Necrotic papulonodules on the legs

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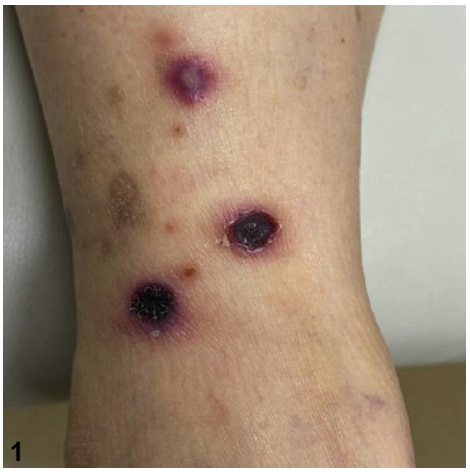
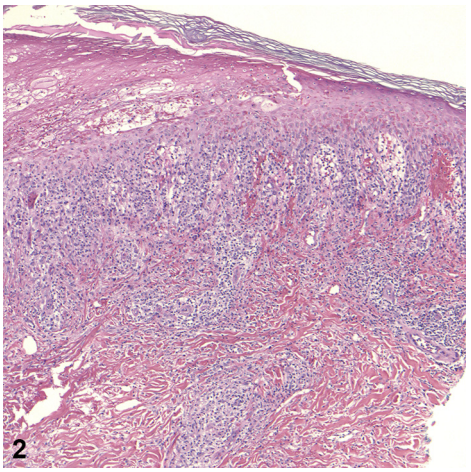
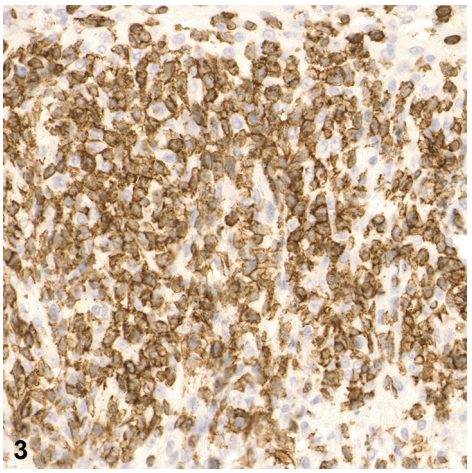
Key words: cutaneous T-cell lymphoma; lymphomatoid papulosis type D; primary cutaneous CD8$^+$ aggressive epidermotropic cytotoxic T-cell lymphoma.







A woman in her 60s presented with 2 years of recurrent lesions on her lower extremities. Each lesion began as a mildly pruritic papule, which progressed to violaceous nodules, ulcerated with central eschar and healing spontaneously over approximately 3 months. Physical examination revealed 3 violaceous papulonodules on her distal right side of her lower extremity; 2 with black eschar formation, in addition to adjacent crusted papules and hyperpigmented macules (Fig 1). A punch biopsy (Fig 2) revealed a moderately dense infiltrate with

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Funding sources: Dr. Vesely and Dr. Damsky are supported by Dermatology Foundation.

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JAAD Case Reports 2021;11:10-2.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.03.012

numerous large, epidermotropic $CD8^+$ (Fig 3), TIA-1^+, and weakly CD30 positive lymphocytes with large pleomorphic nuclei and no evidence of angioinvasion.

Question 1: What is the most likely diagnosis?

A. Necrotic arthropod bites

B. Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma

C. Ecthyma

D. Lymphomatoid papulosis type D

E. Pityriasis lichenoides et varioliformis acuta

Answers:

A. Necrotic arthropod bites — Incorrect. Arthropod reactions typically present histologically with a wedge-shaped dermal infiltrate with eosinophils. Lymphocyte atypia and epidermotropism would not be expected. Additionally, our patient had no intense pruritus or history of exposure to arthropods.

B. Primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma ($CD8^+$ AECTCL) — Incorrect. On histology, $CD8^+$ AECTCL may appear similar to our patient's biopsy, with an epidermotropic $CD8^+$ lymphocytic infiltrate and positive staining with cytotoxic marker TIA-1. However, $CD8^+$ AECTCL is a very aggressive lymphoma, in which the lesions progress rapidly and do not spontaneously resolve.

C. Ecthyma — Incorrect. Ecthyma is due to streptococcal or staphylococcal infection and can ulcerate but typically presents as a single lesion. It usually affects children, elderly patients, immunocompromised patients, or patients with a history of skin trauma. Our patient's 2-year history of self-resolving lesions is more consistent with a chronic process.

D. Lymphomatoid papulosis type D — Correct. Lymphomatoid papulosis (LyP) is a chronic lymphoproliferative disorder presenting with self-resolving papules and nodules. Although LyP type D appears similar on histology to $CD8^+$ AECTCL, LyP type D is distinguished by its benign clinical course. Lymphomatoid papulosis type D is differentiated from other subtypes of LyP by an epidermotropic $CD8^+$ lymphocytic infiltrate.[1]

E. Pityriasis lichenoides et varioliformis acuta — Incorrect. Pityriasis lichenoides et varioliformis acuta, the acute form of pityriasis lichenoides, can present with papules that self-resolve and display a $CD8^+$ lymphocytic infiltrate. However, histology would show keratinocyte necrosis, erythrocyte extravasation, and an absence of lymphocyte atypia.

Question 2: Which of the following is the best treatment option for this patient's condition?

A. Multi-agent chemotherapy

B. Extracorporeal photopheresis

C. Low-dose methotrexate

D. Permethrin

E. Observation

Answers:

A. Multi-agent chemotherapy — Incorrect. Because LyP appears histologically similar to cutaneous lymphoma, patients may be inappropriately prescribed multi-agent chemotherapy. Although this can lead to resolution of lesions, lesions may recur both during and after treatment. Thus, because it has potential for significant side effects and complications, multi-agent chemotherapy should be avoided.[2]

B. Extracorporeal photopheresis — Incorrect. Extracorporeal photopheresis can treat cutaneous T-cell lymphoma but is not used for LyP.

C. Low-dose methotrexate — Correct. Treatment of LyP with methotrexate can help reduce the severity of lesions and prevent new eruptions. However, treatment does not alter the course of the disease, and if treatment is discontinued, LyP lesions may reappear. Additional treatment options include topical ultra-potent corticosteroids, psoralen-UVA light therapy, and brentuximab vedotin in patients with severe or refractory disease.[2,3] Our patient was initially treated with 5 mg methotrexate by mouth twice weekly (Monday and Thursday) with folate supplementation on days when she was not taking methotrexate.

D. Permethrin — Incorrect. Permethrin can treat scabies; however, our patient's case presentation is consistent with a diagnosis of LyP.

E. Observation — Incorrect. Because treatment for LyP is not curative, patients with nonscarring, mild disease may forgo treatment.[2] However, our patient has necrotic lesions that take months to heal and scar. In this case, low-dose methotrexate was started to facilitate healing and reduce the severity of lesions.

Question 3: What condition is known to be associated with this patient's diagnosis?

A. Uterine fibroids

B. Lymphoma

C. Colon polyps

D. Optic glioma

E. Multiple myeloma

Answers:

A. Uterine fibroids — Incorrect. Leiomyomas in the skin, uterine leiomyomas, and renal cell carcinoma are seen in Reed syndrome. Skin findings include firm papules that may be sensitive or painful.

B. Lymphoma — Correct. Lymphomatoid papulosis is associated with an increased risk of developing malignant lymphomas, underscoring the need for continued surveillance. Patients should be monitored once or twice yearly for clinical history and a physical examination focused on the skin, lymph nodes, liver, and spleen. The most commonly associated lymphomas are mycosis fungoides, systemic anaplastic large-cell lymphoma, and Hodgkin lymphoma. Of note, a recent retrospective cohort study found that male gender and having LyP type B or C were significant risk factors for developing a secondary lymphoma, whereas patients with histologic subtype A or D were less likely to develop secondary lymphoma.[4]

C. Colon polyps — Incorrect. In Cowden syndrome, hamartomas may present as gastrointestinal tract polyps. Patients have increased risk of breast, thyroid, colon, renal, and endometrial cancer. Mucocutaneous findings include facial papules, palmoplantar keratoses, and oral mucosal papillomatosis.

D. Optic glioma — Incorrect. Optic glioma is associated with neurofibromatosis type 1. Skin findings include cutaneous, subcutaneous, and plexiform neurofibromas, as well as café au lait macules and axillary freckling.

E. Multiple myeloma — Incorrect. Plasma cell dyscrasias are associated with primary systemic amyloidosis, which often presents with multiorgan involvement. Cutaneous findings may include waxy nodules and plaques with biopsy revealing amyloid deposition in the dermis and subcutis.[5]

Abbreviations used:

$CD8^+$ AECTCL: primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphoma
LyP: lymphomatoid papulosis

Conflicts of interest

None declared.

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