Death from Inappropriate Therapy for Lyme Disease

A 30-year-old woman died as a result of a large Candida parapsilosis septic thrombus located on the tip of a Groshong catheter. The catheter had been in place for 28 months for administration of a 27 month course of intravenous cefotaxime for an unsubstantiated diagnosis of chronic Lyme disease.

A 30-year-old woman was admitted to the Mayo Clinic (Rochester, MN) in May 1999 following a grand mal seizure. She reported a several-week history of anorexia that was accompanied by a 23-kg weight loss over an 8-month period; 4 days before admission, she noticed twitching of her upper extremities. She appeared ill and had a blood pressure of 124/82 mm Hg, a pulse rate of 85, a temperature of 37°C, and a respiratory rate of 20. The patient was confused and unable to provide a coherent history. She was icteric and had diffuse myoclonus. Cardiac auscultation revealed a prominent pulmonary second sound. A Groshong catheter was in place. Hepatosplenomegaly was noted.

Her family provided a pertinent medical history. She had had a history of bilateral knee pain since childhood. She resided in Iowa; however, she had lived in Westchester County, New York, until the age of 16 years and in northern California for a short period thereafter. In 1994, she underwent cholecystectomy and since that time she had had chronic abdominal pain, whole body pain, an episode of Bell’s palsy, occasional headaches, and periods of what were described as “mental fogginess” and “transient numbness.” She also reportedly had a periodic rash and periods of what were described as “mental fogginess” and body pain, an episode of Bell’s palsy, occasional headaches, and periods of what were described as “mental fogginess.”

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Clinical Infectious Diseases 2000;31:1058-1060
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aminotransferase level, 131 U/L; bilirubin level, 5.2 mg/dL; and
creatinine level, 6.5 mg/dL. In our laboratory, EIA was reactive
for B. burgdorferi, but a Western blot assay showed only 1 66-
KDa band. CSF examination was unremarkable, and PCR ass-
ay of CSF was negative for B. burgdorferi.

One day after admission, the patient reportedly became con-
fused, and she fell, pulled and fractured her Groshong catheter,
and became unresponsive. Electromechanical dissociation was
diagnosed, and she died despite aggressive attempts at resus-
citation. After her death, cultures of blood obtained at the time
of admission yielded Candida parapsilosis.

Postmortem examination revealed acute fatal obstruction of
the tricuspid valve orifice by a large infected thrombus located
on the fractured tip of her Groshong catheter (figure 1). Gro-
cott-Gomori methenamine-silver nitrate staining of micro-
scopic sections of the thrombus revealed extensive Candida or-
ganisms (figure 2). Other significant findings at autopsy in-
cluded an old Candida-infected pulmonary thromboembolus
with total occlusion of the left main artery at the hilum as well
as scattered old peripheral emboli bilaterally. Marked spleno-
megaly with reactive follicular hyperplasia and congestion were
noted. At autopsy, there was no myositis, neuritis, meningitis,
vasculitis, or myocarditis suggestive of chronic Lyme disease.

The premature death of our patient resulted from a complica-
tion of her chronic indwelling central venous catheter, which
was used for prolonged iv administration of antimicrobial ther-
apy for a disease that was not fully documented. Lyme disease
is curable with antibiotic treatment, and, although resolution
of true neurological complications of Lyme disease may be slow
after appropriate therapy, there is no evidence that our patient
ever had Lyme disease. Her chronic symptoms were nonspecific,
and results of her laboratory tests were nondiagnostic and did
not fit the criteria for Lyme disease [1]. Furthermore, chronic
antibiotic therapy, such as that described here, is never indicated
for Lyme disease, and such therapy has a significant risk of
side effects. Even in cases of clear-cut Lyme disease, abnormal
test results return to baseline with no measurable sequelae after
appropriate treatment [2].

Lyme disease is primarily a clinical syndrome confirmed by
microbiological tests [3, 4]. For our patient, the diagnosis of
Lyme disease was made despite negative or indeterminate re-
sults of Western blot assays, perhaps because the presence of
only 1 or 2 highly specific bands on a Western blot was con-
sidered a potential harbinger of further expansion over time
[5]. We are of the opinion that acceptable diagnostic criteria
for Lyme disease include the presence of multiple bands of
specific molecular weight and that the serological analysis of
the patient described here did not confirm a diagnosis of Lyme
disease [3]. Notably, in our laboratory, a Western blot assay
showed only 1 66-KDa band, thereby revealing no expansion
over time. The 1 positive PCR assay is intriguing, but this
finding may have been the result of DNA contamination.

It has been suggested that B. burgdorferi infection may trigger
parainfectious pain or fatigue syndromes, which may persist
indefinitely after eradication of the spirochete by antimicrobial
therapy. In addition, fibromyalgia, chronic pain syndromes, and
chronic fatigue syndrome may be incorrectly diagnosed as
chronic Lyme disease [1, 6]. Patients with these disorders have
disabling and generalized symptoms, including marked fatigue,
severe headache, widespread musculoskeletal pain, multiple
symmetrical tender points in characteristic locations, pain and
stiffness in many joints, dysesthesias, paresthesias, difficulty
with concentration, memory loss, and sleep disturbances; their
symptoms are not relieved with antimicrobial therapy [1, 6–8].

Of 788 patients referred to the New England Medical Center
(Boston) with a presumptive diagnosis of chronic Lyme disease,
23% had active Lyme disease, 20% had previous Lyme disease
and another current illness (most commonly chronic fatigue

Figure 1. Opened right atrium from a patient who died because of
inappropriate therapy for Lyme disease. The photo shows a large in-
fected thrombus on the fractured tip of the patient’s Groshong catheter.

Figure 2. Stained section of a right atrial thrombus in a patient who
died because of inappropriate therapy for Lyme disease. The photo-
micrograph shows extensive Candida species (Grocott-Gomori meth-
enamine-silver nitrate stain; original magnification, × 360).
syndrome or fibromyalgia), and 57% did not have Lyme disease (patients in this last group most commonly had fatigue or pain syndromes) [1]. In another study [7], of 209 patients referred to the Yale University Lyme Clinic (New Haven, CT) with a presumptive diagnosis of Lyme disease, 21% had active Lyme disease, 19% had previous but not active Lyme disease, and 60% had no evidence of current or previous Lyme disease. Patients with no evidence of Lyme disease had a median of 4 serological tests for Lyme disease, 7 office visits, and 42 days of antibiotic treatment for Lyme disease and were noted to have high levels of disability and distress.

Appropriate treatment of Lyme disease has been associated with complications (e.g., ceftriaxone-associated biliary complications, iv catheter-associated gram-positive and gram-negative bacterial bloodstream infections, and Clostridium difficile-associated diarrhea). Ceftriaxone-associated biliary complications have been described in patients receiving ceftriaxone therapy for unsubstantiated diagnoses of Lyme disease [9]. Inappropriate antimicrobial therapy for Lyme disease has also been associated with septic thrombophlebitis, neutropenia, serum sickness, and antibiotic-associated colitis [7]. Overall, empirical treatment with iv antibiotics of patients with non-specific chronic fatigue or myalgia, based on positive serological results alone, has been determined to result in many more instances of antibiotic toxicity than cures of atypically symptomatic true Lyme disease [10].

The cost associated with prolonged parenteral therapy can be substantial [10]. The potential for emergence of antimicrobial-resistant bacteria exists with prolonged courses of antimicrobial therapy. Furthermore, the opportunity costs of administering prolonged courses of inappropriate parenteral antimicrobial therapy are enormous. In a study of 30 pediatric patients referred to the Lyme Disease Center at Robert Wood Johnson Medical School (New Brunswick, NJ) for evaluation of ongoing Lyme arthritis who were ultimately diagnosed with fibromyalgia, it was noted that many of the children had been subjected to unnecessary antibiotic therapy, many had missed prolonged periods of school (up to 9 months), and some required home tutoring [11].

Many patients with nonspecific complaints seek an explanation for their fatigue, pain, and mental fogginess [12]. Patients may be more willing to accept a diagnosis of chronic Lyme disease than an alternative diagnosis because Lyme disease is a “real,” potentially curable disease [12]. For some patients, a diagnosis of Lyme disease may be an acceptable end to a search for an explanation of their symptoms; in such a setting, seronegativity may not be viewed as evidence against the diagnosis [12]. Incorrect physician diagnoses, as opposed to self-diagnoses, of chronic Lyme disease may contribute to depression and stress when symptoms do not abate despite protracted courses of antimicrobial therapy [7]. Survey data show that 38% of physicians would recommend >6 months of antibiotic therapy for chronic Lyme disease, and that the most frequently recommended antimicrobial agent for the treatment of chronic Lyme disease would be iv ceftriaxone [13]. The relative ease of administering prolonged courses of iv antimicrobial regimens in the current era has undoubtedly impacted this practice.

Our case report and review of the literature validate the position of the American College of Rheumatology and the Council of the Infectious Diseases Society of America [14], both of which try to discourage the use of antibiotics for a patient with a nonspecific clinical presentation who does not meet the criteria for the case definition standard accepted for Lyme disease. The use of prolonged high-dose iv antimicrobial therapy for our patient’s chronic symptoms of mental fogginess, poor memory, chronic fatigue, and body numbness and pain was, in our opinion, unwarranted and ultimately led to her death.

References