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Case Report

Meningoradiculitis and transaminitis from neuroborreliosis: A case of variant Bannwarth syndrome

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ABSTRACT

Background: Lyme disease is a common vector-borne illness in the U.S. caused by Borrelia species spirochetes. Neuroborreliosis has variable presentations, rarely manifesting as meningoradiculitis or "Bannwarth Syndrome", characterized by painful radiculopathy, neuropathy, varying degrees of motor weakness, peripheral facial nerve palsy and

cerebrospinal fluid (CSF) lymphocytic pleocytosis. We present a case of Bannwarth Syndrome manifesting with transaminitis and significant weight loss.

Case presentation: A 60-year-old man with history of hypertension presented with 3 weeks of progressive back pain, bilateral arm and leg weakness, bilateral hand numbness and a right facial droop in absence of sphincter dysfunction. He reported an 11.3 kg unintentional weight loss and recent holiday to Egypt. Patient was afebrile with normal vital signs but with profound

transaminitis on presentation. Exam revealed a lower motor neuron right facial nerve palsy, diffuse quadriparesis, areflexia but isolated brisk ankle reflexes. A left complete facial palsy developed shortly after admission. Concern for leptomeningeal plus peripheral nerve involvement led to consideration of oncologic, infectious and inflammatory etiologies, along with Guillain-Barre variants. Contrasted MRI of the brain and total spine was normal. CSF revealed lymphocytic pleocytosis (cell count 134), elevated protein (156) with normal glucose, cytology, AFB culture, viral PCRs and paraneoplastic antibodies. Serum and CSF Lyme IgG and IgM were positive. IV Ceftriaxone 2 g daily was started one day after admission. EMG/Nerve conduction studies showed diffuse polyradiculopathy without evidence of Guillain-Barre syndrome. Babesia co-infection was considered given unexplained transaminitis but PCR and quantitation were negative. CSF following 1 week of antibiotics showed improving cell and protein counts with resolving transaminitis. On follow-up at 2 months, facial paralysis, pain, motor and sensory deficits had resolved with return to baseline weight and liver function tests.

Conclusions: Bannwarth syndrome, a subacute painful meningoradiculitis caused by Borrelia species infection, is an uncommon presentation of neuroborreliosis in the U.S. Our case demonstrates previously unreported features such as profound transaminitis and weight loss without evidence of co-infection. Clinical manifestations of neuroborreliosis are variable, thus it is important to consider Bannwarth syndrome in the differential of meningoradiculitis in areas where Lyme Disease is prevalent.

1. Introduction

Lyme disease is the most commonly reported vector-borne illness in the United States, caused by *Borrelia* species spirochetes [1]. About 10–15% of people infected with *Borrelia* species develop involvement of the nervous system, a manifestation of Lyme Disease diagnosed more commonly in Europe [1] and also known as Bannwarth syndrome. It is characterized by painful radiculopathy, neuropathy, varying degrees of motor weakness, lower motor neuron (LMN) facial nerve palsy and cerebrospinal fluid (CSF) lymphocytic pleocytosis [1]. We present an atypical case of Bannwarth syndrome presenting with significant weight loss and profound transaminitis.

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2. Case report

A 60-year-old right-handed man with history of hypertension presented with 3 weeks of gradually worsening midline neck pain progressing into his lower back subsequently associated with numbness and clumsiness of both hands. Over this time period, he experienced an unintentional 11.3 kg weight loss. Just prior to presentation, he developed a complete right LMN facial palsy and bilateral lower extremity weakness without sphincter dysfunction. He is a native of India and had immigrated to the United States 30 years prior, residing in northeastern United States. He had not been to India in 7 years but spent a holiday in Egypt 8 months prior to presentation. The patient did not recall a tick bite or skin lesion suggestive of erythema migrans and did not recall any particular recent outdoor exposures.

On admission, the patient was afebrile with normal vital signs but with profound transaminitis (alanine aminotransferase 1107, aspartate aminotransferase 906) and negative cytomegalovirus and viral hepatitis screening. Creatine kinase (CK) was normal. Neurologic examination demonstrated a LMN right facial nerve palsy with intact corneal reflexes bilaterally but impaired blink on the right, diffuse quadriparesis (right worse than left), and areflexia aside from isolated 3+ ankle deep tendon reflexes bilaterally. Throughout this time, severe central back pain persisted requiring neuropathic pain agents and opiates for adequate pain-control. Concern for a leptomeningeal process with radicular involvement led to the consideration of oncologic, infectious, and inflammatory etiologies, as well as Guillain-Barré variants.

Contrasted MRI of the brain and total spine was normal. CT of the chest, abdomen and pelvis was negative for malignancy as well as pulmonary tuberculosis infection. EMG/nerve conduction study demonstrated prolonged distal latencies in the right median, tibial, ulnar motor studies; slowed conduction velocity in the right tibial motor study; abnormal F waves were noted. A polyradiculopathy affecting both upper and lower extremities was highly suspected based on these nerve conduction findings. A mild to moderate sensorimotor neuropathy with demyelinating features but without evidence of acquired demyelination (i.e. temporal dispersion nor partial conduction block) was also noted, thus Guillain-Barre syndrome was considered unlikely.

Serum Lyme ELISA returned positive, confirmed with positive Western blot IgM and IgG. There were 3 positive IgM bands: 41, 39, 23. IgG bands 93, 66, 45, 41, 39, 23, 18 were also found. *Babesia microti* antibody IgM was 1:320 (Upper limit of normal [ULN] < 1:20) and IgG > 1:256 (ULN < 1:16), but *Babesia* PCRs (*B. microti, B. duncani, B. divergens*) were negative and quantitative buffy coat for blood parasite detection was also negative. Serum *Anaplasma phagocytophilum* IgG and PCR were both negative at the time of admission, approximately 3 weeks after the onset of symptoms. *Ehrlichia* PCR was sent, but unfortunately the test resulted as "invalid" after the patient had already been started on successful treatment and was not resent. QuantiFERON-tuberculosis Gold test was positive, likely due to prior exposure to tuberculosis as a native of India, but as noted previously, CT scan of the chest was normal. Serum GQ1B was tested to rule out Miller-Fischer variant of Guillain-Barre syndrome, although of low concern in this case, and was negative.

CSF revealed a lymphocytic pleocytosis (96%) with nucleated cell count 134, elevated protein (156), normal glucose. CSF cytology, AFB culture, *Mycobacterium tuberculosis* complex detection and rifampin resistance by PCR, viral PCRs and paraneoplastic panel were all normal or negative. CSF Lyme IgG (7 bands: 93,66,58,45,41,39,18) and IgM (1 band: 41) Western immunoblot were positive. A formal CSF:serum antibody index assay was not performed. Note was made of a CSF-unique IgG band, 58, in the CSF sample, performed 1 day after serum studies. IV ceftriaxone 2 g daily was started quickly on hospital day 1 given concern for neuroborrelliosis in the setting of antibodies detected in the CSF, which were the first tests to return. Of note, a left LMN facial nerve palsy developed four days after admission, which was three days following treatment initiation with IV Ceftriaxone. *Babesia* or *Anaplasma* co-infections were considered given unexplained transaminitis, but PCRs for both were negative (as well as quantitative buffy coat for detection of *Babesia)*.

CSF results following one week of treatment with IV Ceftriaxone revealed significant improvement in nucleated cell and protein counts. Following completion of 4 weeks of IV Ceftriaxone, bilateral facial paralysis, pain, motor and sensory deficits had resolved with return to baseline weight and liver enzymes.

3. Discussion

We present a case of Bannwarth syndrome, or lymphocytic meningoradiculitis, with previously unreported features of profound transaminitis and weight loss without evidence of co-infection or clear history of tick bite. As stated, Lyme disease is the most commonly reported vector-borne disease in the United States, caused by *Borrelia* species spirochetes and with the highest concentrations in Northeast, mid-Atlantic, and upper Midwest regions [1]. This patient presented with certain features consistent with Bannwarth syndrome, a form of neuroborreliosis diagnosed more commonly in Europe [1]. Of all Lyme neuroborelliosis cases, about 80% present as Bannwarth syndrome, one-third of which present only with radicular pain preceding motor weakness by about 1–4 weeks [1]. Half of patients with Bannwarth syndrome develop LMN facial nerve palsies, 30% of which are bilateral [1].

The diagnosis requires evidence of intrathecal production of Lyme antibodies or serologic evidence and CSF lymphocytic pleocytosis with a high clinical suspicion. CSF: serum antibody index assay is the preferred method for diagnosis of neuroinvasive borreliosis, which corrects for passive diffusion of serum antibodies into the CSF and detects intrathecal production of antibodies to *B. burgdorferi*. However, we did not perform this test, thus we are unable to distinguish between true intrathecal production of antibodies and passive diffusion across the blood-brain barrier. An alternative diagnosic method, however, includes a high clinical suspicion, appropriate exposure and symptoms consistent with neuroborreliosis and positive serum Lyme ELISA confirmed with positive serum Western blot IgM and IgG. Nevertheless, we believe that the patient had a true CNS infection, given profound CSF lymphocytic pleocytosis, elevated protein, and remarkable neurological recovery with antibiotic treatment. Nerve conduction studies can show decreased CMAPs but normal sensory studies consistent with radiculopathy and lumbar MRI may rarely show contrast enhancement of meninges or nerve roots [1]. In our case, nerve conduction study confirmed a polyradiculopathy with mild demyelinating findings but not acquired demyelination (a feature atypical of neuroborelliosis-related radiculopathy), thus the demyelinating features may have predated the infection. We suspected meningeal involvement given upper motor neuron clinical examination signs (brisk ankle reflexes) despite normal MRI of the brain and total spine.

We suspected co-infection with *Babesia* species (an intracellular parasite of red blood cells) given profound transaminitis, a frequent *Borrelia* co-infection, but *Babesia* PCR and quantitative buffy coat for blood parasites were both negative, making this co-infection less likely. Although the sensitivity of *Babesia* PCR decreases days after initial infection, quantitative buffy coat testing was negative making true infection less likely. Quantitative buffy coat examination is used for the diagnosis of malaria and can also detect red blood cells infected with *Babesia* species [2]. Similar to Lyme disease, *Babesia* species are transmitted by the *Ixodes scapularis* ticks, and has been reported in 27% of serum samples of those with positive Lyme serology [2]. Recently, a review article commented on the polymicrobial nature of neurological diseases caused by infections transmitted via the *Ixodes* tick [3]. Only two prior early studies have reported liver dysfunction as a finding in early disseminated Lyme disease but did not report on associated CNS involvement [4]. In the absence of other coinfection or cause, it appears that the patient's transaminitis was a part of the neuroborreliosis

syndrome and resolved accordingly with antibiotic treatment. The mechanism of liver injury due to Lyme disease is unknown, but may be due to direct invasion of the liver by *B. burgdorferi* or systemic host-mediated immune responses creating a reactive process that leads to hepatocyte injury, as has been previously speculated [4]. There is no standard on length of therapy but the American Academy of Neurology recommends antibiotic treatment duration of 14 days. Some studies recommended up to 28 days [5].

4. Conclusions

Clinical manifestations of neuroborreliosis are variable. Our case demonstrates the importance of consideration of Bannwarth syndrome in the differential of meningoradiculitis, even in the setting of atypical features such as liver dysfunction and weight loss.

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