Tertiary Treponematosis

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Abstract

With recent findings in arthritis and dementia, it has become apparent that Lyme treponemes and oral treponemes have tertiary clinical findings similar to tertiary syphilis. The primary findings are in the skin or mucous membranes with syphilis demonstrating a chancre, Lyme disease erythema chronicum migrans, and oral treponemes dental plaque. Secondary disease is not as clear in Lyme and oral treponematosis as in syphilis, but tertiary is surprisingly similar with treponemes from all three being found in the brain and joints. Lyme and oral organisms have been visualized in the brain and joints by PCR. "Montauk knee" was actually "Lymer" arthritis before the organism was shown to be the causative agent. With the demonstration of the organisms in these locations, treatment should likely be reconsidered. It would seem most logical to prevent them from arriving there in the first place. This would be entirely similar to the prevention of neurosyphilis by appropriate treatment in the earlier stages. Persistence so these organisms is likely due to biofilm production.

Keywords: Treponemes; Borrelia burgdorferi; Treponema denticola; Arthritis; Alzheimer’s disease; Dementia; Penicillin; Primary disease; Secondary disease; Tertiary disease

Commentary

Recent polymerase chain reaction evaluation of brain tissue from patients with Alzheimer’s disease has revealed the presence of two types of spirochetes: Borrelia burgdorferi spirochetes from Lyme disease and oral spirochetes such as Treponema denticola. This makes Alzheimer’s disease similar to the dementia seen in tertiary syphilis caused by the Treponema pallidum spirochete [1]. This analysis followed a previous work in which similar findings were present, also on evaluation by polymerase chain reaction [2]. Both these works clearly implicate Alzheimer’s disease as being an infectious disease with a spirochetal origin.

Interestingly, despite the current guidelines for the treatment of Lyme disease, there is considerable literature on the persistence of Borrelia burgdorferi (as well as other spirochetal entities) in patients and priamtes treated this way. This information suggests that our methods for treating Lyme disease, and likely other spirochetes, may be fundamentally flawed. While antimicrobial therapies generally are effective in treating the symptoms of Lyme disease, some patients continue to show signs of persistent infection. Spirochetes have been shown to persist in the tissues rhesus monkeys treated with ceftriaxone and/or doxycycline [3]. Priem et al found that synovial fluid samples and urine samples were negative in persisting infections, but on PCR they found B. burgdorferi in synovial membranes [4]. Borreliar persistence in vivo was not associated with increasing minimal inhibitory concentrations (MICs) indicating this persistence was not due to acquired resistance [5].

The mechanism which allows these organisms to persist remains unclear. One postulate is spirochetes may enter a dormant state [6-8]. Another possibility for the bacterial evasion of antibiotic therapies is biofilm production. Since it was first shown in 1978 that bacteria made biofilms, [9] spirochetes have also been shown to do similarly [10,11]. Interestingly, biofilms also evade culture detection [12]. Recently bacterial detection by a new technology called Ibis (the Ibis Biosciences T5000 biosensor system) was shown to be effective. In fact, organisms were found in 88% of cases presumed to be aseptic [13]. These joints were in patients with arthritis who either needed a replacement for a failed joint implant or were receiving their first new joint [13]. It is becoming clearer and clearer that our traditional antibiotic therapies are not effective in treating certain types of bacterial/spirochetal communities, namely biofilms, nor is there a standardized modality for detecting organisms in these situations.

While the activity of these spirochetes in the development of AD remains unclear at this point in time, the presence of these organisms in tissue samples from patients with known AD is certainly a cause for concern and further inquiry. Considering the data on spirochetal persistence despite antibiotic therapy, it may be prudent to explore the connection between spirochetes, the production of biofilm that contains amyloid, and the plaques of AD. AD may in fact representative of the ineffective treatment of Lyme as well as other treponenal infections resulting in the neurologic state of dementia.

In syphilis, progression of primary disease to tertiary syphilis is well defined. The chancre (primary) begins approximately 3 weeks after exposure; the papulosquamous rash begins 6 weeks to 6 months later; latent syphilis can last from 5 to 50 years (average, 20 years); then, tertiary disease occurs in the skin, cardiovascular system, or brain in approximately 40% of patients. Sixty percent of patients infected live and die without serious sequelae [14]. The timelines for Lyme disease and periodontal disease are less well understood. The primary manifestations of Lyme and periodontal disease are erythema migrans and dental plaque, respectively. Generalized symptoms (e.g., low-grade fever, lymphadenopathy, malaise) occasionally represent secondary Lyme disease and occur from 2 to 6 weeks after infection. Arthritis and dementia (and likely cardiac disease) are tertiary in both. Secondary periodontal disease is uncharted. Miklossy1 has found that the
plaque, tangles, curly fibers, and deposition of amyloid are the same in Alzheimer’s disease as in syphilis.

We present two patients who may illuminate the problem:

A 42 year old woman, who constantly tended her fruit trees and gardens in rural New Jersey, noted the onset of a non pruritic pink lesion on her upper chest. Two weeks after the appearance of the lesion, she developed a low grade fever, severe arthralgias and malaise. The skin lesion had expanded into a seventeen cm targetoid lesion in the center of which was a tiny, engorged, black-legged organism.

Her dermatologist removed the organism and identified it as an Ixodes tick and identified the rash as erythema chronicum migrans. Although it is always a concern, penicillin resistance has not compromised this concept.

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Fifteen years later, this now 57 year old woman developed Alzheimer’s disease along with a rapid deterioration in her overall health.

The second patient, a 51 year old Pennsylvania businessman and avid golfer, presented with aphthous stomatitis. He was treated for that and referred to the periodontist for treatment of the considerable plaque which had been developing on his teeth. His wife had requested he ask the dermatologist about this. The periodontist and dental assistant removed the plaque, and, at the end of the visit, he was told to “rinse his mouth and spit”. Considerable bright red blood was present in the spittle.

Thirteen years later, he developed Alzheimer’s disease.

Latent disease and persistence of organisms occur in all the untreated, or inadequately treated, treponematoses. Latent syphilis is discovered by a reactive serology; a similar response in the other treponematoses may be present but is not quantifiable. This makes treatment during this period much more difficult, but the simple fact is the organisms persist and ultimately lead to significant disease.

Given that these organisms are present in both the joints of patients with arthritis and the brains of patients with Alzheimer’s disease, it is evident that our traditional antibiotic therapies are not effectively treating these diseases. Alzheimer’s disease and chronic arthritis may in fact be representative of the ineffective treatment of Lyme disease and other treponemal infections. Miklossy’s1 work strongly endorses this concept.

Regardless of the mechanism by which spirochetes survive and cause chronic illness—whether through dormancy or biofilm production—it is clear that patients are not being treated early or aggressively enough to prevent these diseases. In syphilis, penicillin at any stage prior to tertiary is effective in eradicating the disease. The use of penicillin in the treatment of syphilis was not established through a clinical trial, but rather was based on its use in clinical practice [15]. Moreover, because of our aggressive and early treatment of the disease, late neurosyphilis (manifested by tabes dorsalis and general paresis) has become exceedingly rare. Neurosyphilis has resurfaced with the HIV epidemic, but patients with HIV infection and neurosyphilis have been aggressively treated and all have improved [16]. Although it is always a concern, penicillin resistance has not developed in any treponemal infection to date. Also, because of its bactericidal nature, the organisms are not easily able to develop biofilms preventing the sharing of resistance genes in that milieu.

In light of these concerns, we propose that, as a scientific community, we consider an alternative approach to the treatment of Lyme disease as well as of spirochetal infections in general. Rather than treating erythema migrans with the traditional regimen of doxycycline, 7 we should consider a bactericidal approach that may ultimately prevent severe neurologic sequelae. Prevention of these sequelae from oral treponemes is also very important. We might consider pre-treatment with bactericidal antibiotics in patients undergoing dental procedures as a way to protect the brain, similar to the way we protect implanted joints. Moreover, as in syphilis, bactericidal treatment could likely be implemented at any time during the long latent period prior to the appearance of tertiary disease.

For now the most promising, most cost effective, and most rational approach is to prevent these organisms from ever reaching the joints or brains in the first place. We believe it is exceedingly important to kill them before they have the opportunity to do further damage. The need is pressing for more investigation regarding the detection as well as treatment of these chronic infections. Although we are beginning to understand more fully how bacteria are able to evade our current therapies, we currently have neither sensitive detection techniques nor, unfortunately, treatment to rid these infections once established.

References


