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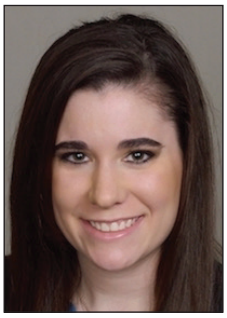
Primary cutaneous T-cell lymphomas

By Georgeanne Cornell, DO, Michael Visconti, DO, and Stephen Olsen, MD

	Clinical features	Course & systemic associations	Histopathology	Immuno-histochemistry	Differential diagnosis	Prognosis	Management
Lymphomatoid papulosis (LyP)	Recurring papules/ nodules, clustering	Regress/recur (frequently) MF/ALCL/ Hodgkin lymphoma in 20%	Five types: A. Large CD30+ lymphocytes with mixed inflammatory cells B. CD4+ epidermotropism C. Mimics pcALCL D. CD8+ epidermotropism E. Angioinvasive	CD30+ phenotypes vary Clonal T-cell gene rearrangement in 50%	PLEVA: Presence of CD30+ blast cells MF with large cell transformation: History of preceding patches/plaques ALCL: No history of recurring lesions	Excellent	Limited or asymptomatic: No therapy/topical steroids Symptomatic, progressive, widespread: Phototherapy and/or low-dose methotrexate (MTX)
Mycosis Fungoides (MF) Variants: folliculotropic MF, pagetoid reticulosis, granulomatous slack skin	Patch/plaque stage: scaly red-brown patches and plaques in non-sun-exposed distribution Tumor stage: nodules with frequent ulceration in a background of patches/ plaques	Benign course in limited disease	Patch/plaque stage: • Atypical lymphocytes with cerebriform, hyperchromatic nuclei • Epidermotropism • Pautrier's microabscesses (clusters of atypical lymphocytes in epidermis) • Linear arrays along basal layer • Superficial banded infiltrate with variable admixed reactive lymphocytes Tumor stage: Loss of epidermotropism	CD3+/CD4+/ CD8-/CD7-	ATLL: Histologically identical Sézary syndrome: Peripheral blood involvement Pagetoid reticulosis: CD8+ phenotype More extensive epidermotropism LyP: Self-healing; Type B histologically indistinguishable Type D: CD8+, CD30+phenotype AECTCL: No cerebriform nuclei CD8+ phenotype		Patch/plaque stage: • Topical/intralesional steroids • Phototherapy (nbUVB, PUVA) • Topical chemotherapy • Topical radiotherapy Erythrodermic: Extracorporeal photopheresis Tumor stage: Systemic multiagent chemotherapy
Primary cutaneous anaplastic large cell lymphoma (pcALCL)	Solitary> multiple Grouping of firm nodules	Unlike LyP, lesions do not rapidly come and go	Sheets of large, atypical CD30+ lymphocytes	CD30+ CD4+/EMA- Lack ALK translocations (vs. systemic ALCL)	Systemic ALCL: EMA+ (negative in pcALCL) LyP: Recurring lesions MF with large cell transformation: No history of preceding patches/ plaques		Solitary or localized disease: Surgical excision, radiotherapy Limited or asymptomatic disease: Radiotherapy, low-dose MTX, brentuximab
Primary cutaneous CD4+ small/ medium T-cell lymphoproliferative disorder (PCSM-TCLPD)	Solitary plaque or nodule	May have aggressive course (need to rule out primary cutaneous peripheral T-cell lymphoma, not otherwise specified)	Dense nodular to diffuse small/ medium lymphocytic infiltrate Minimal to no epidermotropism	CD4+/CD8-/ CD30- (MF-like)	Marginal zone B-cell lymphoma: B-cell immunophenotype		Localized disease: Excision Topical/intralesional steroids Radiotherapy
Primary cutaneous acral CD8+ T-cell lymphoma (ATCL)	Solitary papule/ nodule EAR = most common site	Benign course	• Dense nodular to diffuse infiltrate • Grenz zone • No mitoses, necrosis, ulceration, or angiocentricity	CD3+/CD8+/ CD4-	Other cytotoxic CD8+ cutaneous T-cell lymphomas		



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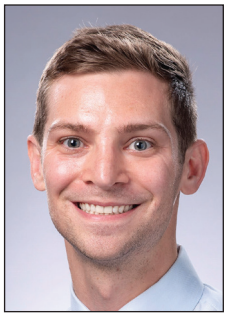

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	Clinical features	Course & systemic associations	Histopathology	Immuno-histochemistry	Differential diagnosis	Prognosis	Management	
Subcutaneous panniculitis like T-cell lymphoma (SPTCL)	Subcutaneous nodules or deep plaques	Hemophagocytic syndrome (HPS) = worse prognosis	Lobular panniculitis of "fat rimming" neoplastic lymphocytes "Bean bag cells" (cytophagocytosis)	CD4-/CD8+/ CD56-/TIA-1+/ granzyme/ perforin+/ βF1+ α/β phenotype	Lupus profundus: Plasma cells, interface change, nodular lymphoid aggregates	Good	w/o HPS: Oral corticosteroids w/ or w/o immunosuppressant (cyclosporine A or low-dose MTX) w/ HPS: High-dose corticosteroids w/ cyclosporine A High-dose chemotherapy with HSCT	
Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma (PC-AECTCL)	Eruptive, ulcerated tumors	Visceral involvement	Malignant infiltrate with epidermotropism and angiodestruction	CD4-/CD8+/ CD56-/TIA-1+/ granzyme+/ perforin+	MF, pagetoid reticulosis, LyP (D): Histologically indistinguishable (all CD8+)	Poor	No well-established therapy	Radiotherapy Multiagent chemotherapy w/ or w/o HSCT
Primary cutaneous γ/δ T-cell lymphoma (PCGD-TCL)	Multiple eroded nodules and plaques	HPS Visceral involvement	• Lichenoid interface • Epidermotropism • Angiodestruction • +/- "fat rimming"	CD4-/CD8- ("double negative")/ CD56+/ βF1-/ EBV- Expression of γ/δ receptor	SPTCL: Does NOT have lichenoid interface Lupus profundus: γ/δ –			
Adult T-cell leukemia/lymphoma (ATLL)	Small, confluent, violaceous papules, or firm/brown nodules	Hypercalcemia HTLV-1+	Floret or clover leaf malignant T-cells	CD4+/CD8-/ CD25+/PD-1+	MF: Lacks floret/ clover leaf cells			Antivirals Multiagent chemotherapy w/ or w/o HSCT
Extranodal NK/T cell lymphoma (ENKTL)	Ulcerating plaques or tumors; May extend into the nose, sinuses, palate	HPS EBV+	• Dense infiltrate with extensive necrosis • Fat rimming • Angiocentricity and/or angiodestruction	CD2+/CD3ε+/ CD56+/TIA-1+/ granzyme+/ perforin+/ EBV+	-			Localized: Radiotherapy Systemic: Chemotherapy
Sézary syndrome	Erythroderma, lymphadenopathy, Sézary cells	Circulating CD4+ neoplastic cells ≥1000 cells/μl	Nonspecific or resemble MF	CD3+/CD4+/ CD8-/PD-1+	Other causes of erythroderma: Will not have identical T-cell clone in the skin and blood		MTX, bexarotene, interferon Mogalizumab (if failed at least one systemic) Extracoporal photopheresis	

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