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Guest Commentary

Rheumatology Research in the 90s

By Allen C. Steere

Syphilis now has a competitor for the title of most complex infection. Because of the neurologic abnormalities it produces, Lyme disease is reminiscent of neurosyphilis.

Once present, the neurologic symptoms follow a slowly progressive course, in some instances for 10 years or longer. Most of these patients have subtle encephalopathy affecting the central nervous system. They have memory difficulty, depression, or sleep distruances but no seizures, myoclonus, or changes in the level of consciousness. They also have sensory symptoms, such as pain in the spine, accompanied by radicular pain in the limbs or trunk, and some have distal parethesias with intermittant tingling sensations in the hands and feet.

These symptoms are perilously close to those that occur in fibromyalgia, with the chronic fatigue syndrome, or instress-induced syndromes- conditions that are ever so much more common than tertiary Lyme disease. How then does one identify the patient with chronic neurologic abnormalities of Lyme disease?

The patients in question have characteristic findings on laboratory
evaluations as follows:
almost all were seropositive by ELISA, half of them had increased
cerebrospinal fluid (CSF) protein,
half had evidence of slight amounts of production of intrathecal
antibody to the spirochete, and 70%
had one or more of both abnormalities. In addition, more than 50% had
abnormal EMGs indicating polyneuropathy affecting both proximal and
distal nerve segments, and MRI brain scans showing areas of increased T2
signal intensity.

In other words, many of our patients had memory impairments on their
psychological assessments, had adnormal CSF anaysis, frequently
accompanies by EMG evidence of an axonal neuropathy. A number of them
also had intermittant attacks of arthritis. Combined with the evidence
of immunity to Borrelia burgdorferi, this is the clinical picture that
is most suggestive of Lyme disease.

There is some provocative information that now suggests that B
burgdorferi infection may cause a multiple sclerosislike picture [sic].
Dr Rudolf Ackermann in Cologne, Germany has described 44 such
patients. So far we have seen only one: 6 years after diseae onset, the
patient experienced progressive stiffness and weakness in the muscles of

his right arm and in both legs; tendon jerks were diffusely brisk, with bilateral ankle clonus and Babinski sign; and there were occasional episodes of incontinence.

MRI of the brain revealed numerous small areas of increased T2 signal intensity in the periventricular region on the right side. This scan is compatible with the diagnosis of multiple sclerosis; however, in the case of this patient, brain stem and auditory-evoked potentials were normal, and he did not have myelin basic protein in CSF. What *did* suggest Lyme disease was the fact that he had a serum IgG antibody response to B burgdorferi of 1 to 12,800 and he had evidence of intrathecal antibody production to the spirochete.

I want to emphasize that it is not yet proved that B burgdorferi causes this syndrome. The patient could have two diseases- Lyme disease and multiple sclerosis. What we lack is the discovery of the spirochete from the brain lesions or the CSF, or perhaps proof of its presence by polymerase chain reaction (PCR) amplification of borrelial gene segments- a technique that is not quite perfected for use in Lyme disease.

***If B. burgdorferi does cause this syndrome, it's absolutely amazing that this spirochete would mimic not only rheumatoid arthritis (RA) but

also multiple sclerosis (MS), two of the most puzzling and devastating
autoimmune diseases.***

***Now I would like to proceed to the issue of seronegative Lyme
disease. I am convinced this entity exists.*** We have evaluated
approximately 200 patients with late Lyme disease in the past 2 years,
and we found that nine, or 5%, were seronegative by ELISA. This finding
coincides with the figure from Ray Dattwyler, MD, at Stony Brook (SUNY),
who first described seronegative Lyme disease. He stressed that this
outcome is more likely to occur in patients who receive antibiotic
therapy during the first several weeks of infection. Indeed, six of our
nine patients (67%) did receive antibiotic therapy during the first
month of illness, a significantly higher percentage than in our
seropositive patients with late Lyme disease.

***I must emphasize the subtlety of the clinical picture in these
seronegative patients. Two had erythema migrans followed months later by
very mild episodes of arthritis lasting only days. Three of the
patients had a subtle encephalopathy/polyneuropathy picture, resulting
in some memory disturbance accompanies by slight numbness and tingling
in the extremities. They also have CSF and EMG abnormalities. **Two of
the patients with neck pain had EMGs that revealed cervical

radiculopathy.** The two final patients had a more generalized pain syndrome with tender points on examination- the clinical picture of fibromyalgia. Three of the patients (one with arthritis and two with neurologic abnormalities) had only a cellular immune response to the spirochete.***

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