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Commentary

Negative impact of the COVID-19 pandemic on the timely diagnosis of tick-borne infections



Gary P. Wormser*, Eliana Jacobson, Elayna M. Shanker

Division of Infectious Diseases, New York Medical College, Valhalla, NY 10595

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ABSTRACT

We describe 3 adult patients who did not have COVID-19 but instead had a treatable tick-borne infection. In each case, however, the duration of time until diagnosis was delayed due to issues that have arisen because of the COVID-19 pandemic. These issues need to be addressed to preserve patient well-being.

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The COVID-19 pandemic has led to many cases of this viral infection in the United States, varying in severity from extremely mild to life threatening (Wormser, 2020). The pandemic has had numerous indirect health effects as well. Concerns about spreading the infection have reduced outpatient visits with health care providers (Rubin, 2020). Even without symptoms, patients are sometimes required to demonstrate negative test results for COVID-19 before they are allowed to undergo certain medical/surgical procedures. Symptomatic patients may also be presumed to have COVID-19 until negative test results are obtained, implying that evaluations for other diseases will be delayed, potentially leading to adverse outcomes. We describe 3 patients who did not have COVID-19 but instead had a treatable tick-borne infection, but in each case, the duration of time until diagnosis was delayed due to issues that have arisen because of the COVID-19 pandemic.

1. Results

Three illustrative cases in which the timely diagnosis of a deer tick-transmitted infection in an adult patient was delayed are discussed here (Table 1). Two of the 3 had had a preceding tick bite. One patient had compelling clinical evidence for cardiac Lyme disease with a coinfection due to *Babesia microti* (Wormser et al., 2019), 1 patient had babesiosis, and 1 patient had human granulocytic anaplasmosis (HGA). Failure to diagnose erythema migrans in a telemedicine evaluation is believed to have played a significant role in the later development of severe cardiac

Lyme disease for case 1. This patient was hospitalized for 6 days due to heart block.

For the 3 patients, the mean time from onset of symptoms to testing for COVID-19 was 14.3 days compared with 23.7 days for testing for the relevant tick-borne infection.

2. Case histories

2.1. Case 1

A 36-year-old man with no significant past medical history presented with an erythematous skin lesion on the anterior aspect of his right thigh on 6/1/20, which increased in size to ~25 cm in diameter by 6/6/20 (in retrospect, the skin lesion was almost certainly an erythema migrans skin lesion based on review by the author [GPW] of a photograph the patient had taken). The patient had no known tick bite but lived in Westchester County, NY, where Lyme disease is endemic. The rash was diagnosed as cellulitis, however, during a telemedicine consult, which was only done because of the COVID-19 pandemic. This was the first telemedicine experience this patient ever had, and it was with a doctor the patient had never met previously. Based on the telemedicine evaluation, the patient was treated for cellulitis with a 5-day course of cephalexin from 6/6/20 to 6/11/20, an antibiotic known to be ineffective for Lyme disease (Nowakowski et al., 2000). Although the skin lesion resolved, he developed multiple symptoms starting on ~6/23/20 that eventually included myalgias, stiff neck, fatigue, low back pain, paresthesias, right knee swelling, inability to concentrate, lightheadedness, palpitations, and dyspnea on exertion. He also had 2

* Corresponding author. Tel.: +1-914-493-8865; fax: +1-914-493-7289.
E-mail address: gwormser@nymc.edu (G.P. Wormser).

Table 1
Delay in diagnosis of deer tick-transmitted infections due to COVID-19.

Case number	Deer tick infection	Number of days from onset of illness until testing for the tick-borne infection(s) listed ^a	Comment
1	Lyme carditis	38 days for both	An erythema migrans skin lesion was misdiagnosed as bacterial cellulitis by a telemedicine consult. The patient later required hospitalization and IV antibiotics for Lyme carditis that progressed to complete heart block; the babesiosis resolved without treatment.
2	Babesiosis	21 days	Patient lost 11 lb in weight, and her hematocrit fell from 47.4% to 29.9%
3	HGA	12 days	

^a If tested the same day the illness began, this would have been tabulated as 1 day of illness.

days of fever to 38.9 °C on 7/6 and 7/7 for which no evaluation was done, except for COVID-19 RNA testing of a nasal swab specimen on 7/7, which was negative.

On 7/8/20, he presented to the Lyme Disease Diagnostic Center (LDDC) located in Westchester County, NY, where he was found to have bradycardia (pulse rate = 48) and advanced first-degree heart block (PR interval = 464 ms). He was hospitalized that day with a presumptive diagnosis of Lyme carditis. Laboratory testing demonstrated 2-tier seropositivity with both IgG and IgM immunoblots positive for antibodies to *Borrelia burgdorferi* (immunoblot testing was done using the MarDx *B. burgdorferi* IgG Western blot and the IgM Western blot [Trinity Biotech], performed according to the manufacturer's recommendations). Complete heart block developed after hospital admission on 7/9/20, and he was treated with intravenous ceftriaxone during his 6-day hospitalization. Including outpatient treatment, he received in total 14 days of ceftriaxone followed by 14 more days of oral doxycycline. As of 8/13/20, the patient's symptoms and the cardiac conduction abnormalities had completely resolved. He was also diagnosed with *B. microti* infection based on a positive polymerase chain reaction (PCR) test on a blood sample obtained while hospitalized, although the blood smear was negative. The babesiosis was not treated and resolved without antiparasitic drugs based on follow-up negative PCR testing performed on 8/13/20 (Wormser et al., 2006).

2.2. Case 2

A 69-year-old woman developed fever, weakness, and anorexia on 7/3/2020, with a peak temperature of 39.4 °C. She reported multiple tick bites in April and May. She had been diagnosed with Lyme disease at least 8 years earlier. The patient herself arranged for a nasal swab RNA test for COVID-19, which was done by a local pharmacy on 7/5/20. The COVID-19 RNA testing was negative, but the results were not known for 14 days. She did not see her primary physician in early July because patients with fever were not allowed into the practice. On 7/22/20, she had an in-person visit with her primary care physician and was seen at the LDDC on 7/23/20. She was diagnosed with *B. microti* infection based on both a positive blood smear and a positive blood PCR. Both smear and PCR testing for *Anaplasma phagocytophilum* were negative on testing performed on 7/23/20. Antibody testing for Lyme disease was performed on 8/11/20 and was negative. The patient cleared the *B. microti* infection with a 10-day course of azithromycin plus atovaquone. Because of this illness, she lost 11 lb in weight, and her hematocrit fell from a value of 47.4% before she developed babesiosis to 29.9% on 7/28/20 (i.e., a 37% drop).

2.3. Case 3

A 56-year-old man was evaluated at the LDDC on 7/14/20. He had had a tick bite approximately 1 month earlier. He had been diagnosed with Lyme disease approximately 10 years earlier. Approximately 11 days before the visit, he became acutely ill with rigors, fevers to 38.9 °C, headaches, and joint pains; the fever lasted approximately 4 days (he had no fevers for the week prior to the LDDC visit with his

other symptoms substantively improved as well). Nine days prior to the LDDC visit, he tested negative for COVID-19 RNA by a nasal swab, with repeat negative testing 6 days prior to the LDDC visit.

The patient was found to be infected with *A. phagocytophilum* based on PCR testing of a blood specimen obtained the day he was seen at the LDDC, in conjunction with positive antibody testing (IgG antibody titer to *A. phagocytophilum* was 1:320, and the IgM antibody titer was >1:256). The patient's HGA resolved without antibiotic treatment.

3. Discussion

Because of concerns about spreading COVID-19, clinical practices are limiting in-person visits, increasing telemedicine visits which preclude performing a complete physical examination, and in some cases requiring negative laboratory testing for COVID-19. Similarly, patients are anxious about becoming infected with SARS-CoV-2 (the cause of COVID-19) by going to the offices of health care providers (Rubin, 2020). This has increased interest in telemedicine visits from the patient's perspective, as illustrated by case 1 in this report. Because of the diversity of symptoms and signs associated with COVID-19, many patients with other conditions are potentially either not being diagnosed at all or not being diagnosed in a timely fashion. We illustrate this issue with deer tick-transmitted infections, but the same concerns would apply to virtually any other type of infection and many other illnesses.

Deer tick-transmitted infections can present with fever, and specifically Lyme carditis, babesiosis, and HGA are each potentially life-threatening, particularly if there is a delay in diagnosis and in initiating appropriate antimicrobial therapies (Wormser et al., 2006; Muehlenbachs et al., 2016). The most severely ill patients with babesiosis or with HGA may also develop acute respiratory distress syndrome similar to COVID-19 (Bayard-McNeeley et al., 2004; De Leon et al., 2019). Health care providers and patients need to be aware of the potential undesirable consequences of just performing COVID-19 tests and, by so doing, delaying a more comprehensive evaluation of a patient's illness. Arguably, all appropriate testing should be conducted at the same time, not sequentially after COVID-19 is excluded.

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Gary P. Wormser: Conceptualization, Writing - review & editing.
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Elayna M. Shanker: Conceptualization, Writing - original draft, Writing - reviewing and & editing.

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