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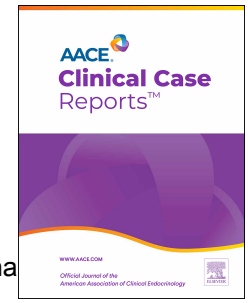

Coexisting Thyroiditis and Carditis in a Patient with Lyme disease: Looking for a Unifying Diagnosis

Paria Zarghamravanbakhsh, MD, Farzane Saeidifard, MD, Gourg Atteya, MD, Swetha Murthi, MD, Ira Nash, MD, Nicholas T. Skipitaris, MD, Leonid Poretsky, MD

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Short title: Lyme carditis and thyroiditis

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Abstract

Background/Objective

Lyme disease, the most common vector-borne infection in the United States, causes multisystem inflammation. We describe a patient who presented with the symptoms of Lyme disease, carditis and thyroiditis.

Case Report

A 53-year-old female developed fatigue and dyspnea on exertion one month after returning from a trip to Delaware, USA. Her electrocardiogram (ECG) showed first-degree atrioventricular (AV) block with P-R interval up to 392 milliseconds, in the setting of an elevated free T4 and undetectable TSH. Lyme serology was positive. She was hospitalized and started on ceftriaxone. During the 2nd day of hospitalization, AV block worsened to 2nd-degree Mobitz type II but converted back to 1st-degree AV block after a few hours. Her 24-hour I-123 thyroid uptake and scan revealed markedly diminished I-123 uptake of 1.2%. On day 4, the P-R interval improved and she was discharged on doxycycline for 3 weeks. P-R interval on ECG and repeated thyroid function tests were normal after finishing antibiotic treatment.

Discussion

In our patient, known exposure to the vector, a classic rash on the chest, improvement in the symptoms and normalization of thyroid function tests after antibiotic therapy support Lyme infection as a cause of carditis and autoimmune painless thyroiditis.

Conclusion

Our case highlights the importance of considering Lyme disease as a cause of autoimmune painless thyroiditis, especially in patients with concurrent cardiovascular involvement.

Keywords: Lyme disease, thyroiditis, carditis.

Introduction

Lyme disease, a tick-borne infection caused by a spirochete Borrelia burgdorferi, is the most common vector-borne infection in the United States, with an approximate incident rate of 300,000 cases annually. Lyme disease can present in 3 stages. Early localized stage (days to weeks after the tick bite) includes skin manifestations and flu-like symptoms. Early disseminated stage (weeks to months after exposure) manifests as systemic inflammation, including cardiac involvement. Late-stage (months to years after exposure) includes neurologic manifestations[1]. Lyme carditis has been reported in 4-10% of the patients with Lyme disease who did not receive treatment in the early localized stage of the infection[2]. Lyme carditis manifests mainly as conduction derangement in the atrioventricular (AV) node. Pericarditis, endocarditis, myocarditis, pericardial effusion, myocardial infarction, coronary artery aneurysm, QT-interval prolongation, and tachyarrhythmia have also been described[2]. Unlike carditis, thyroid dysfunction coinciding with Lyme disease has been rarely reported[3]. To our knowledge, only one publication reported a case of Lyme disease that presented with both carditis and thyroiditis[3]. The definitive unifying diagnosis is complicated because of the possibility of false-positive Lyme serology in patients with thyroiditis [4,5] and AV node block as a result of thyrotoxicosis

Case Presentation

A 53-year-old female with a history of subarachnoid hemorrhage and intracerebral aneurysm initially presented to an urgent care facility because of dyspnea on exertion (DOE) and palpitations occurring several weeks after her return from a 4-week stay in Delaware, USA; where she had several encounters with deer while watching the sunset. Five days after her return, she developed headaches, heat intolerance, near-syncope, and a red 5x5 cm rash on her chest. A few days later, she traveled for 8 days to upstate New York where she developed DOE and palpitations. She presented to an urgent care facility 3 days after her return to New York City. Electrocardiogram (ECG) showed a 1st-degree AV block; thyroid function tests and Lyme serology were obtained. Due to the ECG

findings, she was referred to a cardiologist. She denied any neck or throat pain. She also denied taking any medications or supplements including biotin or iodine. On physical examination, blood pressure was 115/85 mmHg, pulse rate 81 beats/min, and respiratory rate 18/ min. The thyroid was not enlarged or tender. No lid lag or proptosis was observed. Echocardiogram showed a moderate pericardial effusion without signs of tamponade and a mildly dilated aortic root (3.7 cm). Her free T4 was 2.8 ng/dL (normal range (NR) 0.70-1.48 ng/dL) and TSH was <0.01 mIU/L (NR: 0.35-4.94 mIU/L). Thyroid peroxidase antibodies were present at a titer of 444 IU/mL, thyroid-stimulating immunoglobulin was absent (Figure 1). Lyme IgG/IgM test was positive. Repeat ECG showed P-R interval >300 msec (Figure 2). Due to these findings, she was referred to the emergency department. Of note, her TSH was normal at 1.94 mIU/L (NR: 0.49-4.7 mIU/L) in another facility 4 months before her symptoms.

In the hospital, ECG showed first-degree AV block with P-R interval of 322 msec. Repeated TSH was 0.006 mIU/L with a total T4 of 11.78 ug/dL (NR: 4.5-11.70 ug/dl) and free T4 of 1.42 ng/dL (Figure 1). ESR was 55 mm/hr (NR: <26 mm/hr), and CRP was 0.8 mg/L(NR: 0.00-0.40 mg/L). Complete blood count, kidney function and liver function tests were within normal limits. Lyme IgG/IgM test was positive, with a titer of 8.76 units/ml. This result was confirmed with positive Lyme antibody Western Blot for IgG and IgM. With presumed Lyme carditis, she was started on ceftriaxone 2 gm/day. During the 2nd day of hospitalization, AV block worsened to 2nd-degree Mobitz type II (Figure 2) but converted back to 1st-degree AV block after a few hours. During the 3rd day of hospitalization, she remained in normal sinus rhythm with1st-degree AV block, and P-R interval decreased to 320 msec.

Her I-123 thyroid scan and 24-hour uptake showed a decrease in iodine uptake of 1.2%, consistent with thyroiditis. Echocardiogram showed normal left and right systolic and diastolic function with a small pericardial effusion without signs of tamponade.

After starting ceftriaxone her P-R interval on ECG decreased to 316 msec, and symptoms improved. On day 4 of hospitalization, she was discharged on doxycycline 100 mg twice a day for 3 weeks. One week after discharge, she was asymptomatic and ECG showed P-R interval of 234 msec (Figure 2).

8 weeks after treatment, TSH was 2.94 mIU/L with free T4 1.04 ug/dL and total T3 87 ng/dL; after 10 weeks TSH was 2.49 mIU/L and Free T4 1.29 ug/dL (Figure 1). Her TSH was normal at 2.01 mIU/L 4 months after her admission.

Discussion

This case report describes a 53-year-old female who was found to have carditis and autoimmune painless thyroiditis likely due to Lyme infection.

The primary manifestations of Lyme carditis are non-specific and can occur 4 days to 7 months after the initial infection[2,7,8]. Lyme carditis is a potentially fatal condition and its early diagnosis and treatment are essential to prevent complications. Although Lyme carditis usually presents as a form of self-limited conduction derangement, it can worsen and cause complications, including higher grade AV blocks, ventricular or supraventricular tachyarrhythmias, and sudden cardiac death[7,9,10,11].

Previous studies suggested that in Lyme carditis, the deposition of neutrophils, macrophages and lymphocytes produces an inflammatory reaction that contributes to an inflammatory cascade that ultimately causes fibrosis[2,12,13]. Several studies have demonstrated the presence of spirochetes in the biopsies of infected patients' hearts and large vessels[14,15]. It is unknown whether the presence of spirochete is necessary for the continued disease or if the inflammatory cascade itself causes multisystem inflammation.

Previous reports described association between Lyme disease and thyroid disease. Paparone described a case in which Lyme disease was superimposed on primary hypothyroidism and made the diagnosis of Borrelia infection challenging due to similar manifestations in both diseases[16]. Dhliawayo et al reported a case of a 22-year old woman with Lyme disease whose thyroid function tests were consistent with transient thyrotoxicosis and decreased radioiodine uptake in the thyroid[17].

Any form of thyroid dysfunction, especially thyrotoxicosis, can put the patient at risk for further worsening of cardiac function. Deol et al described association of Lyme disease with thyroiditis in a 40-year-old male who presented with night sweats and weakness. The patient also had high-grade 2nd-degree AV block, elevated thyroid hormone levels, suppressed TSH, positive thyroperoxidase antibody, and decreased iodine uptake in the thyroid[3].

The bioinformatics data by Benvnega et al. suggested possible explanation for thyroid involvement in patients with Lyme infection[18]. They reported amino acid sequence homologies between certain microbial proteins

and thyroid autoantigens suggesting that the molecular mimicry between *B. burgdorferi* and human antigens can introduce autoimmunity.

To further complicate the issue, Lyme serology can be false-positive for various reasons, including treponema disease, systemic lupus erythematosus, rheumatoid arthritis, etc. False-positive seroreactivity to B. burgdorferi in a patient with thyroiditis can be caused by the antibodies to self-antigens and to other bacteria cross-reacting with the Lyme ELISA serology[19,20]. When a positive Lyme test is found using a highly sensitive enzyme immunoassay, a Western blot test, which is highly specific for Lyme serology, can be used to differentiate true-positive vs false-positive results.

In our patient, there was a known exposure to the vector, a classic rash, and improvement in the symptoms accompanied by normalization of thyroid function tests after treatment. These findings support a cause-effect relationship between Lyme infection, carditis and thyroiditis. As mentioned above, thyroiditis can produce false-positive Lyme serology and conduction derangements in the heart4,6. For this reason, in patients with abnormal thyroid function tests and positive Lyme serology, but no history of tick bite or no improvement after treatment for Lyme disease, a primary diagnosis of thyroiditis should be considered.

Conclusion

This case report demonstrates the importance of considering Lyme disease as a unifying diagnosis in patients with concurrent carditis and thyroiditis.

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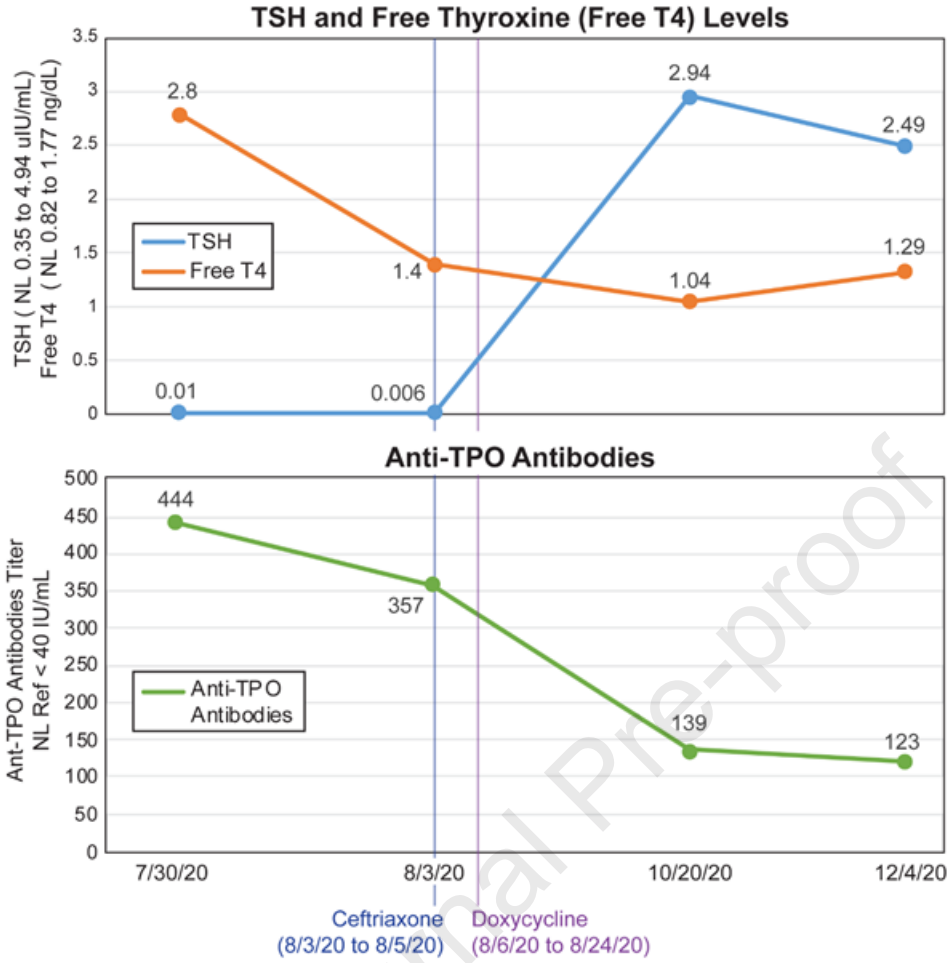
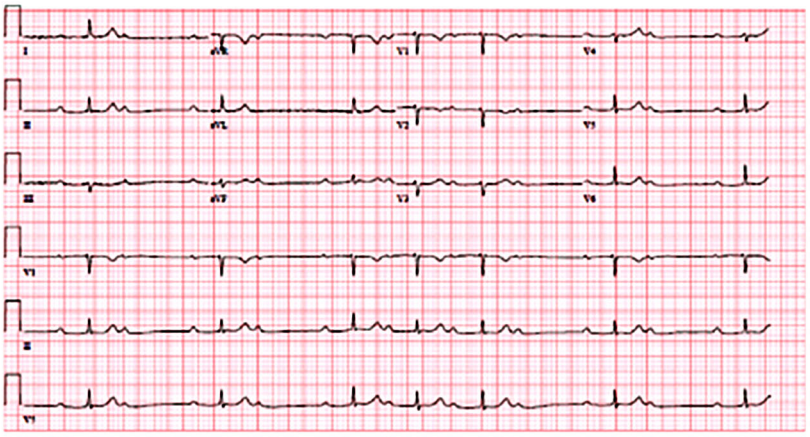
List of Figure Captions

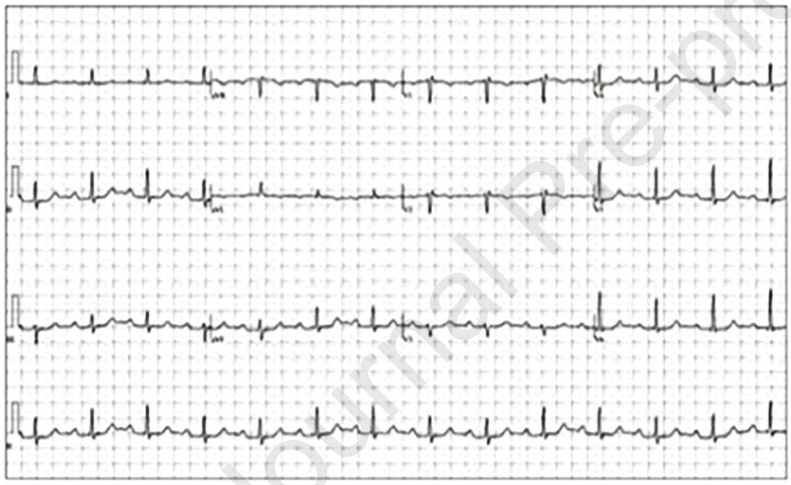
Figure 1. The course of thyroid function tests in a patient with Lyme thyroiditis and Lyme carditis before and after treatment with antibiotics

Figure 2. Electrograms (ECGs) 2 days and then 10 days after starting antibiotics





First ECG 2 days after starting the antibiotics



Second ECG 10 days after starting the antibiotics

Highlights

1. Autoimmune thyroiditis can be caused by Lyme disease.
2. Thyroiditis and carditis can be presenting features of Lyme disease.
3. Treatment of Lyme disease presenting with Lyme carditis and thyroiditis with antibiotics leads to normalization of thyroid function tests and cardiac function.

Clinical Relevance

Our case highlights the importance of considering Lyme disease as a cause of subacute thyroiditis, especially in patients with concurrent cardiovascular involvement which, to our knowledge, was reported only in one case previously.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: