Lyme disease presenting as a stroke in the vertebrobasilar territory: MRI

G. Defer1, R. Levy1, P. Brugières1, D. Postic2, J. D. Degos1
1 Département de Neurosciences, CHU Henri Mondor, Créteil, France
2 Unité de Bactériologie Moléculaire et Médicale, Institut Pasteur, Paris, France

Received: 20 June 1992

Abstract. A 28-year-old female farmer, without vascular risk factors, developed a limited infarct of the pons, associated with a lymphocytic cerebrospinal fluid (CSF) pleocytosis. Titres of specific antibodies against Borrelia burgdorferi were high in serum and CSF. MRI confirmed an infarct in the territory of the medial pontine arteries, but angiography showed no evidence of cerebral angiopathy. Antibiotic therapy rapidly led to a return to normal of CSF cytology and serology. We suggest that Lyme disease is a possible cause of cerebral ischaemia.

Key words: Stroke - Lyme disease - Magnetic resonance imaging

Stroke is one of the least common neurological complications of Borrelia burgdorferi infection (Lyme disease), and poorly documented [1]. We report a case with a temporal relationship between acute neurological manifestations of vertebrobasilar ischaemia demonstrated by MRI and B. burgdorferi infection.

Case report

A 28-year-old right-handed female farmer without previous medical history suffered frontal headache and intermittent muscular pain in the neck for 3 months. She suddenly developed dizziness and an unstable gait, with deviation to the right. Examination showed vertical and horizontal nystagmus, an unstable gait with a wide base and deviation to the right and backwards. There were no signs of meningeal irritation, motor or sensory deficit or cranial nerve involvement, and no fever, skin or joint abnormality; cardiovascular examination, ECG and chest radiography were also normal. After an initial improvement, her condition rapidly worsened, and examination showed complete aponia, major dysphagia, a tetraparesis, predominantly left sided, and mildly impaired sphincter function. Laboratory investigation disclosed 8400 white blood cells/mm³, fibrinogen 2.5 g/l, aspartate aminotransferase 28 IU/l, and alkaline phosphatase 28 IU/l. The erythrocyte sedimentation rate and serum protein were normal. The cerebrospinal fluid (CSF) contained 227 leucocytes (mononuclear cells)/mm³, total protein 0.96 g/l with 22.2 % gamma globulin, glucose 2.06 mmol/l (blood glucose: 4.3 mmol/l). A Gram-stained smear of the CSF and bacteriological cultures were negative, as were serological studies for herpes and cytomegalovirus, Chlamydia and hepatitis B and C. Tests for serum immunofluorescent and rheumatoid factors, syphilitic reactions (TPHA and VDRL) were negative and the angiotensin converting enzyme was normal. The initial titre of specific antibodies against B. burgdorferi [immunofluorescence assay (IFA) after serum absorption by Treponema phagedenis] in serum was 1:1024 (cut-off 1:256) and in CSF 1:256 (cut-off 1:8). Subsequently, the patient received ceftriaxone 1 g twice daily intravenously for 2 weeks, without additional steroid therapy. One week after completion of treatment the CSF showed 37 leucocytes/mm³, total protein 0.45 g/l, and the anti-B. burgdorferi titre (IFA) was 1:1024 in serum and 1:128 in CSF. Thereafter, serology was carried out on defrosted serum by enzyme-linked immunosorbent assay (ELISA) and Western-blot (Table 1).

Three months after antibiotic treatment the patient's clinical condition had greatly improved. She was able to walk alone and had no major difficulty in daily living. She had mild dysarthria and intermittent difficulty in swallowing liquids, a nasal voice, right leg and facial weakness, pyramidal signs including bilateral Babinski signs, knee clonus, mild spasticity, and spasmodic crying and laughing. Contrast-enhanced CT at the onset of neurological symptoms was

<table>
<thead>
<tr>
<th>Antibodies to Borrelia burgdorferi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum 1</td>
</tr>
<tr>
<td>IFA (total Ig) (cut-off serum 1/256, cut-off CSF 1/8)</td>
</tr>
<tr>
<td>ELISA IgM (cut-off 0.300)</td>
</tr>
<tr>
<td>ELISA IgG (cut-off 0.600)</td>
</tr>
<tr>
<td>Western blot (41 kDa)</td>
</tr>
</tbody>
</table>

* The second serum and CSF examinations were 3 weeks after the first and after 2 weeks of antibiotic therapy.

b Results obtained on defrosted serum.

ND, Not done
normal. MRI was performed 3 months after the onset on a 1.5 T superconducting magnet. T1-weighted 600/22/2 (TR/TE/excitations), and T2-weighted (2500/40,90/1) axial images were obtained with an image matrix of 256 x 256. The T1-weighted images were repeated after intravenous gadolinium-DOTA. A sharp, linear, hypointense lesion, medially on the right of the pons, was demonstrated on T1-weighted images (Fig. 1 a). It had no mass effect, did not enhance with contrast medium and was hypointense on T2-weighted images (Fig. 1 b). Angiography showed no vascular occlusion or narrowing in the carotid or vertebrobasilar territories. Nine months after the onset tests for anti-B. burgdorferi (IFA) were negative in serum and CSF, and the latter showed 2 cells/mm³, total protein 0.4 g/l and normal glucose. One year after the improvement following antibiotic therapy the patient's neurological condition was stable, without intellectual impairment.

Discussion

There have been a few reports of abnormalities on MRI during B. burgdorferi infection but not due to cerebral ischaemia [2, 3]. In our patient the acute onset of the neurological disturbance supports the diagnosis of stroke in the vertebrobasilar territory and more precisely in the territory of the medial pontine arteries, as demonstrated by MRI. There were no clinical or radiological features to suggest demyelinating disease, especially there was no previous regressive neurological deficit and T2-weighted MRI showed no other white matter abnormality. The shape and the location of the pontine lesion were also not in favour of demyelination.

This young woman had no vascular risk factors, such as hypertension, smoking or diabetes mellitus and did not take oral contraceptives; cardiovascular examination and the ECG were normal. Her medical history did not reveal any previous cutaneous, rheumatological or cardiac manifestations of B. burgdorferi infection. However, in a rural area where ixodes are common and Lyme disease well known [4], she was exposed at work and had a CSF lymphocytosis at the onset. Antibody determinations provided strong supportive evidence for the diagnosis of Lyme borreliosis. Examination of the patient's serum by IFA and ELISA and of CSF by IFA revealed high antibody titres for B. burgdorferi. Negative syphilis serology allowed definitive interpretation of positive Lyme disease serology and the procedure of absorption with T. phagedenis results in better IFA specificity [5]. The high diagnostic sensitivity of measuring antibodies in CSF by IF or ELISA has already been shown [6]. The appearance of new bands in subsequent serum specimens is a good criterion for a positive immunoblot. Moreover, the disappearance of the CSF lymphocytosis pleocytosis, negativity of IFA in serum and CSF at the last follow-up and the clinical improvement after ceftriaxone therapy also support the diagnosis of Lyme borreliosis [7].

A few possible cases of brain ischaemic lesions in Lyme disease have been published [8–12]. However, in five of cases the temporal relationship between B. burgdorferi infection and the neurological deficit was doubtful, as serological tests for B. burgdorferi were not performed when the latter were present. In another case the patient, a drug addict, had sniffed cocaine the day before the onset of the neurological disturbance and angiography showed appearances suggestive of vasculitis [8]. The case reported by Uldry et al. [10] was more convincing: the patient had recurrent strokes, positive serology for B. burgdorferi and cerebral ischaemic lesions on CT. However, 2 years had elapsed between the first stroke and serological demonstration of infection and antibiotic therapy. Kuntzer et al. [13] recently described a 50-year-old patient with B. burgdorferi infection in whom pathological examination showed spirochaetes in the leptomeninges associated with an obliteratorative inflammatory vasculopathy and two ischaemic infarcts in the myelencephalon; the patient died after a relapsing-remitting hemiparesis over 2 years. May and Jabbari [14] described a young man coming from Europe with a left thalamic stroke, followed 1 month later by a right-sided stroke with lymphocytosis of the CSF and positive Lyme disease serology. Central nervous system manifestations are similar in the United States and Europe, but it seems that cerebrovascular complications were observed only in the latter [9]. They are rare: two recent reviews [15, 16] did not discuss the possibility of cerebral infarction in Lyme disease. In a large number of patients with B. burgdorferi infection no such complication was described [17]. Interestingly most of the documented strokes involved the vertebrobasilar territory [9, 10, 13, 14], as in our patient. Cerebral angiopathy was described on angiography in patients with B. burgdorferi infection [8, 10, 12], and Kuntzer et al. [13] suggested, on post-mortem evidence, that the stroke was related to an obliteratorative inflammatory vasculopathy, as seen in cerebral syphilis. In our case arteriography was normal, but this could be due to the delay between the stroke and the radiological examination. Another explanation is that the small pontine arteries are often not seen on vertebral arteriography. The immediate administration of antibiotics at the onset of disease could have prevented the subsequent development of chronic cerebral angiopathy. From our case and others demonstrating brain ischaemia as a possible manifestation of Lyme disease [1, 15–17], it is tempting to suggest that unrecognized B. burgdorferi infection could lead to ischaemic central nervous system in-