CASE REPORT

Unique expression of chronic Lyme disease and Jarisch-Herxheimer reaction to doxycycline therapy in a young adult

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SUMMARY

I am a 24-year-old male who was diagnosed with chronic Lyme disease after 4 years of multiple, non-specific symptoms. I have written this case as first author with my faculty mentor listed as the coauthor. The objective of this report is to highlight the experience with doxycycline treatment. In 2007, at around age 19 years, I had an acute onset of sore throat, tonsillitis, low-grade fever, stiff upper back and neck muscles, migraines and severely stiff, cracking jaw joints. This led to >24 medical visits, multitudes of tests and examinations, and exploratory surgery over the next 3 years. In 2011, a Lyme-literate medical doctor (LLMD) diagnosed me with chronic Lyme disease. I started taking doxycycline 100 mg by mouth every 12 hours, leading to atypical sequences of events deemed a Jarisch-Herxheimer reaction by a LLMD. This case highlights the unique clinical expression of chronic Lyme disease and the Jarisch-Herxheimer response to doxycycline.

BACKGROUND

Lyme disease, the fastest growing vector-borne disease in the USA, has gained attention due to its increasing prevalence.¹ It is caused by the spirochaete bacteria, *Borrelia burgdorferi*. It is alarming that during 1992–1998, the number of reported cases increased by 70%. Furthermore, studies in Connecticut and Maryland estimated 7–12 unreported cases for every reported case of Lyme disease.² The implications of this are significant and could mean that the true number of annual cases of Lyme disease may be as high as 200 000 rather than 20 000.¹

Lyme disease is most prevalent in its endemic regions of the Northeast, most of North Central and the Northwest part of the USA.³ However, it is often overlooked that Lyme disease has been identified in all 50 states and, therefore, can be found nationwide.⁴

What makes Lyme disease unique is that it can become chronic Lyme disease, or Lyme disease that is persistent despite initial antibiotic treatment. The International Lyme and Associated Diseases Society (ILADS) describes chronic Lyme disease as continuous symptoms, including fatigue, cognitive dysfunction, headaches and sleep disturbance; neurological problems, such as demyelinating disease and peripheral neuropathy; and sometimes motor neuron disease.⁵ There are also neuropsychiatric complications, cardiac presentations such as conduction

delays and dilated cardiomyopathy, and musculoskeletal involvement. These symptoms persist despite 30 days of antibiotic treatment.⁵

The prevalence of chronic Lyme disease has been evaluated by two studies. A retrospective, population-based cohort study found the prevalence of chronic Lyme disease within a Lyme disease population to be 34%.⁶ The second study in a specialised clinic in an area endemic to Lyme disease found the prevalence of chronic Lyme disease to be 62% within a Lyme disease population.⁷ However, the Centers for Disease Control and Prevention states that 'Post-treatment Lyme Disease Syndrome' occurs in 10–20% of Lyme disease patients after 2–4 weeks of antibiotic treatment.⁸

The risk factors for Lyme disease include being in wooded or grassy areas, having exposed skin and not removing ticks properly.⁹ Additional risk factors for chronic Lyme disease include delayed diagnosis, delayed antibiotic treatment, improper dose or duration of treatment and persistent Lyme disease.⁵

One of the most complicating factors with Lyme disease that increases the risk of chronic Lyme disease is the time taken to make a diagnosis, which may be as long as 20 years. The long incubation period and unique, non-specific symptomatic presentation for individual patients make diagnosis difficult.¹⁰ This is especially true since the ELISA and western blot blood tests are not sufficiently sensitive, leaving many patients undiagnosed.⁵ For this reason, chronic Lyme disease is a clinical diagnosis, and laboratory results are used as supporting evidence.⁵

According to ILADS, the best treatment to prevent or treat chronic Lyme disease is prompt and aggressive antibiotic therapy that usually starts with high doses by oral administration. The first-line antibiotic therapies are doxycycline, amoxicillin, azithromycin, cefuroxime, clarithromycin and tetracycline given in higher than normal daily doses, with doxycycline being the most commonly used antibiotic (eg, doxycycline 200–400 mg daily).^{5 11} Furthermore, it is common to consider intravenous antibiotic treatment as first line in the treatment of Lyme disease with central nervous system involvement if the oral regimen fails, leading to refractory or recurrent Lyme disease.⁵ Combination of two or more antibiotics is increasingly used to treat chronic or refractory Lyme disease. The duration of treatment is individualised based on the patient's presentation. This treatment

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approach has proved successful in clinical practice; however, clinical studies are lacking. Therefore, risks versus benefits must be weighed before using such treatment strategies.⁵

A complicating factor of treating Lyme disease with antibiotics is the triggering of the Jarisch-Herxheimer reaction, which may accentuate disease symptoms.¹² The Jarisch-Herxheimer reaction has also been described as a systemic shock-like state following the use of antibiotic therapy. It is believed to be the result of endotoxins released from the spirochaete or, possibly, a cytokine-mediated response. This reaction is associated with fever, myalgia and possibly vascular collapse along with aggravation of the underlying illness.¹³ Jarisch-Herxheimer reactions are unique to spirochaete illnesses including syphilis, louse-borne relapsing fever, yaws, babesiosis and Lyme disease.¹³ Furthermore, a temporal relationship between the initiation of oral tetracycline treatment and the onset of the Jarisch-Herxheimer reaction (rigors and fever) has been reported.¹⁴

I suffered multiple systemic symptoms for several years before being diagnosed with chronic Lyme disease. I wrote this report with assistance from my faculty mentor listed as coauthor. The significance of this case report is that it highlights the unique Jarisch-Herxheimer symptomatology and chronology in greater detail than other case reports. In addition, despite the fact that this reaction may be associated with the use of an antibiotic, the antibiotic therapy should be continued to complete the course.

CASE PRESENTATION

Beginning in 2007, I was a healthy 19-year-old white male, weighing 160 pounds. I was not on any current medications and had no medical conditions. I never used recreational drugs and had no known drug allergies. I was a college student who returned home over summer breaks. My parents' house was located on the edge of a wooded forest heavily inhabited with deer and wildlife.

My present illness began in the autumn of 2007, about a month after cutting down several hundred pine tree branches adjacent to a heavily wooded, deer-inhabited forest. I developed a sudden onset of sore throat, fever, severe pain and crepitus of the jaw joint, twitching eyes, panic attacks, OCD-like behaviour, cluster migraines, tight muscles in the upper back and neck, and thumping in the head with exercise. These symptoms lasted for 3 weeks before slowly decreasing in severity, yet still present through summer 2008. Around this time, I was also diagnosed with mild aortic regurgitation after a stress test was performed by a cardiologist.

In the summer of 2008, I suffered with depression. I also developed the sensations of pressure and fluid in my head and jaw joint regions. These flared in the mornings and lessened by late afternoon and evening. Heart palpitations and irritable bladder symptoms also appeared at this time.

In the autumn of 2008, the depression began to diminish, but all other symptoms remained. In late October, I experienced 2 days of acute pain in left ribcage and left abdominal area. On admission to the emergency room for pain, the triage nurse found it odd that my heart rate was below 40 bpm. The ER physicians found nothing significant causing the pain and recommended analgesia and antacid. The only abnormal finding was elevated granulocytes (73.4%), low lymphocytes (15.9%) and high monocytes (7.7%) on complete blood count (CBC).

Through the winter of 2008 and spring of 2009, the heart palpitations became worse, mainly immediately postexercise, as the heart rate was dropping back to normal. I had one severe episode of tachycardia in early spring 2009 while playing basketball. I remained conscious, but the paramedics took me to

the hospital by ambulance. The tachycardia was self-limiting and I was discharged later that night.

In late spring 2009, I suddenly awoke in the middle of the night with severe lower, left back pain that radiated from the bottom of the rib cage and down into the left buttocks and hip. I had another CBC carried out that showed low lymphocytes (20.5%), high monocytes (8.2%) and high eosinophils (7.8%). All other CBC values were normal. Since that night, I have had lower left back, hip, tailbone and leg pain everyday to date. Severity of the pain fluctuates from day to day and depends on position and activity. I tried to exercise through the pain at first, but experienced severe damage to my left ankle playing basketball.

In the autumn of 2009, I had chronic sinusitis, muscle fasciculations, irritable bowel syndrome, and tingling and pain in my feet and toes. I was placed on 4 weeks of amoxicillin 500 mg every 8 hours orally for chronic sinusitis.

In February 2010, a digital rectal examination by urologist led to diagnosis of prostatitis. Then in summer of 2010, I had another CBC, which showed high monocytes (10.1%) and eosinophils (13.3%). All other CBC values were normal. Abdominal MRI, barium contrast CT scan, colonoscopy, endoscopy and food allergy tests were performed in March 2010. All results were normal. I then had exploratory surgery to investigate a sports hernia, which was absent. The healing from the surgery took much longer than expected, and it left me in more back, hip and tailbone pain than before the surgery. In autumn of 2010, I started prolotherapy injections, receiving six courses over the next 8 months. The lower back and joint pain was reduced by ~50%, but the fatigue became worse. Towards the end of the 8 months of prolotherapy, I saw a Lyme-literate medical doctor.

INVESTIGATIONS

In summer 2011, the Lyme specialist made a clinical diagnosis of chronic Lyme disease. I also had positive antibodies for the Lyme bacteria, *B. burgdorferi*, on the western blot performed by IGeneX. I was started on 3 months of doxycycline 100 mg orally two times per day, 20 billion CFU of a multistrain probiotic and 500 mg of *Saccharomyces boulardii*. By the second dose, I was 'feeling feverish and tired'. By the end of the second day, I had a low-grade fever, sore throat, sinus congestion and loose stools. At the end of the third day, my nose was completely 'blocked of airflow by painful congestion', sore throat, watery diarrhoea, headache, stabbing pain in the upper back muscles, increased fasciculations and fatigue. The nasal congestion led to the sensations of being suffocated, which led to panic attacks. The discomfort was so severe in the evening of the third day that I went to the emergency room, concerned that it was an adverse reaction to the doxycycline. The ER physician sent me home with a few days of lorazepam therapy for sleep. The next day I spoke with the Lyme specialist who suggested that this was a common Jarisch-Herxheimer reaction resulting from the killing of the Lyme spirochaete, *B. burgdorferi*, and that it was not an allergic reaction of the antibiotic, and the antibiotic therapy should be continued to complete the course. The nasal congestion and accompanying symptoms remained acute for days 3–7 of the doxycycline treatment.

As the flare-up of symptoms started to subside, the fatigue remained, and the watery diarrhoea changed to loose stools over the next 2 months. Over the course of the doxycycline treatment, my weight declined from 165 to 130 pounds without significant decrease in caloric intake. I had a CBC with differential performed every 2 weeks while on the doxycycline, and my

eosinophils declined from 14% at the start of treatment to 5% (normal reference range 0–6%) by the seventh week of treatment; however, it increased back to 7% by the ninth week, when I discontinued doxycycline and began to treat the chronic Lyme disease with more natural alternative/complementary therapies. Furthermore, CBCs, liver enzyme tests and basic chemistry tests were ordered by my Lyme disease specialist after the doxycycline treatment was completed. All results from these blood tests were within normal limits.

TREATMENT

In winter of 2011, my Lyme specialist prescribed me cholestyramine for oral suspension USP, one to four 9 g packets per day as tolerated to bind and detoxify the biotoxins associated with *B. burgdorferi*. Pursuant to my own research, I also started Symbiotics Colostrum Plus (bovine colostrum) 5 g orally two times per day, one medium raw garlic clove by mouth with each meal, Lakewood organic aloe vera gel 4 ounces orally two times per day, Sun Chlorella A 3 g orally daily, high doses of probiotic yogurt and Garden of Life's Raw One or Men multivitamin. I once again experienced the Jarisch-Herxheimer reaction when first starting the raw garlic, bovine colostrum and aloe vera gel. The symptoms included bloating, painful gas, diarrhoea, headache, low-grade fever, increased fatigue, waves of depression, vertigo and increased muscle fasciculations. The symptom flare lasted for ~7–10 days, and then dissipated, leading to much improved health. The gastrointestinal symptoms disappeared and stools normalised in consistency and frequency. I also had a substantial reduction in depression, fatigue, pain and muscle fasciculations.

OUTCOME AND FOLLOW-UP

My health has been improving steadily. I keep a medical journal and note a flare in symptoms of fatigue, pain and 'brain fog' with an episode of a migraine roughly every 28 days. A day or two following the migraine I experienced an odd smell from my armpits that 'smelled like formaldehyde'. Since treatment has begun with the natural products, there has been steadily decreasing symptom severity.

My diet included vegetables, fruit, complex carbohydrates and animal protein with about 2000 calories daily. However, consumption of raw fruits and vegetables was hindered due to allergies to fruit and vegetables in the raw form. Since June of 2011, I have consumed mostly organic foods and refrained from high sugar foods, simple sugars and processed foods.

DISCUSSION

With a search of the PubMed database, 35 articles were found that pertained to antibiotic treatment of Lyme disease and/or the Jarisch-Herxheimer reaction as a result of antibiotic treatment. The term searches 'chronic AND lyme AND doxycycline AND case' and 'herxheimer AND doxycycline' on 3 November 2012 provided 20 and 17 references, respectively. One similarity between this case report and the literature is the choice to use doxycycline as the first-line treatment for Lyme disease.^{15–18} Also, the dose of doxycycline found within the literature was comparable to this case, ranging from 100 mg two times per day to three times daily.^{15 16 19 20} Jarisch-Herxheimer reaction occurred in 12% of the cases in one study¹⁹ and 15% of the cases in another study.²¹ However, many patients with Lyme disease were treated with doxycycline without any sign of a Jarisch-Herxheimer reaction.^{22 23}

The significant differences between this case report and the findings in the literature review are the well-defined chronology

of the reaction and the unique symptoms presented. For example, one article states that Jarisch-Herxheimer reactions were considered adverse events and defined simply as an intensification of symptoms within the first day of antibiotic use.¹⁹ A second article stated that the patient probably experienced a Jarisch-Herxheimer reaction after receiving doxycycline, but it did not specify time of onset or patient-specific symptoms of the reaction.²⁰ Another article stated that the 5 patients receiving doxycycline experienced no Herxheimer reaction, but 23 of 46 patients receiving amoxicillin–probenecid experienced Herxheimer reactions at varying times during the first 4–5 days of treatment.²⁴ While there were many references to the Jarisch-Herxheimer reaction in the literature review, none gave a detailed description of patient-specific time frame and symptomatology;^{19 20 24} some received doxycycline treatment without even referencing the Jarisch-Herxheimer reaction.²⁵ The case report we present stands out from these articles by providing detailed description of patient-specific symptoms such as complete nasal congestion, watery diarrhoea, sore throat, low-grade fever, stabbing myalgia, fatigue, headache and increased fasciculations. Furthermore, Jarisch-Herxheimer reaction symptoms in this case stand out by differing from the typical symptoms of sudden rise in respiratory rate, blood pressure and heart rate followed by a phase of flushing, profuse sweating and possibly cardiovascular collapse and death.²⁰ The Jarisch-Herxheimer reaction is a unique response, varying in expression from patient to patient based on their Lyme disease symptomatology. Therefore, healthcare professionals should be knowledgeable as to the possibility and physiological effects of these reactions. It is important to note that the antibiotic treatment should be continued to complete its course even during the presence of Jarisch-Herxheimer reaction, unless doing so increases risk of death. Although natural therapies were used in this case, their efficacy and safety should be systematically evaluated in patients before any of these can be generally recommended for use in patients.

Learning points

- Lack of clinical knowledge regarding the Jarisch-Herxheimer reaction may lead to the assumption that I am experiencing an allergy or an adverse drug reaction. This could lead to the discontinuation of a treatment regimen that is actually effective and necessary for the patient.
- Not all Jarisch-Herxheimer reactions will have the same time of onset or the same presenting symptoms in all patients.
- Jarisch-Herxheimer reaction does not occur in all patients with Lyme disease when receiving doxycycline or other antibiotic treatments.

Contributors CH described the clinical findings and prepared the first draft of the manuscript. MN assisted in planning, organisation and review of the manuscript. Both authors revised and approved the manuscript for submission to the Journal.

Competing interests None declared.

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