Lyme disease or borreliosis, caused by infection with a spirochaete of the genus *Borrelia* and transmitted by tick-bites of the genus *Ixodes*; is the most frequently reported vector-borne disease in the Northern Hemisphere. Borreliosis is a multisystemic disease that can affect skin, joints, heart and central nervous system (CNS). Infection of the CNS by *Borrelia*, called neuroborreliosis (NB) produces multiple manifestations that includes: Encephalitis, myelitis, intracranial hypertension, aseptic meningitis, meningonecephalitis, meningoradicularitis, vasculitis and cranial or spinal nerve neuropathies. The CNS involvement occurs in 15% of cases during early disseminated disease and is manifested predominantly as cranial neuropathies (8 to 10% cases); it is usually unilateral and mainly affects cranial nerve VII (80%). The other common manifestations include motor or sensitive radiculopathy present in 3% of cases and less frequently—Lymphocytic meningitis, mononeuritis multiplex, cerebellar ataxia and myelitis. The classic triad named Bannwarth syndrome, including meningitis, cranial neuropathy and radiculopathy is rare.

Late manifestations usually appear one year after infection, although the average time period is variable. The different symptoms have been explained by persistence of the spirochaete in untreated cases and also have been related to autoimmune phenomena in patients that do not improve after appropriate therapy.

The first challenge when facing this disease is to have a high degree of clinical suspicion for correct diagnosis and beginning antimicrobial therapy. The second is to decide the duration of therapy in patients with NB and immunosuppression, a point where there is controversy among clinicians.

In the present report, a case of patient diagnosed with lymphoblastic leukemia/lymphoma is discussed while she was on a trip in Belgium. On her return to Mexico (Hometown), during the second chemotherapy cycle she developed ascending weakness associated with subcortical microangiopathic lesions, diagnosed in magnetic resonance imaging (MRI) that led to the suspicion of NB; the diagnosis was confirmed by western blot (WB) and polymerase chain reaction (PCR) of serum and cerebrospinal fluid (CSF).

**Case report**

A 30-yr-old healthy woman traveled to Belgium for three weeks during summer. During the trip, she developed acute abdominal pain. She went for laparoscopy and a retroperitoneal mass was diagnosed as lymphoblastic leukemia/lymphoma. Steroid treatment was initiated and she was sent back to Mexico to continue the therapy.

On admission at the National Cancer Institute in Mexico City, she had an Eastern Cooperative Oncology Group (ECOG) score of 1, a mesogastric abdominal mass measuring 14×13 cm was palpable, the rest of the physical and neurological examinations were normal. Her blood count showed 20000 leukocytes/mm³, 12% blasts of lymphoid appearance, haemoglobin 9.5 g/dl, and platelets count of 18000 mm³. Blood chemistry was within normal limits. The bone marrow aspirate revealed minimal residual disease, consequently Phase-B HCVAD (methotrexate, leucovorin and cytarabine) was started.
After 15 days of the Phase-B chemotherapy, she complained of severe headache along with lower extremity weakness with limitation for walking. Rapid deterioration was observed; 48 h later she had progressive generalized weakness. The neurological examination revealed absence of gag reflex without involvement of other cranial nerves, bilateral decreased strength of the distal extremities (4/5), absence of osteotendinous reflexes with normal sensation; however, no abnormal movements, meningeal and cerebellar signs were found.

Human immunodeficiency virus (HIV) test, viral hepatitis profile, venereal disease research laboratory (VDRL) test and toxicology screening were negative. Hypothyroidism and vitamin B12 deficiency were ruled out. A third lumbar puncture showed no evidence of infiltration, protein level was elevated (52 mg/dl), glucose was normal and no cells were observed in CSF. All cultures for bacteria, fungi, mycobacteria, PCR for neurotropic viruses (herpes simplex 1 and 2, cytomegalovirus, Epstein Barr, human herpes virus 6, 7 and 8, varicella zoster, enterovirus, B19 parvovirus and JC) and CSF VDRL were negative. Electromyography reported severe diffuse axonal neuropathy. Brain and spinal MRI findings were reported as compatible with \textit{B. burgdorferi} encephalitis (Fig. 1).

Western Blot IgG antibodies and PCR of serum and CSF were positive for \textit{Borrelia} species. End-point PCR identified \textit{B. afzelli} genospecies. Treatment with intravenous ceftriaxone (2 g per day) was begun, rituximab was withdrawn and the Hyper CVAD regimen was continued. The cardiac MRI excluded the presence of carditis. The patient received treatment with ceftriaxone for 16 wk followed by oral doxycycline (100 mg bid) for nine months. Her neurological status slowly improved over the months while she was treated with oral doxycycline. She completed three cycles of HCVAD and six lumbar punctures with triple intrathecal chemotherapy including methotrexate, cytarabine and dexamethasone. After the third cycle of chemotherapy she developed disseminated herpes zoster that required hospitalization. A control MRI after nine months of antibiotic showed persistence of lesions in brain parenchyma and resolution of abnormalities in spinal medulla (Fig. 2). A fresh CSF sample taken at month 11 of treatment probed negative in Western Blot and PCR. She achieved complete remission of the leukemia and was advised to continue POMP (6-mercaptopurine, vincristine, methotrexate, and prednisone) medication/therapy for 2 yr.

The strength in the upper extremities was completely recovered; she was able to walk without support or assistance and was spending a normal working life.

DISCUSSION

In the United States, \textit{B. burgdorferi} is the most common species causing Lyme disease. In Europe and Asia, other genospecies such as \textit{B. garinii} and \textit{B. afzelli} are reported as the causal organism; epidemiologically, this is relevant because of the travel history of the patient. This is a very unusual case of co-existing leukemia/lymphoma and \textit{B. afzelli} NB that represented a challenge to diagnosis.
and medical management. Several topics are relevant for discussion, especially diagnosis tools and optimal duration of antimicrobial therapy as the patient was immunosuppressed, receiving rituximab, steroids and intrathecal chemotherapy.

NB has been reported in two cases associated with lymphoma and one case with leukemia. The first is a 66-yr-old Dutch female with history of B-cell marginal zone lymphoma; she was on remission with rituximab administered every three months and developed peripheral neuropathy. Serology was negative, but CSF PCR for B. burgdorferi was positive. She received intravenous ceftriaxone for 3 wk and completely recovered1. The second is an 80-yr old Japanese man with coexistent T-cell lymphoma and NB with cranial and peripheral nerve involvement. The diagnosis of lymphoma was made after the diagnosis of Lyme disease and he didn’t receive chemotherapy. The patient died despite treatment with ceftriaxone and steroids8.

The third case is a 63-yr-old German woman with chronic lymphocytic leukemia who developed sensitive neuropathy after the fifth cycle of chemotherapy with fludarabine, cyclophosphamide, rituximab and prednisone. The CSF serology was negative; because of a history of transient erythema on her leg and lymphomononuclear pleocytosis she received ceftriaxone for 3 wk and completely recovered. The diagnosis was confirmed with PCR detecting B. garinii9.

In vitro studies had demonstrated persistence of Borrelia spirochaetes forms in the brain and this can help in explaining the long latent stage and persistence of Borrelia infection; and thus the potential need to prolong antibiotic therapy10. The guidelines recommendations for treatment of acute NB are intravenous ceftriaxone 2 g per day for 10–28 days. An acceptable alternative is cefotaxime or penicillin G. For patients intolerant of beta-lactam, doxycycline 200–400 mg per day might be adequate with the penicillin G. For patients intolerant of beta-lactam, doxycycline was continued; once recovered a new WB and PCR of CSF was performed prior to withdrawal, which were negative. This can be a surrogate marker of resolution of infection to assist in stopping antimicrobials, but this is still an unanswered issue. There are other points to consider such as the use or withdrawal of rituximab that also causes immunosuppression and may compromise the patient’s response and eventually foster relapse. This patient has been followed for over a year with no relapse and complete neurologic recovery.

Conflict of interest
The authors have no any potential conflict of interest.

REFERENCES
Persisting a typical and cystic forms of *Borrelia burgdorferi* and local inflammation in Lyme neuroborreliosis. *J Neuroinflammation* 2008; 5: 40.


*Correspondence to:* Dr Volkow-Fernández Patricia, Department of Infectious Diseases, Instituto Nacional de Cancerología, San Fernando 22, Colonia Seccion XV1, CP 14080, Ciudad de Mexico.
E-mail: pvolkowf@gmail.com

*Received: 30 August 2016*  
*Accepted in revised form: 3 January 2017*