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Case Report Open Access

# Tertiary Lyme Disease

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**Abstract**

Tertiary syphilis is a well-defined spirochete disease occurring many years after the primary infection. It occurs in approximately 30% of untreated syphilis patients and is mostly seen in the cardiovascular system, the brain and the skin. Other organs such as liver of joints show much less frequent involvement. In this discussion, we consider monoarticular arthritis and Alzheimer's disease as tertiary Lyme disease, another spirochete malady. Our patient with so called "Montauk knee" had a positive Lyme serology and negative clinical and laboratory findings of other arthritis's. Treatment with amoxicillin and rifampin led to a cure of her arthritis. We postulate that our patient with dementia had tertiary Lyme disease because Lyme spirochetes have been cultured from Alzheimer's disease brains and because PCR findings have also confirmed the presence of *Borrelia burgdorferi*. We have shown how the spirochetes are likely responsible for the biofilms in the organs involved; such biofilms are integral to the pathology noted in the disorders in question. We discuss how biofilm dispersers together with bactericidal antibiotics are or are not effective in treatment.

**Keywords:** Alzheimer's disease; Lyme serology; arthritis; Amoxicillin

## Introduction

Lyme disease is a spirochete disease transmitted from the bite of a blacklegged tick infected with *Borrelia burgdorferi*. In this regard, it differs from syphilis, the classic spirochete disease, which is usually transmitted sexually. Syphilis can be divided into stages (primary, secondary, latent, tertiary) relatively easily whereas Lyme disease, after its primary stage cannot be as easily categorized. We report herein on two patients with tertiary Lyme disease: one actual with Lyme arthritis and one recreated posthumously from pathology and available information. The only information that was not de-identified in the second patient was age and sex.

## Case Reports

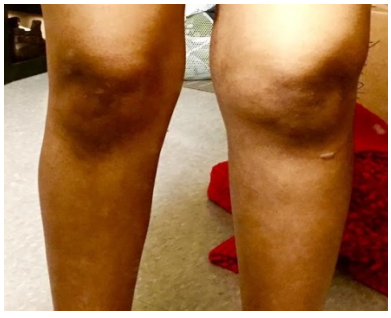

**Figure 1:** Lyme Arthritis, "Montauk" knee; treated for 1 month with 200 mg Doxycycline daily; no resolution.

Patient one, an undergraduate 21-year-old woman of East Asian descent developed arthritis in her left knee. This was characterized by marked swelling (Figure 1) limited range of motion, and pain worsened by motion.

She had no known history of a tick bite or a rash, especially no erythema migrans rash. At the time her arthritis developed, she had a positive Lyme serology and negative ANA, RPR, and rheumatoid arthritis factors. Her routine complete metabolic panel including uric acid was also within normal limits. Therapy, for presumptive Lyme arthritis, with doxycycline 200 mg daily was initiated, and she had been taking this faithfully for one month. The swelling and pain were still present after that course of treatment.

This protocol with doxycycline was considered a treatment failure and was discontinued. She was begun on amoxicillin 500 mg three times daily and rifampin 300 mg daily. After one month of treatment, the swelling and pain were gone (Figure 2) and she wanted to know "when she could begin running again?"

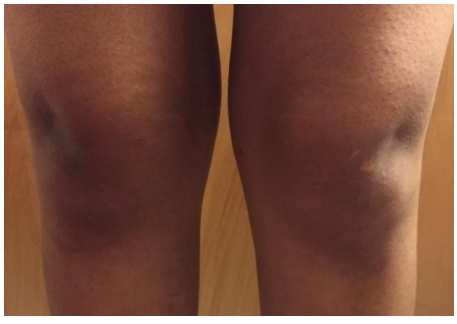

**Figure 2:** Lyme arthritis resolved; treated with Amoxicillin 1500 mg daily and rifampin 300 mg qd.

Patient two was an 83-year-old man with severe dementia. It is unknown whether he had been a smoker, or if he had diabetes, or if he

consumed diet soft drinks as favoured beverages. His hippocampus was shrunken on gross pathology and showed many senile plaques and tangles on routine microscopic pathology (Figure 3).

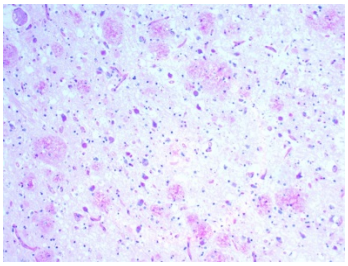

**Figure 3:** Plaques and tangles are clearly noted. PAS stain (10X).

The plaques were formed of biofilms as evidenced by positive staining with PAS and Congo red: these stained the extracellular polysaccharides and amyloid that make up the biofilm (Figures 3 and 4).

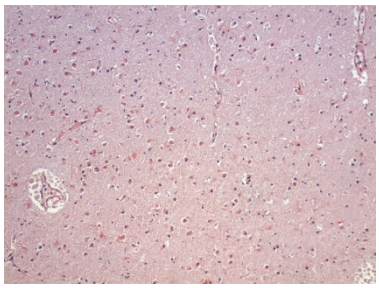

**Figure 4:** Similar staining to PAS; Congo red stains the amyloid that forms the infrastructure of the biofilm (Congo red 10X).

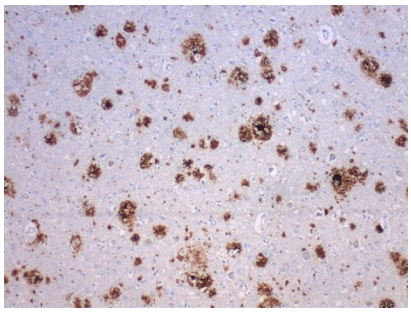

**Figure 5:** Aβ deposits noted throughout the tissue. Aβ immunostain (10X).

Beta amyloid (Aβ) was prominent throughout the tissue (Figure 5). Aβ co-localized with the biofilm (Figure 6). The innate system molecule Toll-like receptor 2 (TLR2) was up regulated throughout the tissue (Figure 7). Biofilms were also present inside the neuronal cells (Figure 8) and Aβ was also noted intracellularly (Figure 4).

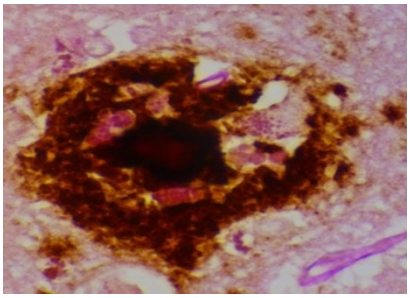

**Figure 6:** Biofilm (pink) and Aβ co-localize and Aβ noted intracellularly (arrows). Aβ immunostain and PAS (40X).

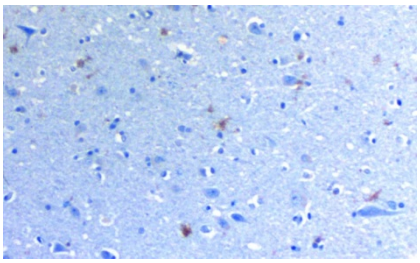

**Figure 7:** Brown-black deposits are TLR2. Toll-like receptor 2 immunostain (10X).

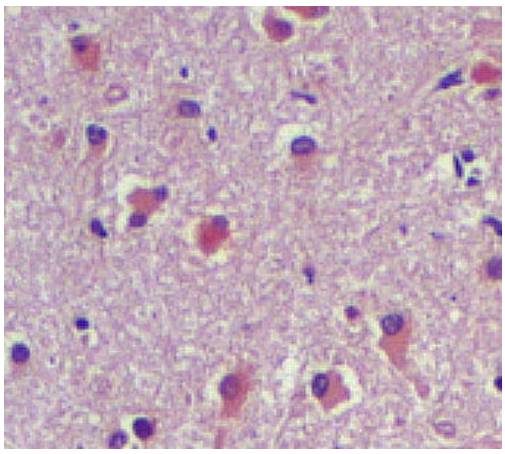

**Figure 8:** Biofilms noted inside neurons (Congo red 40X).

## Discussion

Patient one presumptively had Lyme arthritis because she had a positive Lyme serology and negative syphilis, lupus erythematous, and rheumatoid arthritis serology. Also negative was her uric acid. There were no skin or nail changes of psoriasis. Doxycycline was ineffective, and the regimen of amoxicillin and rifampin cleared the disease.

Ehrlich has shown that nearly all arthritis requiring joint replacement was associated with microbial biofilms [1]. Consequently,

in a patient with arthritis and a known positive serology, it is not unreasonable to postulate that this was Lyme arthritis and was associated with biofilms made by *Borrelia burgdorferi* [2]. Such biofilms would be impenetrable by doxycycline as well as most other antibiotics [3].

Amoxicillin, a known bactericidal antibiotic, along with rifampin, a known biofilm dispersing agent, resulted in effective treatment for our patient. The rifampin "poked holes" in the biofilm allowing the amoxicillin to penetrate and kill the organisms inside [4]. This is similar to the positive effect noted with ameliorating arthritis in a case series of osteoarthritis treated with amoxicillin and citalopram (another biofilm disperser) [5]. It is also similar to the near eradication of leprosy, another chronic biofilm disease, which had responded to rifampin coupled with dapsone [6].

Patient two had Alzheimer's disease (AD) evidenced clinically by severe dementia along with characteristic (post mortem) pathology. Riviera has shown as many as 25% of patients with AD have associated Lyme spirochetes on PCR of brain samples (75% have dental spirochetes) [7].

Miklossy, in confirming the findings of Macdonald, has cultured *Borrelia burgdorferi*, from AD brains [8,9]. For discussion purposes, with many patients having positive PCRs and cultures of *Borrelia burgdorferi*, we will assume our patient had tertiary Lyme disease.

Tertiary syphilis (general paresis) the prototype spirochete disease has been shown to be identical in pathology to AD [10]. Where Lyme spirochetes have been cultivated from AD brains, it is not unreasonable to postulate that Lyme spirochetes in the brain cause similar clinical disease as does syphilis because of the identical pathological findings seen with the spirochetes (*T. pallidum*) in syphilis. Syphilis, in all its stages except for tertiary, is curable by penicillin [11]. Further, since no spirochetes are known to be resistant to penicillin, Lyme spirochetes would be similarly eradicated as are luetic spirochetes in all stages save for tertiary. And, most important, even if the penicillin (plus a biofilm disperser) was effective in killing the Lyme spirochetes in tertiary disease; the debris field (Aβ, biofilm remnants, tangles, and other detritus) would be too extensive for the microglia to clear [12]. Hence, treatment of Lyme disease with penicillin must be given prior to the onset of tertiary disease; i.e. before the AD is evident [11].

This identifies a difference in the treatment approach for different forms of tertiary Lyme disease. In Lyme arthritis, the addition of rifampin to a bactericidal antibiotic was curable; without the rifampin, treatment for syphilitic arthritis - "is in the main not encouraging" [13]. With the rifampin, treatment for arthritis in syphilis would likely respond like the Lyme arthritis in our patient. In AD, treatment with a biofilm disperser and penicillin would likely not be effective and possibly would make the situation worse, conceivably even giving the patient a persistent cerebral Herxheimer reaction [14].

## Acknowledgement

All protocols were done with the approval of the Drexel University College of Medicine Institutional Review Board.

## Conflict of Interest

None of the authors has any conflicts.

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