Vesiculobullous Lyme disease: A case series

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INTRODUCTION

Early-stage Lyme-associated erythema migrans most commonly manifests as a targetoid patch. However, several erythema migrans variants have been reported, which may result in misidentification as well as delayed diagnosis and treatment. This case series demonstrates a rare blistering form of erythema migrans known as bullous erythema migrans.[1]

Abbreviation used:
IgM: immunoglobulin M

CASE SERIES

Case 1

A 54-year-old woman presented to the emergency department of a rural, academic hospital in New Hampshire, with a worsening rash on the lateral aspect of her left ankle. She reported a sudden onset of localized pain and stinging while walking through a corn maze 11 days previously. An enlarging red lesion appeared soon after and became progressively darker (Fig 1). She developed an intermittent, low-grade fever on the fourth day, and the lesion became progressively more painful, swollen, and purpuric.

On examination, she was noted to have a 10-cm edematous purpuric plaque with vesiculobullous changes centrally. Diagnoses of bullous Lyme disease, Sweet syndrome, and herpes zoster were considered. A biopsy of a flat portion of the lesion close to the periphery showed hyperkeratosis and acanthosis with prominent overlying papillary edema along with a histiocyte-rich inflammatory infiltrate. Myeloperoxidase staining was negative. Grocott-Gomori methenamine silver stain and Gram stains were negative for microorganisms (Fig 2). Her symptoms improved rapidly with twice-daily treatment with doxycycline 100 mg for 21 days. Positive immunoglobulin M (IgM) serologies via 2-tiered serologic testing at 3 weeks confirmed a Lyme disease diagnosis. Lyme disease antibody serology 1 year previously was negative.

Case 2

A 49-year-old woman with no known history of tick bite presented to the emergency department 4 days after the appearance of an enlarging, darkening lesion on the posterior aspect of her ankle. On examination, she was noted to have a 9-cm vesiculobullous plaque with erythema (Fig 3). She reported no fever, but slight fatigue. A biopsy of the lesion was not taken. She was treated with a 21-day course of doxycycline and rapidly improved.

Three weeks later, a positive IgM Lyme result via 2-tiered serologic testing confirmed an atypical Lyme disease diagnosis. She did not have previous Lyme disease serology data for comparison.

Case 3

A 65-year-old woman presented to the emergency department with a 3-day history of a red, swollen, painful plaque on the left side of the flank (Fig 4).

Central dusky papulovesicles developed within a day after the appearance of the plaque. She reported a low-grade fever and malaise and denied a known history of tick bite. Treatment for herpes zoster with valacyclovir and for Lyme disease with doxycycline

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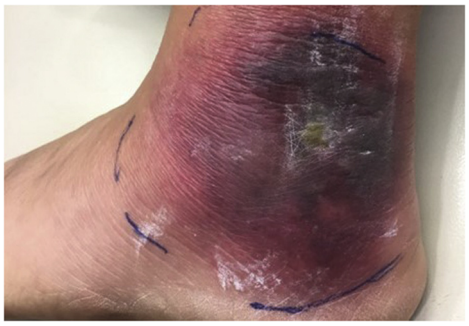

Fig 1. Bright red, annular, edematous, vesicular plaque on the lateral aspect of the left malleolus.

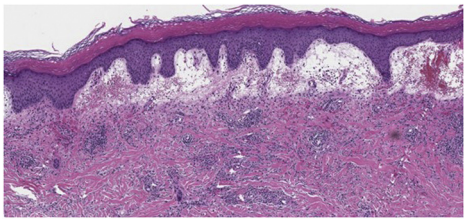

Fig 2. Histopathology demonstrated a dense interstitial and perivascular lymphohistiocytic inflammatory infiltrate within the dermis, extending around adnexal structures and into the deeper aspect of the dermis (hematoxylin-eosin stain; original magnification: ×10).

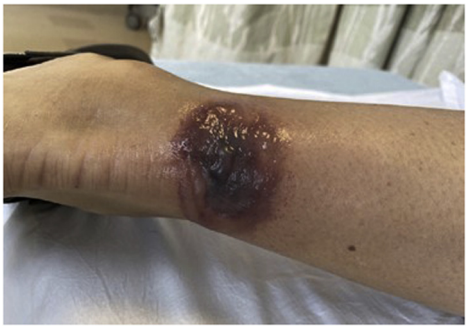

Fig 3. Vesiculobullous plaque on the posterior aspect of the right leg with surrounding erythema.

was initiated. Direct fluorescent antibody staining and viral culture were negative for varicella-zoster virus and herpes simplex virus. Polymerase chain reaction was negative for herpes simplex virus. Lyme serology after 21 days was positive for IgM via 2-tiered serologic testing, confirming a Lyme disease diagnosis. A Lyme disease antibody test 7 years previously had been negative.

DISCUSSION

We report 3 cases of otherwise healthy women with no known history of tick bites who presented with vesiculobullous lesions caused by Lyme disease. All 3 cases were considered likely infectious processes and resolved with empiric doxycycline. Follow-up serologies were positive for IgM at 3 weeks, supporting a Lyme disease diagnosis.

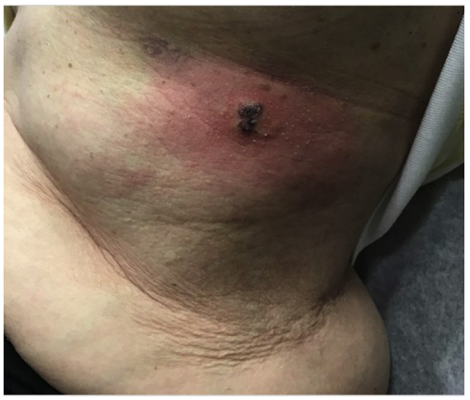

Fig 4. Rash displaying a bright red patch with central dusky papulovesicles.

Lyme disease is an increasingly common diagnosis throughout regions of the United States and Europe, with an estimated 300,000 cases diagnosed annually.[2] The initial stage of cutaneous Lyme is most often characterized by the erythema-migrans patch, which appears within a month of the tick bite. A quarter of these lesions display the characteristic bull's-eye appearance.[3] However, recent publications have also reported urticarial, linear, granulomatous, and bullous erythema migrans presentations.[1,4,5]

This case series demonstrates the rare vesicobullous erythema migrans variant. All 3 cases exhibited rapidly developing bullous lesions in the presence of systemic symptoms, ranging from fatigue and malaise to fever. Histologic findings in the first case displayed relatively nonspecific inflammatory findings; the histologic features of Lyme disease are varied and may be nonspecific.[1,4,5] As such, these lesions were originally considered to represent Sweet syndrome, herpes simplex virus infection, varicella-zoster virus infection, or a spider bite, in addition to atypical Lyme disease. One of the challenges in confirming the diagnosis of Lyme disease is the delayed positivity of Lyme-specific antibodies and the lack of specific findings on histopathology. Histopathologic features of Lyme disease often include a superficial and deep perivascular and interstitial infiltrate consisting of lymphocytes and plasma cells, and may include eosinophils and neutrophils; however, a variety of histopathologic patterns have been described and often suggest a broad histopathologic differential diagnosis.[6,7] The testing options for early-stage Lyme disease (<30 days since symptom onset) include

Table I. Ninety-five percent confidence intervals of sensitivity and specificities of common Lyme disease serology tests for stage 1 disease (adapted from Waddell et al).[8]

Testing method	Sensitivity (95% CI)	Specificity (95% CI)
PCR (blood sample)	33.8%-62.0%	NA
ELISA—pepC10	32.7%-44.0%	97.7%-99.5%
ELISA—VlsE1	47%-77%	98%-99%
ELISA—WCS	60.9%-78.8%	59.5%-83.5%
Western blot (Marblot/GenBio)	42.7%-76.0%	91.9%-98.7%

CI, Confidence intervals; *ELISA*, enzyme-linked immunosorbent assay; *NA*, not applicable; *PCR*, polymerase chain reaction; *WCS*, whole-cell sonicate.

polymerase chain reaction, enzyme-linked immunosorbent assay (ELISA), and Western blot (Table I).[8] The Center for Disease Control and Prevention currently recommends a 2-tier approach, involving an initial serum enzyme immunoassay, followed by IgG and IgM Western blotting or a secondary enzyme immunoassay. All 3 patients underwent 2-tiered serologic testing, using a VlsE1/pepC10 ELISA followed by a whole-cell sonicate ELISA (Zeus Scientific).

This case series highlights a rare variant of cutaneous Lyme disease. Clinicians in Lyme-endemic areas should be aware that Lyme disease might exhibit a broad range of clinical and histologic findings, including bullous presentations. Thus, a low threshold for considering Lyme disease in the differential diagnosis of bullous lesions is warranted in endemic areas with empiric treatment and follow-up serologies for disease confirmation.

Conflicts of interest

None disclosed.

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