Letters

RESEARCH LETTER

Neoplasms Misdiagnosed as “Chronic Lyme Disease”

Clinical features of Lyme disease include erythema migrans rash, facial palsy, arthritis, and peripheral neuropathy. In endemic areas, patients with erythema migrans can be diagnosed clinically. Otherwise, diagnosis is based on the history of possible exposure, compatible clinical features, and positive 2-tier serologic testing.1

Chronic Lyme disease is a loosely defined diagnosis given by a small number of physicians—who are not usually infectious disease experts—to patients with various nonspecific symptoms, including patients with no objective evidence of Lyme disease.2 In addition to adverse outcomes from unconventional treatments for chronic Lyme disease,3,4 patients misdiagnosed with chronic Lyme disease may be harmed when their actual condition remains untreated.

We report 3 cases in which diagnosis of the patients’ actual conditions was delayed due to the misdiagnosis of chronic Lyme disease. Institutional review board approval was not obtained for this case series because it did not meet the regulatory definition of research and was outside the scope of institutional review board requirements. All 3 patients gave written informed consent to share their medical records for this case series.

Report of Cases | Case 1. A man in his late 30s presented with a 12-year history of joint pain and memory loss, as well as 2 years of paresthesias in both hands. A physician diagnosed him with chronic Lyme disease and prescribed oral tetracycline hydrochloride after a telephone consultation despite negative Lyme serologic test results. Following an in-person evaluation 2 months later, the physician initiated extended antibiotic treatment (Table). The patient’s symptoms gradually worsened, and he developed syncope and visual field deficit. Evaluation by a different physician revealed a 1.4 × 0.8-cm pituitary tumor and elevated insulin-like growth factor 1 (835 ng/mL [to convert to nanomoles per liter, multiply by 0.131]), consistent with acromegaly. Successive Lyme serologic test results were negative. Only a portion of the tumor could be removed; the patient has permanent facial changes, cardiomyopathy, joint pain, and obstructive sleep apnea.

Case 2. A man in his late 30s presented with a 4-year history of fatigue, abdominal pain, and loose stools. Previous evaluations demonstrated stable mesenteric lymphadenopathy. Although he lived in an area where Lyme disease is rare, reported no history of erythema migrans, and had negative Lyme serologic test results, he was diagnosed with chronic Lyme disease by a physician and treated with antibiotics (Table). Subsequently, the patient discontinued treatment and was re-evaluated by a gastroenterologist and an oncologist. Findings from a gastric biopsy demonstrated stage IV mucosa-associated lymphoid tissue lymphoma; successive Lyme serologic test results were negative. Findings from a mesenteric lymph node biopsy and positron emission tomographic scan demonstrated stage IV classic Hodgkin lymphoma, for which the patient underwent chemotherapy. He died 2 years later of complications of advanced lymphoma.

Case 3. A man in his late 50s presented with a 2-week history of fatigue and a 3-day history of fever, headache, and myalgias. He had no known tick bite but worked outdoors in a Lyme disease-endemic area. Serum enzyme immunoassay results for Lyme disease were positive, and he was prescribed doxycycline.

Table. Test Results and Treatments Prescribed for Patients Misdiagnosed With Chronic Lyme Disease

<table>
<thead>
<tr>
<th>Test Result and Treatment</th>
<th>Case No. 1</th>
<th>Case No. 2</th>
<th>Case No. 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lyme test results</strong></td>
<td>EIA: not performed</td>
<td>C6 EIA: positive</td>
<td>Initial test: Whole-cell sonicate</td>
</tr>
<tr>
<td></td>
<td>Western blot: IgG 1/10 scored bands (negative)</td>
<td>Western blot: IgG 1/10 scored bands (negative)</td>
<td>EIA: positive</td>
</tr>
<tr>
<td></td>
<td>Subsequent test: C6 EIA: positive</td>
<td>Western blot: IgM 3/3 scored bands (positive), IgG 2/10 scored bands (negative)</td>
<td></td>
</tr>
<tr>
<td>Interpretation in clinical context</td>
<td>Negative</td>
<td>Negative</td>
<td>Initial test: Consistent with early Lyme disease (although reflex Western blot should have been performed)</td>
</tr>
<tr>
<td>Antibiotic treatments received</td>
<td>Various combinations of tetracycline (500 mg 3 times a day, then 1500 mg/d), clarithromycin (500 mg twice daily, then 1500 mg/d), and hydroxychloroquine (200 mg twice daily) for 3 y</td>
<td>Various intravenous and oral antibiotics (including metronidazole) for 4½ mo*</td>
<td>Doxycycline (100 mg twice daily) for 28 d, plus 2 additional 21-d courses of doxycycline</td>
</tr>
</tbody>
</table>

Abbreviations: EIA, enzyme immunoassay; Ig, immunoglobulin.

* Additional information on medications not available from the treating physician.
Non-small cell adenocarcinoma of the lung (arrowhead) that caused symptoms attributed to chronic Lyme disease.

Shortly afterward, an expanding 18 × 15-cm erythematous rash appeared below his left shoulder. The rash resolved but malaise and fatigue recurred. Two additional doxycycline courses provided only transient improvement. Five months after his initial diagnosis, the patient was referred to an infectious disease specialist for presumed chronic Lyme disease.

The results of the physical examination and laboratory evaluation were normal except for a slightly elevated white blood cell count. Results of serologic testing for Lyme disease were consistent with previous infection (Table). The patient had a remote 18 pack-year history of smoking. The chest radiograph revealed a 1.1-cm nodular mass in the right upper lobe confirmed by computed tomographic scan (Figure). Further evaluation demonstrated stage 1 non-small cell adenocarcinoma, which was successfully resected.

Discussion | Patients 1 and 2 had no evidence of ever having Lyme disease. Patient 3 likely had true *Borrelia burgdorferi* infection for which antibiotic therapy was appropriate; however, subsequent symptoms were incorrectly attributed to persistent infection.

Chronic *Lyme* disease is a misleading term that should be avoided. Posttreatment *Lyme disease* syndrome is the proper term for patients with a verified previous *B burgdorferi* infection who experience fatigue, arthralgias, or other symptoms 6 months or more after antibiotic treatment when all other conditions have been ruled out.

We are not suggesting that every patient with nonspecific symptoms, such as fatigue, joint pain, or abdominal pain, should be aggressively evaluated for cancer. Rather, we present these cases to demonstrate delays in diagnosis that come from assuming that patients have chronic Lyme disease.

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Author Contributions: Dr Nelson had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Nelson, Elmendorf. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Nelson, Elmendorf. Critical revision of the manuscript for important intellectual content: All authors. Administrative, technical, or material support: Nelson, Elmendorf. Study supervision: Mead.

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Secondhand Tobacco Smoke Exposure Among Hospitalized Nonsmokers With Coronary Heart Disease

Exposure to secondhand tobacco smoke (SHS) increases adult nonsmokers’ risk of cardiovascular disease by 25% to 30%. Among nonsmokers hospitalized with acute coronary syndrome, SHS exposure is associated with a higher likelihood of subsequent cardiovascular and all-cause mortality as well as reinfarction.2,3 Hospitalized nonsmokers with coronary heart disease (CHD) should avoid SHS exposure after discharge, but little is known about the frequency of SHS exposure in this population or whether clinicians (including nurses, nurse practitioners, physician’s assistants, and physicians) address it. The present study assessed self-report and biochemical measures of SHS exposure among hospitalized nonsmokers with CHD and explored patients’ beliefs and the clinicians’ actions about SHS.

### Methods

The study was approved by the Massachusetts General Hospital/Partners Health Care System Institutional Review Board. Participants provided oral consent; they re-