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A case of rapidly progressive Lyme disease masquerading as cellulitis

Julian Campillo Luna[1], Lauren Hartz[2], and Christine Ngaruiya[3]

[1]University of Michigan Michigan Medicine
[2]Yale University
[3]Stanford University School of Medicine

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Authors and affiliations: Julian Campillo Luna, MD, MHS, Department of Emergency Medicine, University of Michigan, Ann Arbor, Michigan, USA; Lauren Hartz, Yale University, New Haven, Connecticut, USA; Christine Ngaruiya, MD, MsC, DTM&H, Department of Emergency Medicine, Stanford University School of Medicine, Palo Alto, California, USA.

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Correspondence to:

Dr. Julian Campillo Luna

1500 E Medical Center Dr.

B1-380 Taubman Center, SPC 5305 Ann Arbor, MI 48109

United States

Phone: (650) 723-5111

Email: jucampil@med.umich.edu

ORCID: https://orcid.org/0000-0001-8509-0700

Email Addresses of Authors:

Julian Campillo Luna: jucampil@med.umich.edu

Lauren Hartz: lauren.j.hartz@yale.edu

Christine Ngaruiya: cngaruiy@stanford.edu

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INTRODUCTION

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Lyme disease is a disease transmitted by the *Ixodes scapularis* tick, the majority of cases occur in the northeast region of the United States.[1] There were over 250,000 cases between 2008-2019[2]. The disease is caused by the spirochaete*Borrelia burgdorferi* and other species of the same genus.[3] Approximately 75% of cases of early Lyme disease are diagnosed at the emergency department or urgent care by identifying the characteristic skin findings of early Lyme disease, which necessitates no further serological testing.[3]

The characteristic rash of Lyme is erythema migrans (EM), a "bullseye" shaped area of redness with central clearing.[3]However, the appearance of the rash can differ, including the appearance of a necrotic center that mimics envenomation by the American brown recluse spider, *Loxosceles reclusa* .[4] In this report, we describe an instance of Lyme disease masquerading as cellulitis which resulted in a diagnostic delay and complications that might have been prevented with earlier diagnosis. This is of particular importance during the COVID-19 pandemic, during which febrile illnesses can often lead to misdiagnoses.[5] Verbal consent was obtained from the patient in preparation of this case report.

CASE HISTORY: Background

This patient was an otherwise healthy 36-year-old male from Connecticut who began experiencing fevers and body aches. He reported that a week prior to the case visit he was bitten by an insect or spider on the back of his left knee, which did not bother him until two days later. He denied any hiking in the area, though had traveled to Massachusetts recently.

On day two of illness, he experienced increasing pain, warmth and swelling to the area. That day, he went to an urgent care clinic, where he was prescribed a course of 500mg of cephalexin 4 times a day for 5 days for presumed cellulitis. He began treatment but noticed no improvement. The next day he developed a fever of 103F, and began having body aches as well as nausea, vomiting, chills, and headaches. He ascribed his symptoms to a viral upper respiratory infection (URI), noting that his son was also sick and not vaccinated for COVID-19. On day two after presumed infection, his physical exam was only notable for an area of erythema to the left popliteal fossa, with warmth and induration, and consistent with cellulitis (Figure 1).

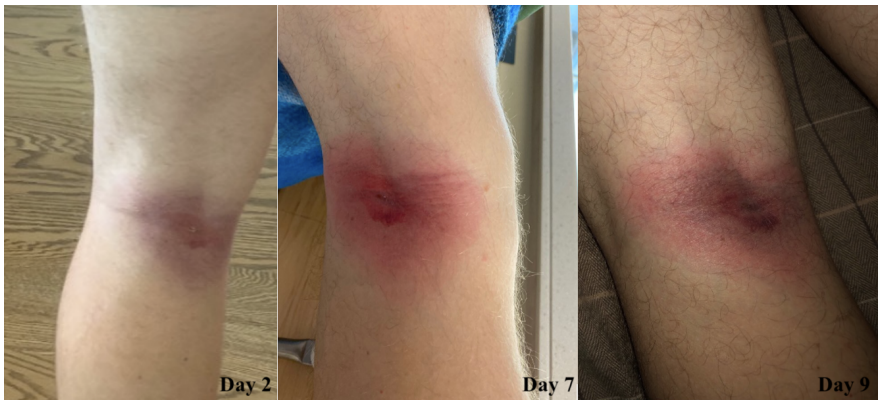

Figure 1: Patient's left popliteal fossa on days 2, 7, and 9 (from left to right) after presumed infection.

CASE HISTORY: First Presentation

He presented to our ED on day 7 of illness with fever, malaise, body aches, and pain and swelling behind the left popliteal fossa. His heart rate was 96, blood pressure of 135/76, temperature of 99.5F and an O2 saturation of 96% on room air. The differential at the visit included cellulitis, COVID-19, tick-borne illnesses, and viral respiratory infection. A COVID-19 PCR test was ordered and resulted negative during his ED stay. The rash had evolved into an erythematous rash with a necrotic-appearing center and crust (Figure 1), consistent with a potential variant of EM.[6]

METHODS: First Presentation

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Given a high index of suspicion for potential tick-borne illness based on the history of possible bite, the rash appearance and worsening symptoms despite appropriate treatment for cellulitis, we obtained a complete blood count, basic metabolic panel, liver function testing, and a tickborne panel (Table 1). All testing was done in-house through Yale New Haven Hospital's Department of Laboratory Medicine. He was found to be thrombocytopenic with a platelet count of 117x1000/uL (Table 1). He also had mild elevations of his liver enzymes (AST of 58U/L and ALT of 74U/L) (Table 1). The Babesia smear was negative during the course of stay (Table 1).

Table 1: Laboratory values obtained during the patient's two admissions to the emergency department.

Laboratory tests	Day 7	Day 9
Sodium (mmol/L)	136	140
Potassium (mmol/L)	4.1	4.3
Chloride (mmol/L)	102	104
CO2 (mmol/L)	23	25
Anion Gap	11	11
Glucose (mg/dL)	147	105
BUN (mg/dL)	16	18
Creatinine (mg/dL)	0.98	1.02
WBC (x1000/μL)	4.9	4.9
RBC (M/μL)	5	4.7
Hemoglobin (g/dL)	15.1	14.1
Hematocrit (%)	43.2	40.9
Platelets (x1000/μL)	117	145
MPV (fL)	10.7	10.5
Neutrophils (%)	81.7	57.3
Lymphocytes (%)	11.2	31.8
Monocytes (%)	6.3	9.3
Eosinophils (%)	0.2	1.2
Basophils (%)	0.2	0.2
Bilirubin (mg/dL)	0.5	0.3
Direct Bilirubin (mg/dL)	<0.2	<0.2
Alk phos (U/L)	58	67
ALT (U/L)	74	78
AST (U/L)	58	54
Lyme Ab by ELISA (LI)	1.47	3.7
Lyme IgM by western blot	Negative	Positive
Lyme IgG by western blot	Negative	Negative
Borrelia Ab, IgG and IgM by western blot	Negative	Negative
Babesia smear	Negative	Negative
Ehrlichia PCR	Not detected	Not detected
Anaplasma PCR	Not detected	Not detected
Anaplasma and Ehrlichia smear	Negative	Negative
CSF protein	Not Done	26.7
CSF glucose	Not Done	65
CSF Culture	Not Done	No Growth
SARS-CoV-2 by PCR	Not detected	Not detected

The patient was treated symptomatically with 975mg of acetaminophen, 15mg of ketorolac, and 4mg of ondansetron. At this point, the decision was made with the patient to empirically begin a course of 100mg of doxycycline twice daily for 10 days with the first dose given in the emergency department (standard

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treatment for uncomplicated Lyme disease), and the patient discharged with strict return precautions. This was based on a characteristic (albeit variant) rash, laboratory tests, and regional epidemiology that supports this diagnosis.

METHODS: Second Presentation

A second set of lab studies was obtained, similar to the one obtained the day before except for the platelet count returning to normal at 145x1000/uL (Table 1). By this time his tickborne panel had fully resulted with positive Lyme antibodies on Enzyme linked immunosorbent assay (ELISA) screen, but negative IgM and IgG on the western blot reflex (Table 1). A second sample was drawn at the time, which resulted in positive IgM and negative IgG (Table 1). Due to the concern for meningitis, a lumbar puncture was performed with the opening pressure measured as normal. The cerebrospinal fluid (CSF) was sent for analysis and culture, resulting in a CSF glucose of 65mg/dL (normal), a CSF protein of 26.7mg/dL (normal), and no culture growth (Table 1). Given that he was well-appearing, the cultures could be followed outpatient. He was discharged with a course of 60mg of prednisone daily for 10 days for the Bell's palsy and precautions to tape his right eye shut while sleeping, and instructions to extend the course of his doxycycline from 10 to 21 days since he was now being treated for presumed neurologic Lyme disease rather than uncomplicated Lyme disease.

CONCLUSION AND RESULTS

Following the course of treatment, the patient's dermatologic symptoms successfully resolved two weeks after presentation and his Bell's palsy successfully resolved 4 months after presentation. The patient did not display any additional sequelae of Lyme disease.

Because of its constellations of non-specific findings, Lyme disease remains a diagnosis that can be difficult to make without supporting lab results. For any patients in Lyme-endemic areas, as well as patients with recent travel to these, the differential diagnosis for a rash should include Lyme. Given the debilitating consequences of Lyme carditis and neuroborreliosis, prompt recognition and treatment of this disease process is paramount.

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