Rare disease

Protracted neuroborreliosis – an unusual cause of encephalomyelitis

Saif Huda, Udo Carl Wieshmann

Neurology Department, Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Correspondence to Dr Saif Huda, shuda@nhs.net

Summary

A 58-year-old lady with waxing and waning of non-specific symptoms including fatigue, dizziness, hearing loss and unsteady gait for 15 months, became acutely confused 12 h prior to presentation. On admission to a district hospital she was feverish and unresponsive. Her travel history consisted of visits to Argentina, Chile and the Outer Hebrides. CT of the brain was normal. Lumbar puncture demonstrated a lymphocytic pleocytosis of 500 cells, protein of 1 g/l, a low glucose ratio with negative cytology and viral PCR (including herpes simplex 1 and 2). MRI revealed multiple abnormal areas of high signal on T2 fluid attenuated inversion recovery sequencing within the cerebellum, temporal lobes and periventricular areas. Western blotting of serum and cerebrospinal fluid for *Borrelia burgdorferi* were both positive. She was treated with cefuroxime and aciclovir and within 24 h she was alert and responsive. She received 4 weeks of cefuroxime in total and made a good recovery.

BACKGROUND

Neuroborreliosis, is a rare complication of *Borrelia burgdorferi* (Bb) infection, more commonly known as Lyme disease. Bb is a spirochete that is typically transmitted by the ixodes tick.¹ Typical manifestations include erythema chronicum migrans, radiculopathy, arthritis and cranial neuropathies. Encephalomyelitis is rare. A travel history to an endemic area and history of tick bite is key to the diagnosis. This case illustrates the importance of considering Lyme disease in patients with a history of fatigue, cranial nerve palsies including the vestibulocochlear nerve, and an acute confusional state with cerebrospinal fluid (CSF) lymphocytic pleocytosis.

CASE PRESENTATION

A 58-year-old keen traveller and horse rider presented with waxing and waning of non-specific symptoms for 15 months. These consisted of malaise, headaches, dizziness and balance difficulty. No rash or fever was noted. Initially symptoms fluctuated but at times were severe, interfering with activities of daily living. Four weeks later the headaches resolved but balance difficulty and malaise persisted. In the following months symptoms continued to fluctuate but gradually worsened. She noted increasing difficulty with horse riding and a reduction in her auditory acuity. She was seen by an ear, nose and throat (ENT) specialist, who found evidence of bilateral sensori-neural hearing impairment. She also had an admission to a hospital and was reviewed by a neurologist as an inpatient. A different consultant neurologist later saw her as an outpatient. A tentative diagnosis of postviral syndrome was made although the patient herself raised the possibility of Lyme disease. MRI of her brain was reported as normal and she was referred to physiotherapy for her balance. Over the next 2 months she developed short-term memory difficulty, urinary hesitancy and lost a stone in weight.

She was admitted to a district general hospital in an acute confusional state. Her husband had found her attempting to defecate in the kitchen with incomprehensible speech. On arrival her Glasgow coma scale was recorded as eyes 2, motor 4 and verbal 2. Initial neurological examination

Figure 1 T2 weighted magnetic resonance axial brain imaging demonstrating increased signal in periventricular and subcortical areas.

Table 1 Serial cerebrospinal fluid results

	CSF 1	CSF 2	CSF 3	CSF 4
Red blood cells	783	456	535	80
White blood cells (lymphocytes)	465	157	91	52
CSF glucose (mmol/l)	1.7	2.4	2.3	2.5
Serum glucose (mmol/l)	Not recorded	6.3	7.2	5.9
CSF protein (g/l)	6.3	2.75	2.44	2.44

CSF, cerebrospinal fluid.

documentation was limited. She was noted to be feverish, without evidence of seizure activity, focal sensory or motor disturbance. Empirical treatment with cefuroxime and aciclovir was commenced. Within 24 h her level of consciousness normalised and she was transferred to the Walton Centre for Neurology and Neurosurgery. Cranial nerve examination demonstrated a sensori-neural pattern of auditory impairment with intact facial nerves. Gait ataxia was noted without evidence of truncal or appendicular ataxia. Power was preserved with clonus noted at the right ankle, and an extensor right plantar response.

INVESTIGATIONS

The following investigations were negative or within normal limits: baseline bloods, inflammatory markers, thyroid antibody and function tests, serum and CSF ACE, auto-antibody screen, antivoltage gated potassium channel antibodies, treponemal antibodies, HIV, CSF viral PCR, antineuronal antibodies, CSF bacterial serology (including listeria and tuberculosis), ECG and MRI spine.

The EEG showed occasional slow wave activity in the δ range intermittently over left temporal region and at times had a sharpened appearance. T2 weighted magnetic resonance axial brain imaging demonstrating increased signal in periventricular and subcortical areas (figure 1).

CSF demonstrated a lymphocytic pleocytosis with a low glucose ratio (table 1). Type 2 oligoclonal bands were detected. CSF index was tested on the second CSF sample and was 1.78 (0.3–0.7). CSF Bb immunoglobulin (Ig)G and IgM ELISA with immunoblot confirmation was strongly positive.

DIFFERENTIAL DIAGNOSIS

Viruses	Other
Herpes simplex virus 1,2	Mycobacteria
Enteroviruses	Listeria
Varicella Zoster	Syphilis
Arboviruses	Leptospira
HIV	Toxoplasma
Epstein–Barr Virus	Fungi for example, <i>Cryptococcus</i>
Mumps	Carcinomatosis
Measles	
Lymphocytic choriomeningitis virus	
Adenovirus	Partially treated bacterial meningitis
Cytomegalovirus	
Influenza A,B	
Parainfluenza	
Rubella	

OUTCOME AND FOLLOW-UP

Following the diagnosis of Neuroborreliosis, a 4-week course of intravenous cefuroxime was completed. A

marked improvement in functional status was noted. One year following the acute presentation, the patient notes that her hearing has improved, but that bladder dysfunction and non-specific malaise have persisted.

DISCUSSION

Neuroborreliosis is caused by Bb, a tickborne spirochete.¹

The vector of transmission is the Ixodes tick, and commonly the primary reservoir host is the white-footed mouse.²

Bb sensu stricto is commonly seen in North America. The most common strains in Europe are *Borrelia afzelii* and *Borrelia garinii*. Common neurological presentations include cranial neuritis, radiculoneuritis, multiple mononeuropathies and lymphocytic meningitis. The variation in strains explains the varied presentations between North American and European subsets. In Europe the most common presentation is a painful meningoradiculitis (Bannwarth's syndrome).³ In North America presentation is usually with erythema migrans, arthritis and meningitis without painful radicular symptoms. Approximately 10–15% of patients will develop nervous system involvement with early dissemination.⁴ Parenchymal brain or spinal cord involvement is rare. A prospective study in Denmark of 187 patients with Lyme disease found only one case of encephalitis.³ Typical findings of *Borrelia* encephalomyelitis include ataxia, bladder dysfunction, auditory and cognitive impairment.

A diagnosis of neuroborreliosis can be fraught with difficulty and may be complicated by current diagnostic methods. A standard two-tiered approach using ELISA for screening followed by Western blot for confirmation aided by CSF antibody index is widely used. In late Lyme disease the diagnostic sensitivity of the ELISA screening assays for IgG is >90%.⁵ In our case the test was strongly positive (Susan O'Connell, personal communication). The clinical presentation, epidemiological context and imaging findings were classical for a *Borrelia* encephalomyelitis. The CSF pattern was also characteristic, although a low glucose ratio is atypical and thus *Listeria* and *Tuberculosis* were initially also considered. Our investigation was extensive and some investigations such as the nerve conduction studies and electromyogram were unnecessary. The diagnosis was missed by ENT and neurology consultants prior to her acute presentation, despite the patient considering the diagnosis herself.

PostLyme disease syndrome (PLDS) is often used to describe subjective complaints and symptoms described by patients following standard treatment regimens (eg, fatigue, headache, myalgia and memory impairment). The term 'chronic Lyme disease' (as opposed to PLDS), its existence, and whether it is due to the persistence of the Bb spirochete has been the subject of much debate. Clinically this can be a particular problem when the issue of long-term or repeated antibiotic treatment is raised. The guidance published in the New England Journal of Medicine (NEJM), the European Federation of Neurological Societies and the Infectious Diseases Society of America review panel discourage the use of long-term antibiotics in patients whose symptoms persist after standard treatment.^{5–7} However, there is no doubt that in untreated patients the organism can persist in the long term and cause serious deterioration as illustrated by our case.

Learning points

- ▶ Neuroborreliosis should be considered in cases of encephalomyelitis, with a long prodrome of non-specific symptoms and cranial nerve palsies in the appropriate clinical context.
- ▶ A travel history with direct enquiry related to tick bite is crucial for establishing an index of suspicion.
- ▶ Antibiotic treatment is highly effective and results in marked improvement of the condition. At present there is insufficient evidence to warrant the use of long-term or repeated courses of antibiotics.

Acknowledgements The authors are grateful to Consultant Microbiologist Dr Susan O'Connell for the analysis of the patients' samples and her helpful comments in the drafting of this manuscript.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Burgdorfer W**, Barbour AG, Hayes SF, *et al*. Lyme disease—a tick-borne spirochetosis? *Science* 1982;**216**:1317–9.
2. **Halperin JJ**. Neurologic manifestations of Lyme disease. *Curr Infect Dis Rep* 2011;**13**:360–6.
3. **Hansen K**, Lebech AM. The clinical and epidemiological profile of Lyme neuroborreliosis in Denmark 1985–1990. A prospective study of 187 patients with *Borrelia burgdorferi* specific intrathecal antibody production. *Brain* 1992;**115** (Pt 2):399–423.
4. **Bacon RM**, Kugeler KJ, Mead PS; Centers for Disease Control and Prevention (CDC). Surveillance for Lyme disease—United States, 1992–2006. *MMWR Surveill Summ* 2008;**57**:1–9.
5. **Mygland A**, Ljøstad U, Fingerle V, *et al*.; European Federation of Neurological Societies. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. *Eur J Neurol* 2010;**17**:8–16, e1–4.
6. **Feder HM Jr**, Johnson BJ, O'Connell S, *et al*.; Ad Hoc International Lyme Disease Group. A critical appraisal of “chronic Lyme disease”. *N Engl J Med* 2007;**357**:1422–30.
7. **Lantos PM**, Charini WA, Medoff G, *et al*. Final report of the Lyme disease review panel of the Infectious Diseases Society of America. *Clin Infect Dis* 2010;**51**:1–5.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Huda S, Wieshmann UC. Protracted neuroborreliosis – an unusual cause of encephalomyelitis. *BMJ Case Reports* 2012;10.1136/bcr.11.2011.5206, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>