Treatment of Amyotrophic Lateral Sclerosis and Multiple Sclerosis With Antibiotics

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INTRODUCTION

The concept of treating infections and other serious diseases based on possibility rather than probability is not new. Who among the readers of this essay have not added an antibiotic to the treatment of fever of unknown etiology because of the possibility that it may be associated with a bacterial infection?

Have not most oncologist given patients with serious cancer chemotherapy because of the possibility that it might help them? It is in this frame of reference that this essay suggests that ceftriaxone should be added to treatment programs for amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) because of their possible relationship to Lyme disease.

First we will discuss the lessons that can be learned from syphilis, which is the spirochetal disease most closely related to Lyme disease.[1] Then, we will present anecdotes of cases of ALS and MS seen at the Waisbren Clinic. These anecdotes support the conclusion that there is a possibility that treatment for Lyme disease might help some patients who live in areas where Lyme disease is endemic and who present with syndromes compatible with MS and ALS. [2] Finally, articles in the literature will be alluded to that may help explain the anecdotes in this article.[3-20]

SYPHILIS AND LYME DISEASE

Lessons from syphilis might well be applied to consideration of Lyme disease because both of these conditions are caused by spirochetes. Both disease have primary, secondary, and tertiary manifestations.[3,4,5] Both have elements of autoimmunity. In the case of syphilis, the tertiary phase may respond to antibiotic treatment given many years after the first phase.[5] That spirochetes can remain alive in the body in the quiescent state for years may validate the treatment of Lyme disease after a long interval after onset.[5] Both syphilis and Lyme disease respond with a Herxheimer reaction to antibiotic therapy given long after exposure.[6,7] Both syphilis and Lyme disease respond to the same type of antibiotics.

ALS AND LYME DISEASE

In 1988, a woman whose mother was in the last stage of ALS asked me if it were possible that her mother's clinical picture was caused by Lyme disease. Prior to the rapid advance of ALS, Lyme disease was suspected because her immunofluorescent antibody titer to Borrelia was over 1:1000.[21] Because of the rapid progression of the disease and the demonstration of anti-Borrelia antibody, the patient, her daughter, and myself decided that a course of ceftriaxone might be worthwhile. This was because the drug had recently been found to be active against Borrelia.[22] Ceftriaxone was given intravenously at a dose of 2 gms. per day. On the fourth day, six hours after a dose of ceftriaxone, the patient was found dead in bed. At that time, all concerned felt that her death was due to a manifestation of the ALS. In the face of present knowledge that the Herxheimer reaction occurs after ceftriaxone treatment for Lyme disease, we now know that Herxheimer reaction might have occurred and been involved in the fatal outcome.[6,7]

I then learned that Dr. Neil Cashman, a neurologist at the University of Wisconsin Medical School, had saved 54 sera obtained from patients with ALS. He was kind enough to ask Dr. Ronald Schell, a microbiologist at his University, to do anti-Borrelia immunofluorescent antibody titers on this serum. Four of these titers were positive for anti-Borrelia antibodies. We published these findings in *The Lancet*, with the suggestion that it might be worthwhile to treat some cases of ALS with ceftriaxone for presumed Lyme disease.[8] In 1990, Halperin and his associates confirmed our findings that anti-Borrelia antibodies were not infrequently found in cases of ALS.[9] They treated nine patients who had ALS and antibodies against Borrelia with antibiotics. Three patients appeared to improve. Three progressed. Three apparently were unaffected. Carelli reported that six patients with ALS failed to respond to treatment with ceftriaxone.[23] Thus the basis for treating ALS with ceftriaxone are hearsay reports, the relationship of Borrelia burgdorferi to Treponema pallidum, the fact that Borrelia burgdorferi shows molecular mimicry with human tissue, and the fact that cases of ALS exhibit antibody titers against Lyme disease.[8,9] The possibility that Borrelia burgdorferi can affect human nerves is illustrated by its activity against nervous tissue in the neurologic network of the heart in patients who develop heart block from Lyme disease.[24]

MULTIPLE SCLEROSIS AND LYME DISEASE

In 1994, I saw two cases of classic severe far advanced MS that followed documented Lyme disease that they had suffered many years before. I treated both of these with ceftriaxone with indifferent results.

In 2001, I saw in close succession, two patients who had exposure to tick bites that had resulted in a classic Lyme disease dermatologic reaction.

The first patient had been sick for a year with fatigue, fever, paresthesia, and unsteadiness on her feet. An MRI of her brain had revealed findings consistent with MS. Her search of "the web" convinced her that she had Lyme disease because she had been exposed to ticks and had a bull's-eye rash just before becoming ill. Serologic tests were equivocal. I agreed with her diagnosis and arranged for her to have a 21-day course of ceftriaxone 2 grams intravenously. She became afebrile, her joint pain disappeared and she became essentially asymptomatic. Within several months she was able to resume her fulltime employment from which she as on disability leave. MRIs done yearly since then have shown no progression of the abnormalities that were considered consistent with MS. She remains on suppressive doxycycline therapy.

On July 4, 2001, the second patient had a tick bite followed by a bull's eye rash. The rash persisted for a month and her mild arthritis flared to the point that she was becoming unable to work. She concluded that she might have Lyme disease and I agreed. She was given a 21-day course of ceftriaxone 2 grams intravenously with gradual improvement and she returned to work. She was maintained on oral doxycycline, azithromycin, and cefuroxime. After the initial clinical response she developed paresthesias and balance difficulty, and in July 2003, became so ataxic that she had difficulty in standing. She was hyperreflexic. Her MRI showed findings compatible with MS. At that time, I decided to treat her with glatiramer acetate and another course of intravenous ceftriaxone.[25] She stated five days after the start of glatiramer acetate that her balance greatly improved. She is now back to work fulltime but she is still somewhat ataxic and has joint pains more typical of Lyme disease then of MS. She is being maintained on oral doxycycline and azithromycin. A delay in getting the intravenous ceftriaxone started, allowed her to observe a rapid clinical response of her ataxia that possibly was because of the glatiramer acetate. The tantalizing aspect of this part of her history is that it raises the speculation that in cases of Lyme disease with autoimmune features, glatiramer acetate might be worthwhile as part of the initial preventive therapy.

ARTICLES THAT SUPPORT THE HYPOTHESIS

There are articles in the medical literature that are consistent with the hypothesis that Lyme disease can cause a clinical picture almost identical to MS. Pachner has called Lyme disease the great imitator.[3] Chmielewska-Badora has questioned whether there is a connection between Lyme disease and MS.[10] Lakos has stated that Lyme disease may imitate MS.[11] Lana-Peixoto has reported positive serology for Lyme disease in MS.[12] Garcia-Monco has found antibodies to myelin basic protein in Lyme disease.[13] Martin has demonstrated that Borrelia burgdorferi can act as a trigger for autoimmune T-cell reactions within the central nervous system.[14] A possible explanation for this phenomenon is that Borrelia burgdorferi exhibits molecular mimicry with human nervous tissue.[16] Molecular mimicry might evoke antimyelin T-cells against myelin basic protein.[14] Baig, et al demonstrated cells secreting antibodies to myelin basic protein in cerebrospinal fluid in patients with Lyme neuroborelliosis.[17] Gay and Dick have referred to literature that suggests that Borrelia burgdorferi can cause demyelination as a sequel Lyme disease.[18,19,20] They stated, "It seems inevitable that some patients, especially in area where

Lyme disease is endemic, who have been labeled as “possible MS”, will ultimately be shown to have Lyme demyelinating encephalopathy.” They further suggested that, “A search for these patients should be undertaken in endemic areas.”[18] The endeavors reported here appear to have supported their suggestions.

DISCUSSION

If there are physicians who feel that the possibility of ALS and MS syndromes are worthy of a trial of ceftriaxone therapy, there are some caveats that should be kept in mind.

The patients and their families must be made aware that there is only a possibility that being treated with ceftriaxone might be beneficial. It must be emphasized to the patient that this is an attempt to help them and not an experiment. The relative safety of the ceftriaxone can be emphasized. The patient should have possible exposure to Lyme disease, but serologic tests do not have to be positive to be considered for treatment. In addition, they are now medications that have been shown to have utility in the treatment of ALS and MS. They must eventually be included in the treatment plan. Riluzole has been found by some to be helpful in ALS and glatiramer acetate and beta interferon have utility in the treatment of MS.[25,26] When and how ceftriaxone should fit into the treatment program must be considered. In most cases a 30-day trial of ceftriaxone before using riluzole or glatiramer acetate does not seem unreasonable.

The possibility of a severe Herxheimer reaction should be considered.[6,7] ALS patients should be carefully monitored for this because of the respiratory difficulties inherent in this disease. A Herxheimer reaction must be prepared for in pregnant women because pregnancy has been found to be a high risk factor in women treated with penicillin for syphilis.

Kuhn has expressed the opinion that good hypothesis must be innovative enough to create an interest and open ended enough to invite further study.[27] The further study suggested by our hypothesis could be a mega analysis of patients treated for ALS and MS with ceftriaxone. These patients might be found through reports on the internet and in reports made to the societies dedicated to ALS and MS. These national ALS and MS organizations might be willing to act as a clearinghouse to find patients in whom a relationship between ALS or MS and Lyme disease seems likely. They might also be willing to solicit reports regarding the results of ceftriaxone therapy in patients with ALS and MS. This could be done by a questionnaire sent to patients in data banks.

The caveat regarding trying to evaluate treatment of ALS with ceftriaxone is that more than one precipitating cause of ALS probably exists. They include geographic, genetic, electrical and other microbial influences. [28,29,30] It may well be that only a minority of ALS syndromes are involved with Borrelia organisms. If so, only a small number of cases may respond to ceftriaxone. Treatment of only those patients with solid serologic evidence of disease or those from heavily infected areas may be most fruitful. Since ALS is almost inevitably fatal, only a few long-term survivors who received ceftriaxone will be of particular interest.

In cases of MS who are treated for the possibility of Lyme disease, evaluation of serial studies of the number of anti-myelin T-cells in their blood might be helpful.[14] In the case of ALS, molecular mimicry between the polypeptide in Borellia and in the lateral nerve cells will be worthwhile to ascertain.

A physician and his/her patient who consider treatment of ALS and MS with ceftriaxone must weigh pros and cons. The pros are that there are some rational reasons to do this and these

patients have enough to lose for them to “grasp at safe straws”. The cons are that hearsay evidence is always suspect, although one only has to hark back to the discovery of digitalis to realize that paying attentions to hearsay evidence has yielded results in the past.[31]

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