CASE REPORT

Disseminated Lyme disease presenting as multiple non-target cellulitic-appearing skin lesions and oral pseudomembrane

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SUMMARY

A 45-year-old man was presented with 3 weeks of fever, chills, headache, myalgia and sweats after returning from a camping trip. He had multiple erythematous, blanching, non-target lesions on back and lower abdomen and oral pseudomembrane. He was empirically started on doxycycline for presumed Lyme disease and hydration for management of acute renal failure. Next day, he was started on vancomycin for worsening rash and coverage of methicillin-resistant *Staphylococcus aureus* skin infection and fluconazole for possible thrush and tested for HIV, syphilis, tick-borne diseases, arboviral panel, Epstein-Barr virus, rapid plasma reagin and rheumatoid factor. Initial Lyme's screening test was negative. Over the next 4 days, rash and headache improved significantly and Epstein-Barr DNA and immunoglobulin M Lyme antibody came back positive. After discussion with Infectious Diseases colleagues, doxycycline was continued for 3 weeks for management of early disseminated Lyme disease. Patient had no recurrence of his symptoms at 4 week follow-up visit.

BACKGROUND

Disseminated Lyme disease typically presents with features of prodromal syndrome and target lesions with other system involvement like cardiovascular and neurological system.

Our case did not exhibit typical target lesions but more of cellulitis-appearing lesions with oral pseudomembrane; initial Lyme screening test was negative, but western blot was positive along with Epstein-Barr nuclear antigen, confounding the diagnosis with infectious mononucleosis.

CASE PRESENTATION

A 45-year-old previously healthy white male presented to the emergency department (ED) with generalised weakness and chills. Three weeks prior, he had been on an outdoor camping trip in northern Minnesota and on return had headaches, fever, malaise, fatigue, generalised weakness and generalised joints, muscle and back pain. Taking ibuprofen every 4 hours for 3 days led to symptomatic relief. However, his symptoms recurred 3 days prior to admission with addition of chills, shaking, alternating with cold feeling and warm, profuse sweating, retching, blurry vision, stomach pain, leg cramps and chest pressure. Headache was generalised without neck rigidity or photophobia.

Patient denied sinus pressure, drainage, shortness of breath, illicit drug use, penile discharge, testicular pain, sick contacts, spending time in caves, tick bite, oral or anal sex with same or opposite gender or travel outside the country.

He had no allergies and a medical history significant for Achilles tendon repair. He had received appropriate vaccinations and lived in a monogamous relationship with his wife. A full systems review did not reveal any further information.

Blood pressure was 123/71 mm Hg, heart rate of 94 beats/min, respiratory rate of 16 and temperature of 40°C. Clinical examination revealed an ill-appearing young male with large erythematous, warm, rash without central clearing over the left lower quadrant, with similar but smaller rashes on abdomen and back (figure 1) and scattered white patches on surface and side of tongue. (figure 2) Cardiovascular, respiratory, genital, neurological examination was unremarkable. Meningeal signs were absent.

Laboratory examination revealed normal haemogram and lactate, elevated creatinine of 1.37 mg/dL and a C-reactive protein of 40.6 mg/L. CT neck, chest, abdomen done in ED as part of sepsis workup was remarkable for a few enlarged non-specific axillary lymph nodes. ECG confirmed a normal sinus rhythm at 68 beats/min without any heart blocks or QT prolongation.

Patient was admitted to hospital for workup of fever of unknown origin and management of acute kidney injury. He was empirically started on doxycycline for presumed Lyme disease and hydration for management of acute renal failure.

Next day his renal failure resolved, but his rash worsened; hence, vancomycin was started for possible methicillin-resistant *Staphylococcus aureus* skin infection and fluconazole was initiated for management of oral thrush.

On fourth day of hospital stay, Epstein-Barr immunoglobulin (Ig)G and nuclear antigen were positive but IgM was negative. Lyme's western blot serology was reported positive for IgG p23, IgM p41 and p39 bands. After discussion with Infectious Diseases colleagues, it was determined that patient had early disseminated Lyme disease. By this time, he had significant improvement in his symptoms and rash (figure 3); hence, vancomycin was stopped and the patient was discharged home to complete 3 weeks of doxycycline and 7 days of fluconazole.

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Figure 1 Day 1 rash.

He returned 4 weeks later to the infectious disease clinic, had complete resolution of his rash and had no recurrence of his symptoms.

INVESTIGATIONS

Following tests: urine analysis, urine culture, blood cultures, Lyme screen, HIV ELISA, syphilis arboviral panel, rheumatoid factor, strep screen, malaria-babesia screen were reported to be negative.

Figure 2 Oral pseudomembrane.

Figure 3 Day 4 rash attached.

On fourth day of hospital stay, Epstein-Barr IgG and nuclear antigen were positive, but IgM was negative. Lyme western blot serology was reported positive for IgG p23, IgM p41 and p39 bands.

DIFFERENTIAL DIAGNOSIS

1. Acute HIV- based on prodromal symptoms, oral pseudo-membrane, but was ruled out with negative HIV test.
2. Infectious mononucleosis: based on prodromal symptoms and positive nuclear antigen, but ruled out by negative IgM titer and not ruled out by positive Lyme western blot.

TREATMENT

After discussion with Infectiologists, it was determined that patient had early disseminated Lyme disease. Patient had significant improvement in his symptoms and rash ([figure 3](#)); hence, vancomycin was stopped and the patient was discharged home to complete 3 weeks of doxycycline and 7 days of fluconazole (for possible thrush).

OUTCOME AND FOLLOW-UP

Patient returned 4 weeks later to the infectious disease clinic, had complete resolution of his rash and had no recurrence of his symptoms.

DISCUSSION

Lyme disease is a zoonosis caused by *Borrelia (burgdorferi* in North America, *garinii* and *afzelii* in Asia and Europe). Minnesota had 1176 confirmed Lyme's cases in 2015 (20.7 cases/100 000

people). Over the last 20 years, the median incidence has risen from 464 cases (1996–2005) to 1121 (2006–2015).¹

This disease can have symptoms ranging from classic prodromal syndrome (fever, chills, myalgia, arthralgia, malaise, weakness) and skin lesions, to involvement of other organ systems like cardiovascular and nervous system, etc. The disease typically starts as a classic bull's eye or target lesion called erythema migrans and if untreated progresses to early disseminated and then late infection.^{2,3}

Skin manifestations include erythema migrans, borreliolymphocytoma or as a late manifestation: acrodermatitis chronica atrophicans.⁴

Diagnosis is made based on classic symptoms and signs and serological tests like ELISA screen and western blot. Serology is not always positive in early Erythema Chronicum Migrans; hence patients should be treated based on clinical suspicion alone. Within the first 4 weeks of illness, both IgM and IgG western blot tests should be performed for confirmation of initially positive enzyme immunoassay (EIA) screening test results. EIA lacks the specificity; hence, a two-step approach including the initial EIA and second-step western Blot for positive or borderline EIA

tests is recommended to diagnose majority of Lyme cases. After 4 weeks, results of the IgM western blot should be ignored and only the IgG western blot results considered, along with the EIA results. A Lyme disease IgG western blot test that is 'positive for IgG p23' is in fact negative—an additional four reactive bands are required.^{3,5}

Case reports of false-positive Epstein-Barr virus in patients with early disseminated Lyme's disease have been reported.⁶

Treatment includes 2 week treatment with doxycycline, amoxicillin or cefuroxime for early disease without cardiac or nervous system involvement and intravenous ceftriaxone for cardiac or nervous system involvement. Late Lyme disease with arthritis is treated with 28 days of oral doxycycline, amoxicillin or cefuroxime and intravenous ceftriaxone for nervous system involvement.^{2,3}

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Learning points

- ▶ Disseminated Lyme disease can present without the classic bull's eye/target lesions and may mimic cellulitis.
- ▶ Lyme disease can have unrelated findings like oral pseudomembrane, lymphadenopathy that may lead one to suspect alternative diagnosis like acute HIV or infectious mononucleosis
- ▶ Lyme screen may be negative in some cases; hence, western blot is necessary to confirm diagnosis of suspected Lyme disease if initial screen is negative depending on clinical pretest probability.
- ▶ Disseminated Lyme disease typically involves other organ systems like cardiovascular or nervous system.

REFERENCES

- 1 Lymes disease statistics. Minnesota department of health. <http://www.health.state.mn.us/divs/idepc/diseases/lyme/statistics.html>.
- 2 Steere AC, Strle F, Wormser GP, *et al.* Lyme borreliosis. *Nat Rev Dis Primers* 2016;2:16090.
- 3 Wormser GP, Dattwyler RJ, Shapiro ED, *et al.* The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006;43:1089–134.
- 4 Müllegger RR, Glatz M. Skin manifestations of lyme borreliosis: diagnosis and management. *Am J Clin Dermatol* 2008;9:355–68.
- 5 Canadian Public Health Laboratory Network. The laboratory diagnosis of Lyme borreliosis: guidelines from the Canadian Public Health Laboratory Network. *Can J Infect Dis Med Microbiol* 2007;18:145–8.
- 6 Pavletic AJ, Marques AR. Early disseminated Lyme disease causing false-positive serology for primary Epstein-Barr virus infection: report of 2 cases. *Clin Infect Dis* 2017;65:336–7.

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