DERMATOLOGY WORLD
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Chemotherapy-specific cutaneous reactions

by Parin Pearl Rimtepathip, MD, Janna Vassantachart, MD, and G. Alden Holmes, MD

Cutaneous reaction	Clinical description	Most commonly associated drug	Special notes
Acral reactions			
Neutrophilic eccrine hidradenitis	Erythematous papules and plaques on extremities and trunk	Cytarabine	-Most notable in treatment of AML, Hodgkin lymphoma, and solid tumors
Acral erythema, Hand-foot syndrome (HFS), or Palmar-plantar erythrodysesthesia	Prodrome of pain and dysesthesia followed by symmetric, sharply demarcated erythema of palms and soles (diffuse)	5-FU, Capecitabine > Doxorubicin, Cytarabine	-Grade 1: Mild erythema without dysesthesia -Grade 2: Erythema, pain, and dysesthesia -Grade 3: Blistering, pain, and impaired function -Treatment: High-potency steroids, moisturizers with keratinolytic properties, and possible cessation of therapy
Atypical Hand-foot syndrome (HFS)	Similar findings to HFS but on the DORSAL surface of hands, Achilles tendons, and malleoli	Taxanes	
Hand foot skin reaction (HFSR)	Less severe acral dysestheisa and swelling compared to HFS with prominent hyperkeratotic plaques on frictional areas ONLY	Multi-kinase inhibitors, BRAF inhibitors	-Grade 1: Absence of pain -Grade 2: Mild to moderate pain -Grade 3: Severe pain -Treatment: High-potency steroids, topical retinoids/urea, fluorouracil, and temporary chemotherapy dose reduction → chemotherapy cessation
Sticky skin syndrome	Affects entire skin but exaggerated effect on acral surfaces	Doxorubicin with Ketoconazole	-Most notable in patients with androgen-independent prostate cancer simultaneously receiving ketoconazole and doxorubicin
Truncal reactions			
Acneiform rash	Monomorphic, folliculocentric papulopustular eruption distributed on the face, scalp, chest, and back	EGFR inhibitors, BRAF inhibitors	-Grade 1: Topical antibiotics, antiseptic creams, and low-potency corticosteroids -Grade 2/3: Doxycycline and/or low-dose systemic isotretinoin -Avoid topical benzoyl peroxide and retinoids due to severe irritation
Hypersensitivity reaction	Typically appear after multiple infusions. Flushing/rash → anaphylaxis-like reaction	Platinum agents	-Treatment: slowing infusion densitization → chemotherapy cessation -Allergy testing is not needed prior to chemotherapy initiation
Sclerodermoid changes		Bleomycin, Taxanes	-Has been observed to improve with chemotherapy cessation and course of high-dose steroids
Reactions predominantly noted on extremities			
Xerosis	Fissuring and easy bruising commonly observed on extremities contributing to pain and pruritus	EGFR inhibitors, MEK inhibitors	-Treatment: Avoiding dehydrating skin practices, moisturization, and antihistamines
KP-like reaction	Generalized folliculocentric keratotic, pruritic papules	BRAF inhibitors, Multi-kinase inhibitors	-Treatment: Topical retinoids, urea, alpha-hydroxy acids, or salicylic acid
Lichenoid/DM-like	Overlying joints with PIH	Hydroxyurea	-Most common cause of drug-induced Dermatomyositis (>50%) with latency period of 60 months on average, longer than non-hydroxyurea induced DM
Pseudocellulitis, Erysipeloid		Gemcitabine	-Risk factors include pre-existing lower extremity edema and impaired lymphatic drainage

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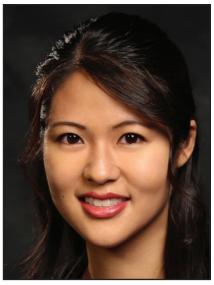

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Cutaneous reaction	Clinical description	Most commonly associated drug	Special notes
Dyschromia			
Hyperpigmentation	Generalized (Addison-like)	Busulfan	-May also have pulmonary fibrosis
	Intertriginous/occlusive areas	Ifosfamide, Thiotepa	
	Serpentine supravenous	Fluorouracil	-Distributed over infused veins
	Linear, flagellate, or whipped-like patches on trunk	Bleomycin > Docetaxel	-Skin and lungs susceptible to bleomycin toxicity due to absence of bleomycin hydrolase -Similar findings with raw shiitake mushroom consumption
	Palmar creases, skin over joints	Bleomycin, Doxorubicin	
	Acral and mucosal	Capecitabine, Tegafur, Cyclophosphamide	
	Site of topical application	Carmustine, Nitrogen mustard	-Increases both melanocytes as well as melanin in keratinocytes
Hypopigmentation	Localized to diffuse effect ranging from hypopigmentation to depigmentation that can affect the skin, nails, hair, and oral mucosa	Tyrosine kinase inhibitors (Imatinib), Multi-kinase inhibitors, Imiquimod, PD-1 Inhibitors	-Caused by an inhibition of c-kit -More commonly observed in patients with darker skin -Course typically reverses with dose reduction or chemotherapy cessation
Yellow skin, white hair	Yellow discoloration intensifies with treatment duration typically sparing mucous membranes and sclera	Multi-kinase inhibitors (specifically Sunitinib)	-Spontaneously resolves with chemotherapy cessation
Other			
Hair effects	Anagen effluvium	Tyrosine kinase inhibitors, EGFR inhibitors, Vismodegib, Multi-kinase inhibitors	-TKI: Dose-dependent response -EGFRI/Vismodegib: Typically reversible hair loss -Treatment: Topical minoxidil shortens hair loss duration, dose reduction/ chemotherapy cessation
	Nonreversible alopecia	Busulfan, Docetaxel	
	Excessive growth (trichomegaly, hypertrichosis of upper lip)	EGFR inhibitors	-Treatment: Eye lash trimming, depilatory creams, laser epilation, interruption of treatment
	Flag sign (alternating bands of dark/light hair)	MTX	
Nail effects	Pitting and onycholysis → nail loss, paronychia, discoloration	EGFR inhibitors, Taxanes	-Treatment: Warm compresses, antibacterial soaks, topical corticosteroids, and/or systemic tetracyclines
	Melanonychia	Doxorubicin >	
	Subungual splinter hemorrhages	Multi-kinase inhibitors	-Spontaneous resolution with therapy cessation
	Exudative hyponychial dermatitis (pain with hemorrhage)	Docetaxel, Capecitabine	-Most notable in treatment of breast cancer -Chemotherapy cessation if severe

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Mucosal effects	Mucositis including aphthae, xerostomia, and geographic tongue. Rarely vulvovaginitis/balanitis	EGFR inhibitors	-Aphthae treatment: Topical steroids, antiseptic washes, and palifermin (recombinant human keratinocyte growth factor). -Typically resolves within 3 weeks
	Mucocutaneous hemorrhage (epistaxis and/or cutaneous hemorrhage)	Anti-angiogenesis agents	-Therapy should be reconsidered in existing hemorrhage
	Oral leukoplakia resembling flat warts	Palifermin	
Reactions Involving Skin Lesions	Inflammation of AKs and DSAP	Fluorouracil, Capecitabine	
	Inflammation of SKs	Cytarabine, Taxanes	
	Eruptive nevi	Multi-kinase inhibitors	-Spontaneous resolution with therapy cessation
	Keratotic lesions including Acantholytic dermatosis, SKs, Verrucous keratosis, Hypertrophic AKs, KAs, and Cutaneous SCC	BRAF inhibitors, Vismodegib	-Regular dermatologic follow-up with excision of malignancies. -Vismodegib is more specifically associated with SCC and KA
Scrotal reactions	Scrotal erythema (with pain)	Sunitinib	
	Scrotal eczema (without pain)	Sorafenib	
Radiation-related reactions	Photosensitivity with hyperpigmentation, telangiectasias, and photosensitive reactions	Fluorouracil, EGFR inhibitors, BRAF Inhibitors, MTX, Hydroxyurea, Docetaxel, Dacarbazine	-Treatment: Sun protective measures -EGFR inhibitors: hyperpigmentation and telangiectasias fade with chemotherapy cessation -BRAF inhibitors: increased susceptibility to UVA
	Sunburn recall and Radiation recall	MTX	
Ulcerative reactions	Extravasation reaction with ulceration or indurating red plaques at chemotherapy administration site	Fluorouracil, Anthracyclines	
	Pyogenic granuloma	EGFR inhibitors, MTX, Multi-kinase inhibitors (specifically Sunitinib), Capecitabine	-EGFRI lesions are found on the great toes
	Lower extremity foot ulcers	Hydroxyurea	-Inhibits DNA synthesis by disrupting the S phase of the cell cycle resulting in basal keratinocyte damage and hindered collagen production -Treatment: Wound care, chemotherapy cessation if severe

References:

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