The Clinical Spectrum of Lyme Neuroborreliosis

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Abstract

Lyme disease is a multisystem infectious disease, endemic in parts of Europe, including the West of Ireland. Neurological manifestations (neuroborreliosis) are variable. Presenting neurological syndromes include meningitis, cranial neuropathies, myeloradiculitis and mononeuritis multiplex. A lack of specificity in serological diagnosis may add to diagnostic confusion. We reviewed thirty cases of acute Lyme disease in the West of Ireland and found neurological syndromes in 15 (50%), with partial radiculopathy (13 patients; 80%), and cranial neuropathy (7 patients; 46%) occurring frequently. Neuroborreliosis needs to be considered in the differential diagnosis of these neurological syndromes in the appropriate clinical context.

Introduction

Lyme disease is a multisystem infectious disease caused by the Borrelia spirochaete genus. The predominant species in North America is Borrelia burgdorferi sensu stricto, and in Europe the predominant species are B. afzelii and B. garinii. Deer and other mammals are the intermediate hosts - Lyme disease is the most frequently reported arthropod-borne infection of the nervous system in Europe and USA. Ehrhema migrans (EM) is regarded as the most common clinical marker of infection and is estimated to occur in 60-80% of patients with Lyme disease (neuroborreliosis; NB). Multiple areas of both central and peripheral neurological involvement are reported, mimicking a variety of common disorders. Typical neurological presenting syndromes include meningitis, cranial neuropathies (with a predilection for the facial nerve), myeloradiculitis and mononeuritis multiplex. Difficulties in the diagnosis and management of patients with Lyme disease are compounded by a lack of specificity of serological tests and lack of sensitivity of serological tests in active disease.

Seroprevalence studies report the Republic of Ireland as having one of the highest rates of Lyme disease in Europe. In the West of Ireland, Lyme disease is considered endemic. We undertook a retrospective analysis of the clinical characteristics of Lyme NB in the West of Ireland. We conducted a retrospective review of the clinical presentation of patients with serologically confirmed Lyme disease diagnosed over a five-year period at a single referral centre in the West of Ireland. We identified the proportion of patients presenting with NB, we define the neurological syndromes at presentation, and report the clinical outcomes.

Methods

The study population included those patients who had a serological testing consistent with Lyme disease, based on referrals to the department of Medical Microbiology, University Hospital Galway. The period studied extended from January 1996 to August 2002. During that period, approximately 2,100 sera were tested using the screening ELISA. All sera were tested using the screening ELISA. A two-tier diagnostic process was utilized in accordance with the World Health Organization (WHO) guidelines, comprising an initial screening enzyme-linked immunoblot assay (ELISA) for anti Borrelia antibodies, in those patients who had positive screening ELISA tests, and a confirmatory ELISA immunoblot assay at the Lyme Borreliosis Unit, Southampton, UK. We identified 42 samples over the sixty-six month study period with serology consistent with Lyme disease. After obtaining Ethical Committee approval and written informed consent from the referring physician, we obtained a detailed clinical data for 32 patients. Data was collected from chart review and included demographic characteristics, potential exposure to tick bite, clinical presentation and results of investigations.

Results

Baseline characteristics

Antibody subtypes directed against B burgdorferi in the thirty patients included in the study were determined as follows: seventeen patients (57%) had both IgM and IgG antibodies; six patients (20%) exhibited anti IgM antibodies only, and seven patients (23%) had only IgG anti-Borrelia antibodies. Patients ranged from 26 to 80 years of age, with a mean of 52.5 years, 50% were male. Twenty-two patients (67%) were resident of western counties of Ireland. Only one patient was resident outside the state. Recent travel outside Ireland was documented in seven cases. Nine patients (30%) had polyarthralgia at presentation; 11 patients (34%) had joint swelling, none of these had cardiovascular syndromes.

Neurological Manifestations

Fifteen patients (50%) had neurological manifestations at presentation (Table). The most common symptom was headache (12/15 patients; 80%). Cranial neuropathy occurred in seven patients, among whom unilateral facial palsy was present in six patients (40%) with neurological manifestations. Bilateral facial palsies were documented in only one patient. Four patients had headache at presentation. Psychoaffective disturbances, in the form of marked irritability and reduced concentration, were noted in one patient.

Clinical Presentation

The majority of patients (25/27, 93%) presented between the months of May and October. While two patients (7%) had a rash at presentation, only 43% of patients presented with EM rash. Fatigue was a prominent symptom in more than half of the patients (16/30), but fever >38°C degrees C was reported in only four patients (13%). Seven patients (23%) had polyarthralgia at presentation; one patient had anterior uveitis. None of the patients had cardiovascular syndromes.

Laboratory Findings in NB patients

Eleven patients with Lyme NB had both anti-Borrelia antibodies for IgM and IgG; two patients were IgM positive (two patients were IgM positive only, and two were IgG positive only. Concomitantly performed CSF analysis was carried out in five of the fifteen patients with NB and was abnormal in all five (Table). We had raised CSF protein levels ranging from 0.6 g/l to greater than 1g/l. Four had CSF pleocytosis (>4 cells/mm³) comprising an initial screening enzyme-linked immunoblot assay (ELISA) for anti Borrelia antibodies, in those patients who had positive screening ELISA tests, and a confirmatory ELISA immunoblot assay at the Lyme Borreliosis Unit, Southampton, UK. We identified 42 samples over the sixty-six month study period with serology consistent with Lyme disease. After obtaining Ethics Committee approval and written informed consent from the referring physician, we obtained a detailed clinical data for 32 patients. Data was collected from chart review and included demographic characteristics, potential exposure to tick bite, clinical presentation and results of investigations.

Discussion

We identified forty-two patients with serological evidence of acute Lyme disease over a five-year period presenting to a single referral laboratory in the West of Ireland. Fifty percent of the patients on whom clinical data was available had evidence of Lyme NB. Both the incidence of Lyme disease in the West of Ireland and the proportion of patients with NB in our study appears to be higher than in previous reports. The first reported cases of Lyme disease in Ireland appeared in the late 1980s. The incidence of Lyme disease in the state of East of Ireland has been identified as a high-risk area because of high rates of sero-prevalence among asymptomatic adults. The highest sero-prevalence was documented in the west and south-west of Ireland (9.8% and 11.2%, respectively). A prospective sero-prevalence study in 2006 documented a seropositivity for Lyme antibodies, primarily from patients attending Dublin hospitals, but Galway area hospitals formed the second largest group despite its much smaller catchment population (11.5% vs. 9.6%). The given apparent high incidence of Lyme disease in Ireland, information on patients with Lyme NB in the region is sparse. Kelly and Hanrahan in 1997 described the clinical presentation of six cases of Lyme disease diagnosed in Ireland over a 4-year period, five of whom contracted the disease in the West of Ireland. The larger number of patients in our study may reflect a combination of higher awareness among physicians, as well as more reliable serological diagnostic techniques.

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The proportion of patients with Lyme NB in our cohort is high, amounting to 50% of patients presenting with confirmed Lyme disease. Although estimates vary, previous studies in Ireland and Europe report rates of neurologic involvement in Lyme disease ranging from 18% to 31%.

Sensory motor radiculitis and facial palsy were the two most common neurologic presentations in these patients: we have recently reported perineuritis as a pathological finding in one of this cohort. 1. Lyme neuroborreliosis (Bannwarth's syndrome) is a radicular neuropathy associated with a chronic lymphocytic pleocytosis in cerebrospinal fluid and frequently with unilateral or bilateral peripheral facial palsy 15 is one of the most common neurologic manifestations of Lyme disease in clinical studies conducted in Ireland and other parts of Europe.

In one of our patients was severe enough to prompt investigation for a cardiac cause. All patients with Lyme facial palsy in our cohort had additional neurologic symptoms, and 87% reported constitutional complaints. This highlights the fact that while NB may be responsible for up to 10% of cases of facial palsy, Lyme disease should be considered in a patient with facial palsy when it is associated with other signs or symptoms of borreliosis. A relatively small number of our patients had symptoms of meningism. Meningitis in NB seems to cause less pronounced meningeal symptoms than asymptotic meningitis. Only one third of our patients with symptoms suggestive of NB had a lumbar puncture and cerebrospinal fluid analysis; however, CSF was abnormal in all of these cases. Oligoclonal bands were present in cerebrospinal fluid and not serum in one case. Current guidelines consider the presence of intrathecal specific antibodies as essential laboratory evidence for the diagnosis of early Lyme NB and the absence of specific CSF oligoclonal bands as supporting evidence. 16 Given the relatively high yield of CSF for identification of Lyme antibodies physicians should be encouraged to carry out CSF analysis in all patients with symptoms suggestive of NB even in the absence of meningism.

This study has some inherent limitations due to its retrospective design and potential for ascertainment bias. However the potential for overestimation of disease incidence through the use of serology as part of patient selection is more than offset by the fact that only about 40-45% of patients with early Lyme disease EM have positive serology. Moreover, serology may not be requested in patients with typical clinical disease and typical serologic grounds. However in patients in whom the duration of illness is 4 weeks or more, the sensitivity and specificity of IgG response is in the range of 90%-97% as determined by the 2 test approach and thus a single test (for IgG only) is usually sufficient for diagnosis if the clinical picture is compatible. We believe our results indicate a relatively high incidence of neurologic complications in patients with Lyme disease, particularly in patients with serologically confirmed disease. There is a high incidence of Lyme NB among patients with Lyme disease in the West of Ireland, higher than that suggested by previous studies. The absence of a history of tick bite, potential exposure to ticks or EM is not reliable in the exclusion of the diagnosis. CSF analysis and serology testing is recommended in all suspected cases of neuroborreliosis, even in the absence of meningial symptoms.

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References
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