules and pustules in a seborrheic distribution, and affects 50-100% of patients
- Other notable dermatologic side effects of treatment with EGFR inhibitors include xerosis, paronychia, and mucositis
- Consider entities on the differential diagnosis when evaluating patients for cutaneous toxicity to cancer therapy

Dermatology Week

Guidelines for Identification, Management, and Prevention of Dermatological AEs

Grading of Cutaneous Toxicities

- Common terminology criteria for adverse events (CTCAE)
  - Common language to communicate with oncology partners
  - Can inform management decisions

Grading Acneiform Rash

Acneiform rash	Grade 1	Grade 2	Grade 3	Grade 4
Disorder characterized by an eruption of papules and pustules, typically appearing in the face, scalp, upper chest and back	Papules and/or pustules covering <10% BSA, which may or may not be associated with symptoms of pruritus or tenderness	Papules and/or pustules covering 10-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL; papules and/or pustules covering >30% BSA with or without mild symptoms	Papules and/or pustules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated	Life-threatening consequences; papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated

BSA = body surface area; ADL = activities of daily living.

Basse C, et al. *Lung Cancer*. 2022;173:116-123. National Cancer Institute Cancer Therapy Evaluation Program. Accessed April 28, 2025. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.

Preventing Acneiform Rash

- Systematic review, 26 studies, 1926 patients
- Oral antibiotics: Greatest efficacy in preventing both **severe** (grade 2 or higher) acneiform eruptions with relative risk reduction of 40% (RR = 0.6, 95% CI, .46-.79, $p < .01$) and **any** acneiform eruptions, with relative risk reduction of 22% (RR = .88, 95% CI .82–.94, $p < .01$)
  - Primarily tetracycline antibiotics

CI = confidence interval; RR = relative risk.
Gorji M, et al. *Asia Pac J Clin Oncol*. 2022;18(6):526-539.

Preventing Acneiform Rash

Prophylactic skincare recommendations

- Use of a daily topical emollient
- Sun protection with SPF > 30 regularly
- Avoidance of irritative products, (i.e. salicylic acid)

Pre-emptive pharmaceutical recommendations

- Use medium-potency topical steroid twice-daily (i.e. methylprednisolone aceponate 0.1%)
- Use of 100 or 200 mg/d of doxycycline
- Administer pre-emptive treatment with oral antibiotics for at least 6 weeks following the initiation of EGFRi
- Do not consider topical antibiotics as a pre-emptive or curative modality

Apalla Z, et al. *J Eur Acad Dermatol Venereol*. 2025;39(4):730-741.

Treating Acneiform Rash

Management individualization
- Management should be individualized based on the severity and extension of the rash

Topical rash management
- Medium-potency steroids should be used for acneiform rash on the trunk and extremities
- Mild-potency steroids should be used for the face and anatomic folds

Systemic antibiotics
- Doxycycline as Pre-Emptive Treatment should be offered at a dose of 100 mg or 200 mg/d
- Minocycline should be used over doxycycline in patients with a history of photosensitivity or in regions with high UV index
- Doxycycline (200 mg/d) is recommended as a reactive treatment for grade 2/3 rash, but not for grade 1
- Topical Antibiotics should not be offered as reactive treatments

Duration of antibiotic treatment
- Discontinuation of pre-emptive treatment with oral antibiotics after 6–8 weeks if no clinical signs of acneiform rash develop
- Continuation of systemic antibiotics for more than 8 weeks if acneiform rash develops

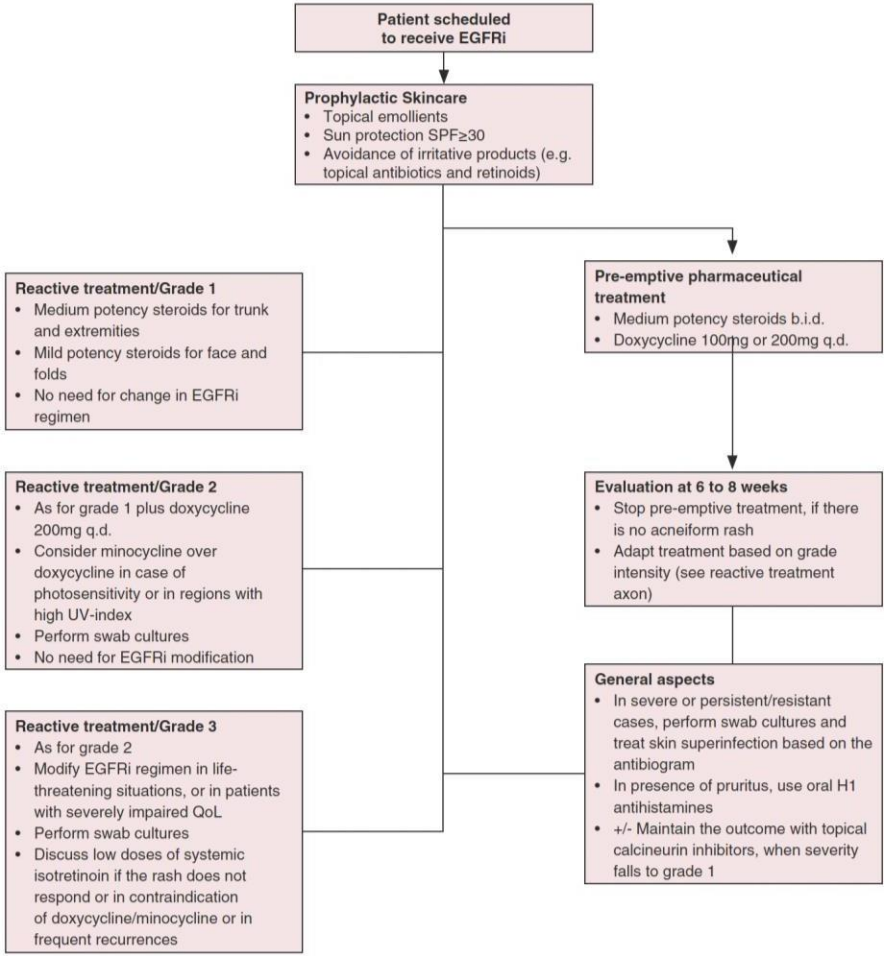
Skin superinfection
- In severe or resistant cases, treat skin superinfections (most common Staphylococcus aureus) based on the antibiogram

Systemic retinoids
- Systemic isotretinoin or acitretin are not recommended as a first-line treatment for grades 1 to 3 rash
- Consideration for low dose of oral isotretinoin (0.3 mg/kg) is suggested as a second line in grade 2/3 cases not responding to or contraindicated for doxycycline/minocycline

Pruritus management
- Oral H1 antihistamines

UV = ultraviolet.

Apalla Z, et al. *J Eur Acad Dermatol Venereol*. 2025;39(4):730-741.



QoL = quality of life.

Apalla Z, et al. *J Eur Acad Dermatol Venereol*. 2025;39(4):730-741.

Grading Xerosis

Dry skin	Grade 1	Grade 2	Grade 3
Disorder characterized by flaky and dull skin; the pores are generally fine, the texture is a papery thin texture	Covering <10% BSA and no associated erythema or pruritus	Covering 10-30% BSA and associated with erythema or pruritus; limiting instrumental ADL	Covering >30% BSA and associated with pruritus; limiting self care ADL

National Cancer Institute Cancer Therapy Evaluation Program. Accessed April 28, 2025. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.

Preventing and Treating Xerosis

- Shower/wash hands with lukewarm water
- Keep showers/baths short
- Wear gloves when washing dishes
- Avoid harsh soaps
- Avoid fragrances
- Moisturize daily
- Use cream-based moisturizers
- Use moisturizers at night with white cotton gloves (occlusion)

Oakley A. DermNet. Accessed May 8, 2025. https://dermnetnz.org/topics/dry-skin.

Grading Paronychia

Paronychia	Grade 1	Grade 2	Grade 3
Disorder characterized by an infectious process involving the soft tissues around the nail	Nail fold edema or erythema; disruption of the cuticle	Local intervention indicated; oral intervention indicated (eg. antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL	Operative intervention indicated; IV antibiotics indicated; limiting self-care ADL

Basse C, et al. *Lung Cancer*. 2022;173:116-123. National Cancer Institute Cancer Therapy Evaluation Program. Accessed April 28, 2025. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.

Preventing and Treating Paronychia

- Moisturize to improve skin barrier, avoid irritants, trim nails, use gloves
- Antimicrobial soaks (diluted bleach, vinegar soaks, hypochlorous acid spray), topical antibiotics, topical antifungals
- Oral antibiotics
- Topical steroids for inflammation
- Intralesional steroids
- For pyogenic granuloma-like lesions: Topical timolol, silver nitrate, cautery

Liu TH, et al. *Medicine (Baltimore)*. 2022;101(42):e31208. Olamiju B, et al. *J Am Acad Dermatol*. 2021;84(3):806-808.

Preventing and Treating Paronychia

Table 1 Interventions for chemotherapy-associated paronychia

Intervention	Dose/Frequency	Evidence	Patient population
Prophylactic doxycycline + daily moisturizer, sunscreen, 1% hydrocortisone	100 mg twice a day	• Lacouture et al. (2010). • 6-week phase II, multicenter, open label, randomized clinical trial • 17% incidence in paronychia (control: 36%)	95 patients receiving panatimumab for metastatic colorectal cancer
2% PVP-I	Two drops twice a day	• Capriotti et al. (2019). • 8-week phase II, multicenter, double-blind, randomized clinical trial • 52.7% grade 2 reduction on CTCAE adapted grading scale (control: 37.9%)	102 patients receiving an EGFR, MEK, or mTOR inhibitor, or taxanes
Minocycline	50 mg twice daily	• Goto et al. (2018). • Retrospective, single center case series • 40% incidence of paronychia (no control)	25 patients receiving afatinib for nonsmall cell lung cancer
Corticosteroid ointment	Unspecified	• Goto et al. (2015). • Retrospective, single center case series • 27% of patients still required medication discontinuation or dose reduction	127 patients receiving EGFR inhibitors, taxanes, and/or capecitabine for breast, lung, colorectal, or pharyngeal cancer
Autologous PRP Therapy	0.3 ml daily	• Kwon et al. (2012). • Case report • Reduction in edema, redness, and granulation after 3 months	68-year-old female on gefitinib for metastatic lung cancer
Adapalene	0.1% applied daily	• Hachisuka et al. (2011). • Case report • Reduction in pain and inflammation	49-year-old male on cetuximab for metastatic colorectal cancer

CTCAE, common terminology criteria for adverse events; EGFR, epidermal growth factor receptor; MEK, mitogen-activated protein kinase; PRP, platelet-rich plasma.

Gupta MK, Lipner SR. *Int J Dermatol*. 2022;61(4):410-415.

Grading Oral Mucositis

Mucositis	Grade 1	Grade 2	Grade 3	Grade 4
A disorder characterized by ulceration or inflammation of the oral mucosa.	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated

National Cancer Institute Cancer Therapy Evaluation Program. Accessed April 28, 2025. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.

Treating Oral Mucositis

Table 1 The main components of the management approach for various oral complications of targeted therapy

Oral complication	Main components of the management approach
For all oral mucosal complications	• Maintain good oral hygiene • Avoid irritating food • Use mild-flavored fluoridated toothpaste • Use topical anesthetics for pain control, if needed • Rinse with saline or sodium bicarbonate solution to improve OH • Maintain hydration
Aphthous-like lesions	• Corticosteroids (topical, intralesional, and/or systemic)
Oral mucositis or stomatitis due to targeted therapy	• Corticosteroids (topical, intralesional, and/or systemic) • Antifungals if oral candidiasis is superimposed (topical or systemic)

OH = oral health.
Villa A, et al. *Support Care Cancer*. 2024;32(8):549.

TABLE 3. Topical Treatments Proposed for the Management of Targeted Therapy Related-Oral Mucosal Toxicities and Oral Ulcerative Mucosal Immune-Related Adverse Events[a]

DRUG	CONCENTRATION	TYPE OF PREPARATION[b]	PROPOSED DAILY DOSE[d]	AVAILABLE COMMERCIALLY IN THE US	COMMENT
Dexamethasone	0.1 mg/mL (0.01%)	Solution	10 mL 3-6 × d	Yes	Available as an elixir or as an alcohol-free solution
Dexamethasone	0.4 mg/mL (0.04%)	Solution	10 mL 3-6 × d	No	
Prednisolone	3 mg/mL (0.3%)	Solution	5 mL 3-6 × d	Yes	
Budesonide	0.3 mg/mL (0.03%)	Solution	10 mL 2-4 × d	No	The low bioavailability provides a broader therapeutic range (ie, a longer rinse poses a smaller risk for systemic adverse events compared with other steroid rinses)
Clobetasol	0.5 mg/mL (0.05%)	Solution	5 mL 3× d	No	
Triamcinolone	10 mg/mL (1%)	Solution	5 mL 3-6 × d	No	
Betamethasone	0.5 mg/mL (0.05%)	Solution	10 mL 3-4 × d	No	
Clobetasol	0.05%	Cream, gel	2× d	Yes	
Triamcinolone	0.1%	Cream, dental paste[c]	2× d	Yes	The dental paste's semisolid consistency may limit its use on friction-bearing oral soft surfaces
Triamcinolone	0.5%	Cream	2× d	Yes	
Halobetasol	0.05%	Cream	2× d	Yes	Limited information about flavor acceptance
Betamethasone	0.05%	Cream, gel, ointment	2× d	Yes	Limited information about flavor acceptance
Betamethasone	0.1%	Cream, ointment	2× d	Yes	Limited information about flavor acceptance
Fluocinonide	0.05%	Gel	2× d	Yes	

[a] Modified from: Elad S, Zinchuk K, Li S, Cutler C, Liesveld J, Treister NS. Economic and practical considerations in the treatment of oral mucosal chronic graft-versus-host disease. *Biol Blood Marrow Transplant*. 2018;24:1748-1753.[87]
[b] Applying a topical steroid over a large oral surface on a regular basis may increase the risk for oral candidiasis. In patients with a history of repeated oral candidiasis, anti-*Candida* prophylaxis may be needed.
[c] The dental paste is the only steroid preparation that is cleared for topical oral use by the US Food and Drug Administration; the remaining commercially available topical agents are prescribed off-label.
[d] Oral solutions are administered topically (swish and spit).

Elad S, et al. *CA Cancer J Clin*. 2022;72(1):57-77.

Key Takeaways

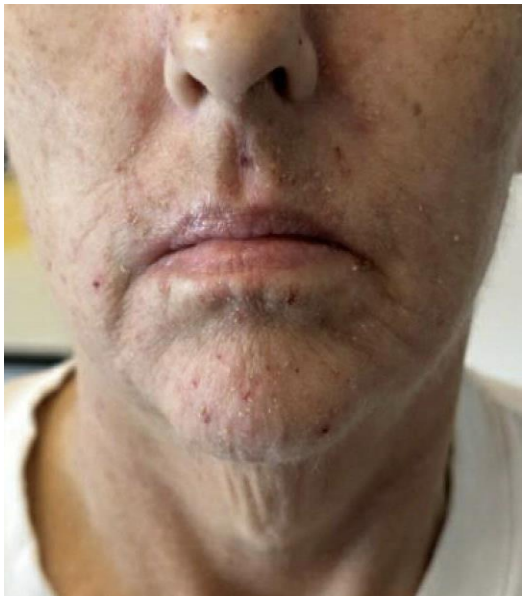
- Common Terminology Criteria for Adverse Events is a useful tool to communicate with oncology partners and guide toxicity management
- Preventive strategies should ideally be implemented prior to initiation of an EGFR inhibitor
- Management of dermatologic toxicities associated with EGFR inhibitors is influenced by patient preferences, patient co-morbidities, oncologist preferences, and grade of toxicity, among other variables

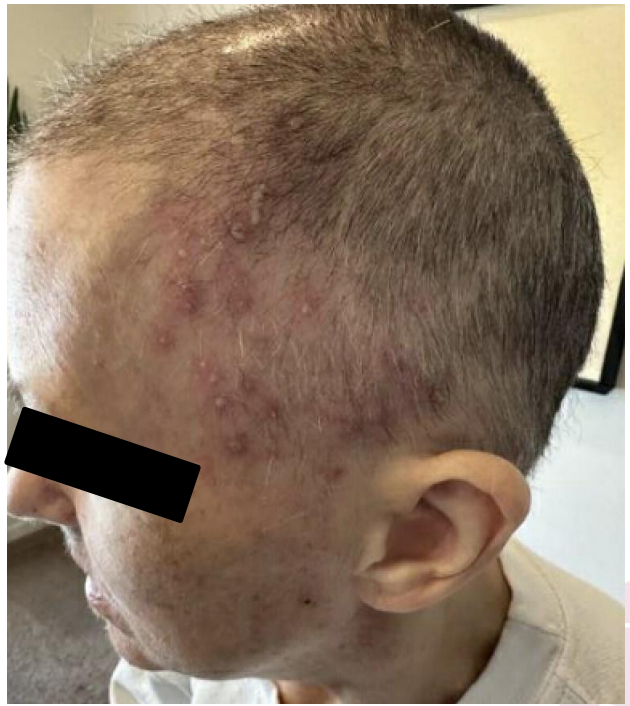
Dermatology Week

Patient Cases

Patient #1

- 55-year-old female with history of metastatic ileocecal adenocarcinoma, on FOLFIRI with recent addition of panitumumab
  - Oncodermatology e-consult for rash





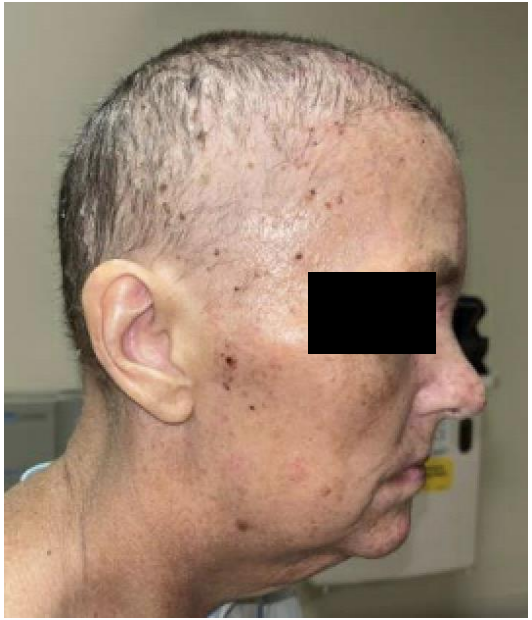
Patient #1

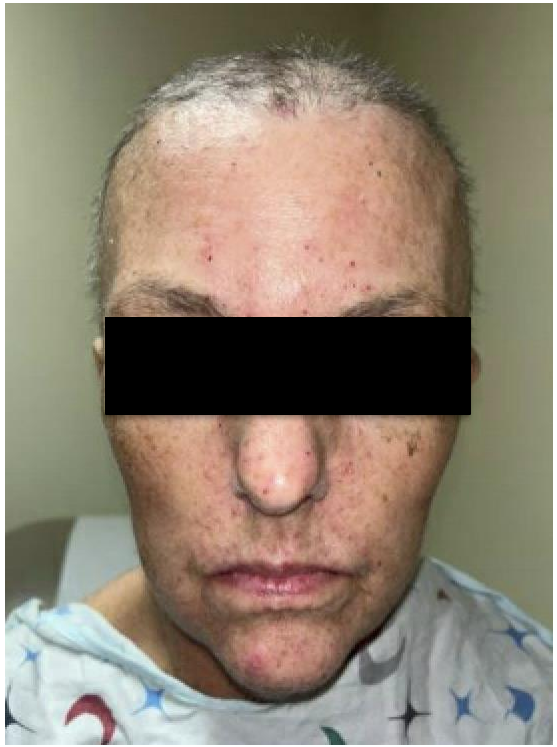
- No preventive therapy

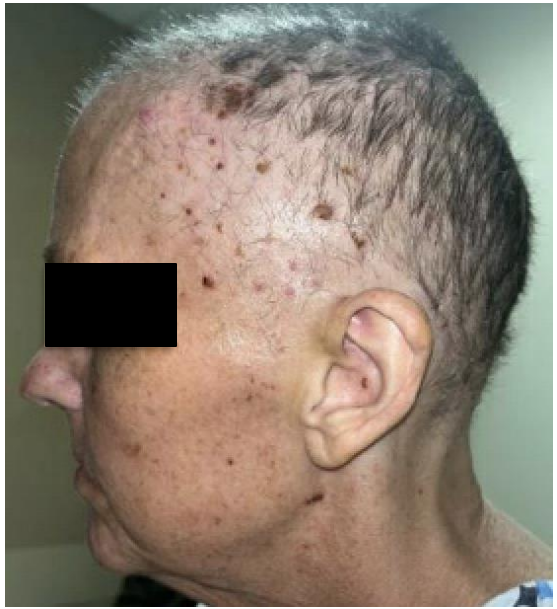
- E-consult recommendations
  - Start clindamycin 1% solution BID OR doxycycline 100mg PO BID
  - Start fluocinonide 0.05% solution BID to scalp
  - Start desonide 0.05% cream BID to face

Patient #1

- Acneiform rash, grade 1
- Clinic visit ~1 week later

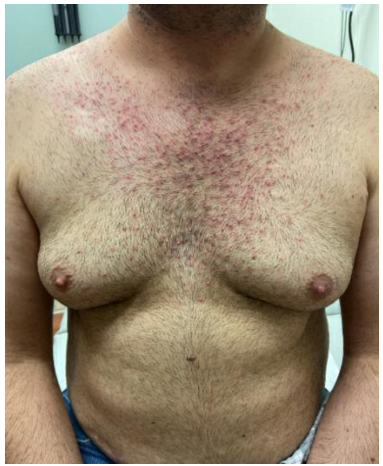


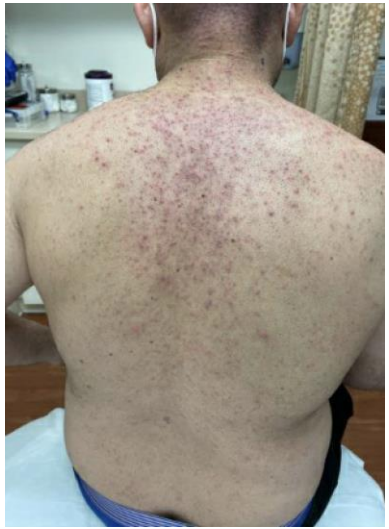


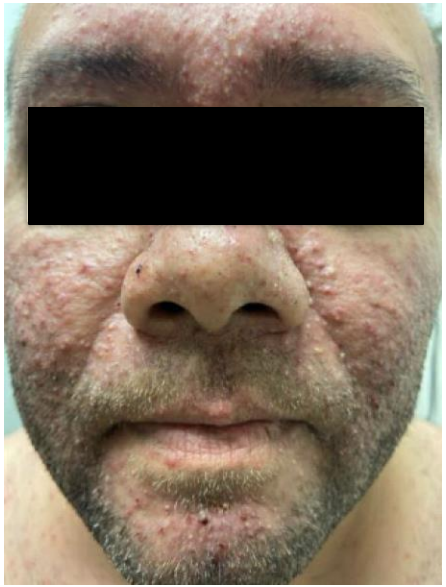


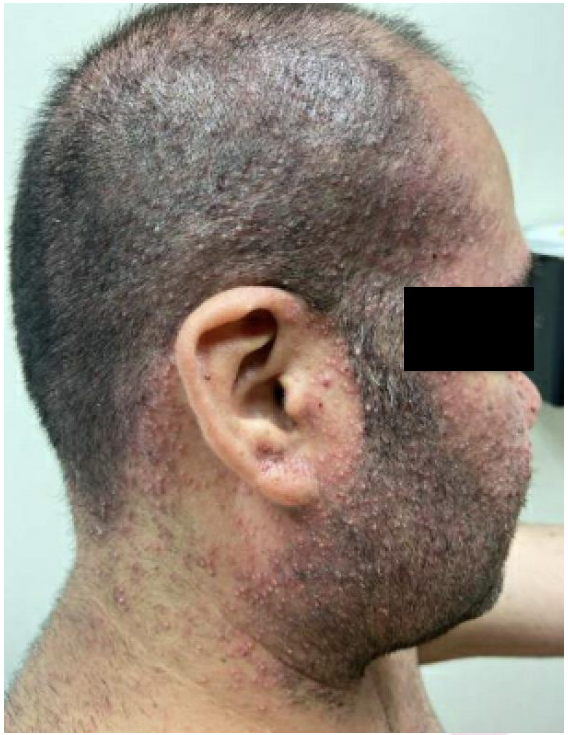
Patient #2

- 39-year-old male with history of metastatic sigmoid adenocarcinoma, on FOLFOX and cetuximab
  - Referred to dermatology for ongoing rashes









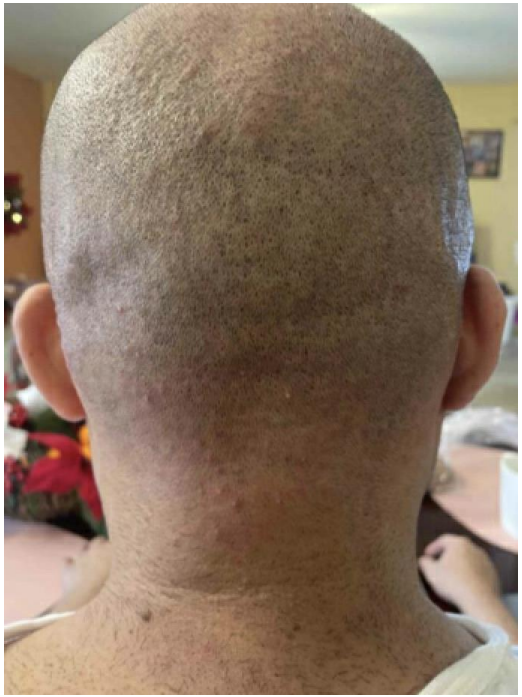
FOLFOX = folinic acid, fluorouracil, oxaliplatin.

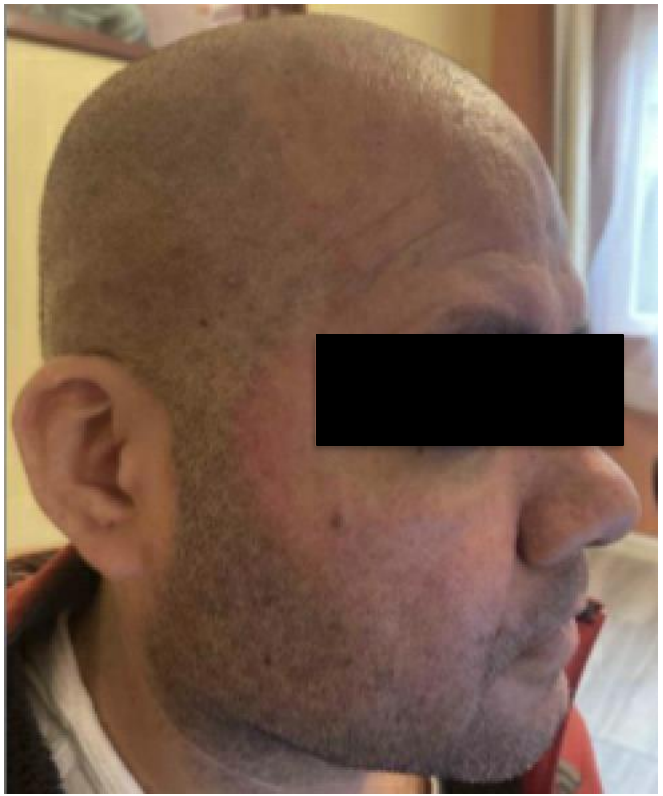
Patient #2

- Acneiform rash, grade 3
- Had tried/failed: clindamycin 1% lotion, hydrocortisone 2.5% cream, triamcinolone 0.1% ointment, doxycycline 100mg BID for ~6-7 months
- Wound culture: Pseudomonas aeruginosa
- Biopsy: Ruptured folliculitis, bacteria, and demodex
  - Treated with levofloxacin and oral ivermectin
- Improved when cetuximab was held but recurred upon restarting

Patient #2

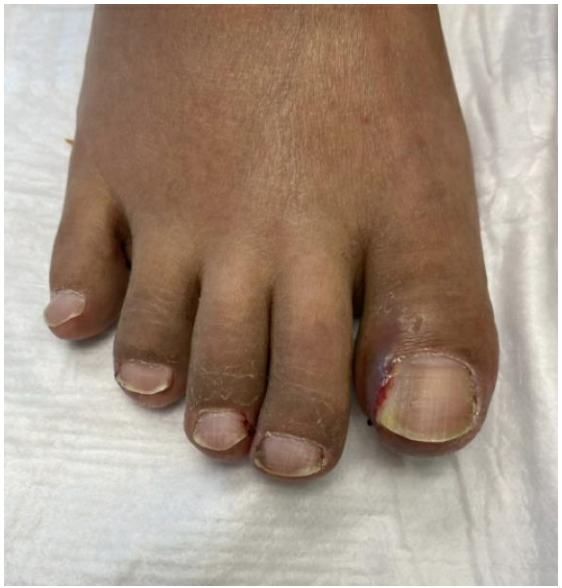
- Prednisone – short course
- Isotretinoin 20mg

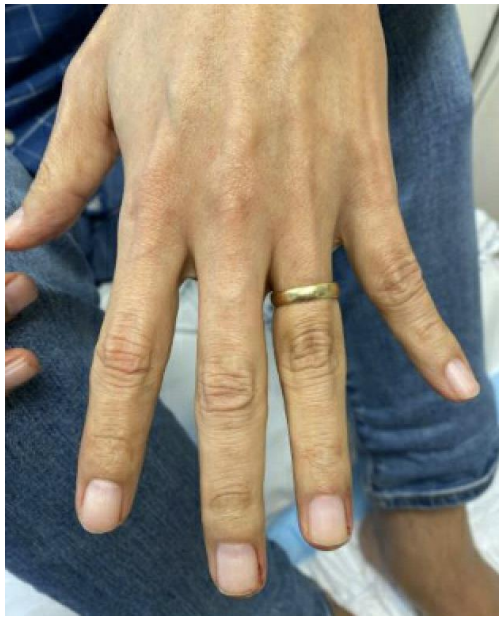




Patient #3

- 55-year-old male with history of EGFR L858R positive stage IVb NSCLC, on lazertinib and amivantamab
  - Presents with painful, bleeding fingernails and toenails

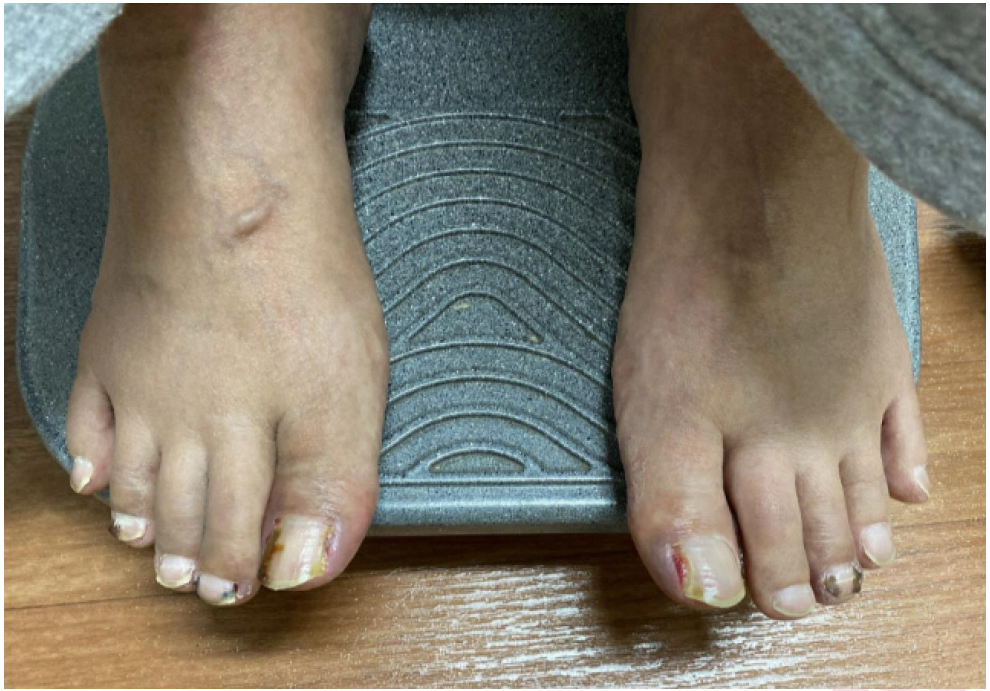




Patient #3

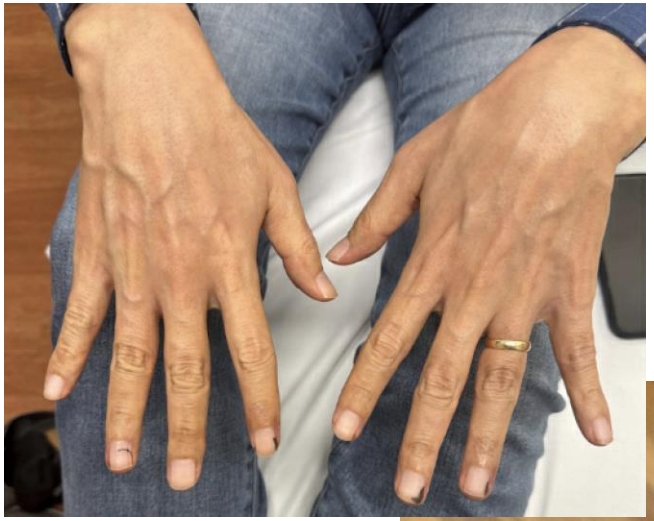
- Paronychia, grade 2
- No preventive therapy

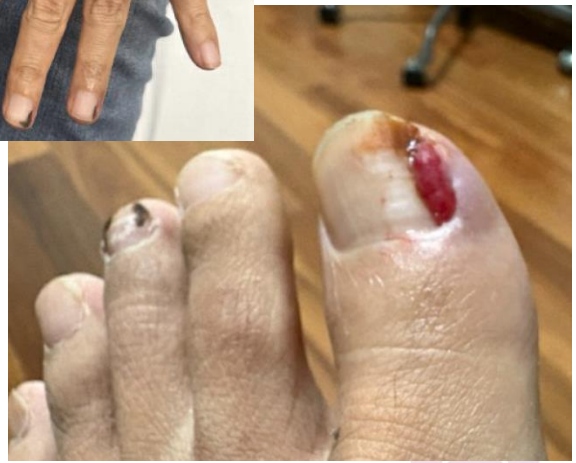
- Initial therapy (patient opted for topicals)
  - Paronychia: Triamcinolone 0.1% ointment BID
  - Pyogenic granuloma-like lesions: Timolol 0.5% gel BID
- Secondary therapy (ongoing bleeding): Silver nitrate
  - Culture



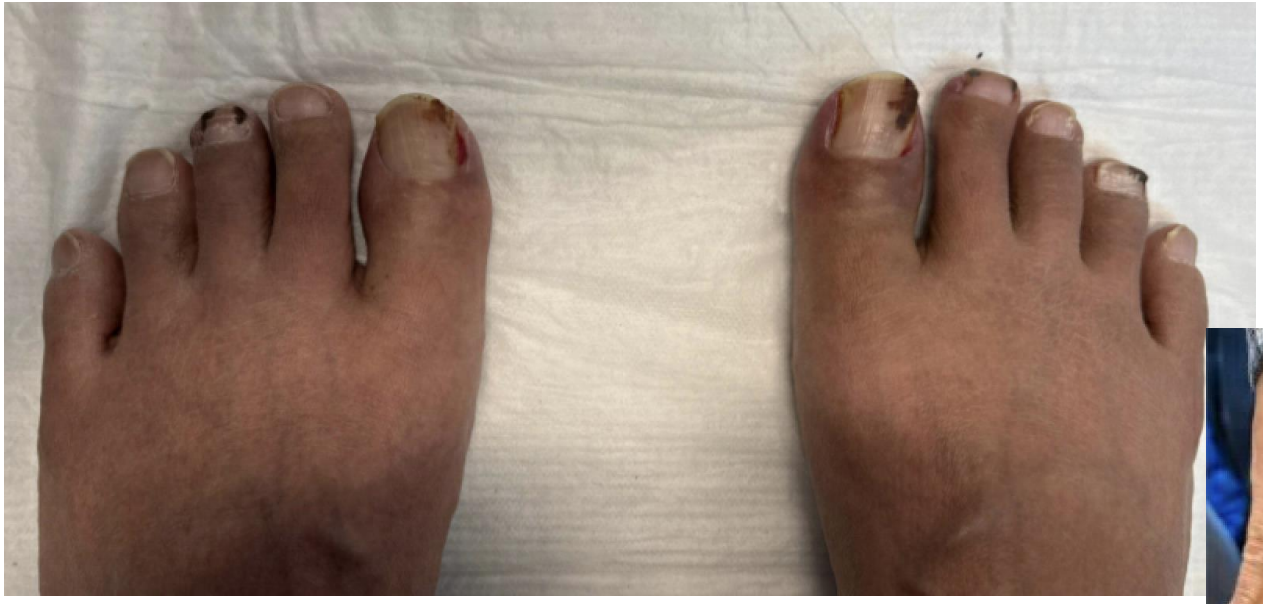
Patient #3

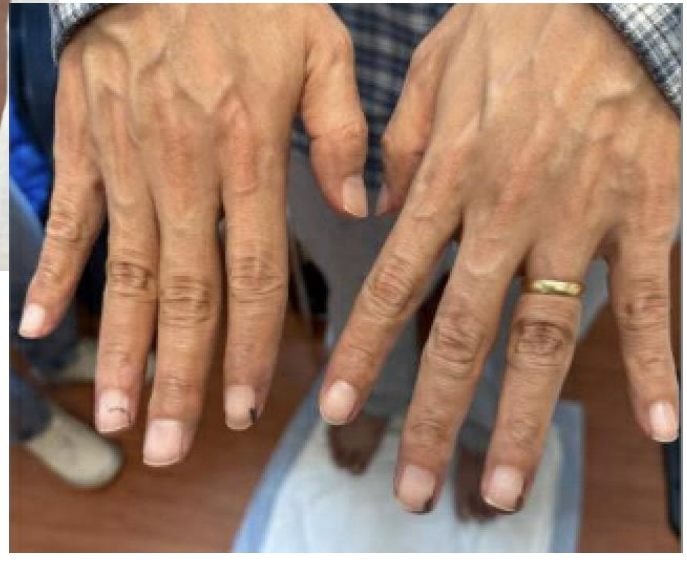
- Improvement after 2 treatments with silver nitrate (especially hands), but L1T continued to worsen
  - Started on doxycycline (could not tolerate due to gastrointestinal side effects)
  - Switched to cephalexin
  - Intralesional steroid injection to nail fold





Patient #3

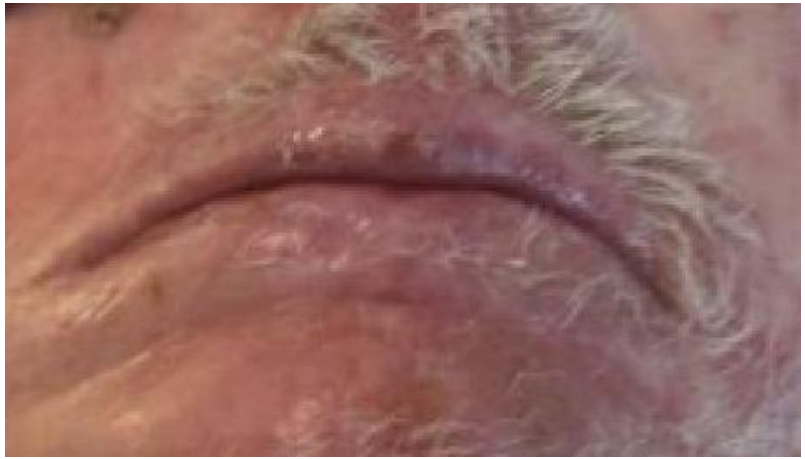




Patient #4

- 80-year-old male w/ CLL and multiple NMSCs, including multiply recurrent SCC with perineural invasion, undergoing treatment with cetuximab and radiation
  - Presents with pain and reduced oral intake

- Oral mucositis, grade 3
  - Cultures: Wound, fungal, HSV
  - Topical steroids
  - Nystatin s/s, clotrimazole troches
  - Consider nutritional deficiency work-up



CLL = chronic lymphocytic leukemia; NMSC = non-melanoma skin cancer; SCC = squamous cell carcinoma; HSV = herpes simplex virus.

Key Takeaways

- E-consults can be an effective way to provide prompt treatment recommendations if patients have not been seen for preventive counseling
- Treatment regimens for acneiform rash, paronychia, and mucositis are highly individualized

Dermatology Week

The Role of Dermatologists in Cancer Care

Impact of Cutaneous Toxicities on Patients

- Cutaneous side effects of EGFR inhibitors have a significant impact on patient quality of life
  - Cause pruritus
  - Cause pain
  - Impact ADLs
  - Alter appearance

- *"The sight of my altered body shocked me. Up until this moment, with the exception of the mouth sores, my illness had been largely invisible. On some level, I was starting to realize that the life I'd had before was shattered, the person I'd been buried. I would never be the same." – Suleika Jaouad*

Jaouad S. *Between Two Kingdoms*. Random House; 2021.

Impact of Cutaneous Toxicities on Treatment

- Patients and oncologists may pause or stop treatment in cases of cutaneous toxicity. This may not always be warranted
- One major goal of oncodermatology is to prevent and treat cutaneous toxicities so patients are able, if willing, to (most comfortably) stay on the recommended therapy to effectively treat their cancer
- Interdisciplinary collaboration is key to the treatment of cancer patients

Dermatologists Add Tremendous Value

- Your expertise in the management of dermatologic conditions transfers naturally to the diagnosis and management of EGFR inhibitor dermatologic side effects
  - Identifying morphology
  - Utilizing BSA
  - Teasing out other entities on differential diagnosis
  - Performing common procedures (cultures, biopsies)
  - Recommending skin-directed therapies
  - Assessing for treatment response

Patient Education Is Key

- Grade of cutaneous toxicity can be mitigated by preventive methods
- Patients need to know about these methods prior to treatment initiation

Key Takeaways

- Ideal management of cutaneous toxicities to EGFR inhibitors involves multidisciplinary collaboration and comprehensive patient education

- Your expertise in dermatology is crucial to help cancer patients effectively manage dermatologic side effects and continue their recommended therapy

Dermatology Week

Thank you

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