Acute ischaemic pontine stroke revealing Lyme Neuroborreliosis in a young adult

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Abstract

We report the case of a 23-year-old male patient who suddenly developed right hemiparesis, cerebellar ataxia, dysarthria, and bilateral dysmetria. Brain magnetic resonance (MR) examination demonstrated hyperacute ischaemic lesions within the pons. CSF analysis revealed a high protein content, lymphocytic pleocytosis, and oligoclonal IgG bands not present in the serum. Elevated IgM and IgG anti-Borrelia burgdorferi antibodies were shown in both serum and CSF samples, associated with an intrathecal synthesis of these antibodies. Ischaemic CNS lesions have been rarely observed as the first manifestation of Lyme neuroborreliosis. The putative mechanism for parenchymal ischaemia is the local extension of inflammatory changes from meninges to the wall of penetrating arterioles.

Key words : Borrelia Burgdorferi ; Neuroborreliosis ; stroke.

Introduction

Lyme disease is a multisystemic disorder caused by an epizootic organism of the spirochete group, called *Borrelia Burgdorferi* (Bb), which is transmitted to humans by ticks of the genus Ixodes. Three sequential clinical stages have been described : i. early localised ; ii : early disseminated ; iii : late persistent disease. Lyme neuroborreliosis may occur during the early dissemination phase, most often as a painful meningo-radiculitis, whereas encephalomyelitis is observed in the late phase (Hengge *et al.*, 2003). Very rarely, the disease may present as a meningovascular process leading to an acute stroke. The posterior circulation could be preferentially involved.

We report a patient with acute brainstem dysfunction due to pontine lesions, and a serologically proven Lyme neuroborreliosis.

Case report

A previously healthy male student of 23 years of age was admitted to our Neurology Department for gait ataxia, right kinetic hemiataxia, homolateral hemiparesis and dysarthria of two days duration. Symptoms had appeared suddenly in the afternoon while patient was resting on an Egyptian seaside beach.

At admission, the patient was apyretic at 36.8° C, had blood pressure at 103/51 mm Hg and normal sinusal heart beat rate. Neurological examination demonstrated wide-based gait, right hemiparesis and bilateral dysmetria. Cerebellar dysarthria but with only mild dysphagia, and a bilateral Babinski sign were present. No facial palsy, oculomotor disorder, nystagmus nor sensory deficit were observed.

Brain magnetic resonance (MR) work-up at admission demonstrated bilateral acute ischaemic damage within the pons, but with normal intracranial angiogram (Fig. 1a-d). Contrast-enhanced scans failed to detect other brain lesions or meningeal involvement. A MR angiogram of the neck performed 24 hours later failed to reveal any abnormality (not illustrated). A conventional catheter angiography was not performed. Transoesophageal ultrasonography and 24-hour Holter monitoring electrocardiogram were unremarkable.

Routine blood tests and biochemical assays were normal. Because of the unexpected occurrence of ischaemic lesions in a young adult, a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis demonstrated 160 cells/mm^3 with 70% lymphocytes, 3% reactive lymphoblasts, 9% neutrophils and 18% monocytes. The total protein content was elevated at 137 mg/dl (normal range : 20-55). An important intrathecal synthesis of IgM (intrathecal fraction at 58%), of IgA (79%) and to a lesser degree of IgG (10%) was present. In addition, several CSF oligoclonal IgG bands were detected, which were not present in the matched serum.

These results prompted us to perform serological tests for Lyme disease (Euroimmun Anti-Borrelia plus VlsE ELISA IgG and Euroimmun Anti-Borrelia ELISA IgM, Lübeck, Germany). Strongly positive reactions were detected in the serum for both IgM (IgM ratio of 4.04, Nl < 1.0) and IgG (167 Relative Unit/mL, Nl < 20) antibodies. The
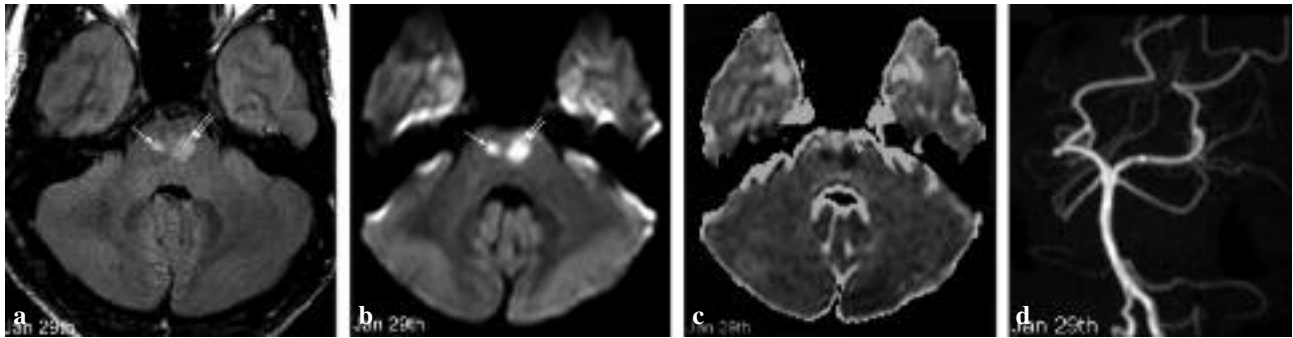
Fig. 1. — MR work up at admission

1a : Transverse Fluid-Attenuated Inversion Recovery (FLAIR) image showed bilateral abnormally hyperintense foci within the pons with a smaller right parasagittal lesion (arrow) and a larger left parasagittal one (paired arrows). Remainder of cerebral examination was unremarkable.

1b : Transverse Diffusion-weighted (DW) image in a similar slice location showed strongly hyperintense signal intensity within abnormal pontine areas on both sides.

1c : Apparent Diffusion Coefficient (ADC)-mapped image showing decreased ADC value within pontine lesions with an average of 513 mm²/s corresponding to a 73% reduction when compared to normal mean values within normal adjacent parenchymal tissue (700). This is pathognomonic for cytotoxic oedema reflecting acute ischaemic damage.

1d : Left oblique antero-posterior image from Time of Flight (TOF) angiogram demonstrated normal status of the posterior circulation.

ELISA tests were confirmed by a commercial Western Blot assay (Euroline-WB, Euroimmun AG) showing specific patterns (OspC for IgM antibodies, VlsE, p39, p30, OspC for IgG antibodies).

Native CSF contained 124 RU/mL of anti-Bb IgG antibodies confirmed by Euroline-WB, whereas serum diluted at the same IgG concentration was equivocal (21.9 RU/mL), thereby demonstrating an intrathecally-restricted production of these antibodies, which is a key feature for Lyme neuroborreliosis (Sindic *et al.*, 1987). PCR for Bb in CSF remained negative.

In contrast, serology was negative for HIV and *Treponema pallidum* (TPHA and VDRL tests). Rheumatoid factor, antinuclear and antiphospholipid antibodies were negative too.

Intravenous ceftriaxone (2 g daily) was given for two weeks according to current guidelines (Wormser *et al.*, 2006). The patient recovered completely within the month. A follow-up MR examination performed almost four months later demonstrated the appearance of a small gliotic scar on the right side of the pons and of a encephalomalacic cyst on the left one (Fig. 2a-c).

Retrospectively orientated anamnesis revealed a tick bite six months before admission with subsequent backache and unusual posterior headache. *Erythema chronicum migrans* was never observed throughout whole disease course.

Discussion

Arterial wall dissection, haemostatic dysfunction and connective tissue disorders are the most frequent etiologies of ischaemic stroke in young adults followed by vasculitis and CNS infections involving *Borrelia burgdorferi*, *Treponema pallidum*, *Mycobacterium Tuberculosis, Mucormycosis* and pyogens of which diagnosis mainly relies on CSF analysis.

May and Jabbari (1990) reported one case of ischaemic stroke in the frame of Lyme neuroborreliosis in 1990 and made a review including 11 previously published cases. Since then, only 18 additional patients have been reported (Lock *et al.* 1989 ; Olsson and Zbornikova, 1190 ; Defer *et al.*, 1993 ; Reik, 1993 ; Keil *et al.*, 1997 ; Schmitt *et al.*, 1999 ; Deloizy *et al.*, 2000 ; Zhang *et al.*, 2000 ; Heinrich *et al.*, 2003 ; Romi *et al.*, 2004 ; Schmiedel *et al.*, 2004 ; Habek *et al.*, 2007), 5 of them involving children below the age of 15 (Oksi *et al.*, 1996 ; Laroche *et al.*, 1999 ; Wilke *et al.*, 2000 ; Klingebiel *et al.*, 2002 ; Cox *et al.*, 2005). Another patient who suffered from a transient ischaemic attack characterized by dysphasia for a few hours with complete subsequent recovery had positive anti-Bb serology and lymphocytic meningitis (Hammers-Beggren *et al.*, 1993). Two cases of intracerebral haemorrhage and three of subarachnoid haemorrhage have also been described (Scheid *et al.*, 2003).

Among the 31 patients with a stroke event including ours, 18 were males, 23 had less than 50 years of age (range : 5-74 years) and 13 had between 15 and 28. Hemiparesis was the inaugural symptom in 22 (71%). Posterior circulation was involved in 13 cases (42%), with a frequent occurrence of uni- or bilateral thalamic infarction (6 cases). Basal ganglia, periventricular white matter and more rarely cortical areas can also be involved.

Conventional catheter angiography was performed in 9 cases and showed diffuse signs of vasculitis in four, signs restricted to vertebro-basilar
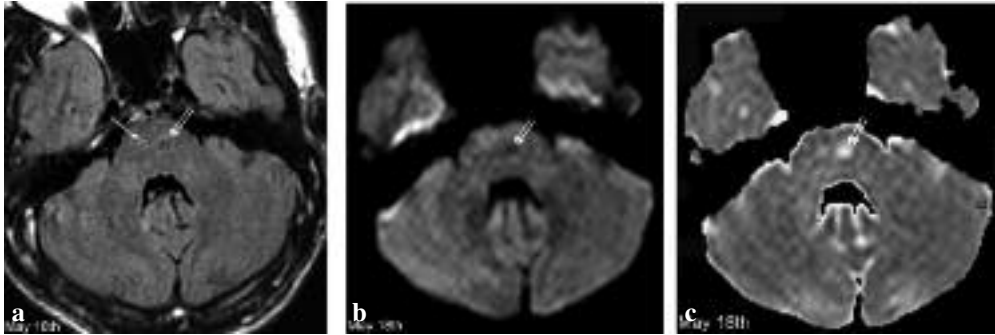
Fig. 2. — Follow-up MR work up 4 months later

2a : Transverse FLAIR image in a similar slice location as in Fig. 1a showed the persistence of a slight hyperintense gliotic scar on the right side (arrow), and the appearance of a hypointense encephalomalacic cyst on the left side (paired arrows).

2b : Transverse DW image in similar slice location failed to reveal any right abnormality corresponding to the gliotic scar but revealed an hypointense left cleft well corresponding to the cystic sequella (paired arrows).

2c : ADC-mapped image confirmed abnormally increased ADC value (bright signal intensity) within left cystic area with an average of 2000 mm²/s (+220%) reflecting increase in free-water diffusivity (paired arrows).

vessels in three others, to thalamic vessels in one, and was normal in the last case. Magnetic resonance angiography (MRA) was consistent with vasculitis in six cases and normal in three. Cerebral biopsy confirmed focal vasculitis in one case (Oksi *et al.*, 1996), and transcranial Doppler ultrasonography revealed severe stenosis of middle cerebral arteria in another (Lock *et al.*, 1989).

The delay between tick bite and stroke onset may range from three weeks (Hanny *et al.*, 1987) to 18 months (Reik *et al.*, 1993), thereby suggesting that Borreliosis-related acute cerebral infarction may occur at either early disseminated, or late phase of the disease course.

In all cases, CSF analysis revealed a high cell count, a high protein content and an intrathecal anti-Bb antibody synthesis. A slight hypoglycorrhachia may be observed. These abnormalities were resolved by appropriate antibiotic treatment and the clinical outcome was favorable in the majority of the cases. Results of CSF analysis were not reported in one case, except for positivity for Bb PCR It should be stressed that diagnosis of Lyme neuroborreliosis is made by inflammatory CSF abnormalities (lympho-monocytic pleocytosis and plasma cells), and by intrathecal production of Bb-specific antibodies ; only in early cases could PCR be helpful. Intrathecal antibodies without CSF pleocytosis exclude active neuroborreliosis and point to previous infection or blood-brain barrier disruption.

Our patient shares the similar characteristics to many of previously reported patients : young age, abrupt onset of neurological deficits, prior chronic headache, tick bite(s) 6 months before, typical CSF abnormalities, involvement of the posterior circulation with bilateral pontine infarction, good clinical outcome after antibiotic treatment. MRA was normal as in some other reported cases. The pathogenic mechanism for such localized vasculitic process could be a selective inflammatory involvement of perforating arteries emerging from either the basilar trunk or the middle cerebral arteries ; these thin vessels have a relatively long course through inflammatory meninges, thereby enabling easier inflammatory contamination by contiguity to arteriolar walls.

Although a screening for anti-Bb antibodies is of little value in unselected stroke patients (Hammers-Berggen *et al.*, 1990), Lyme neuroborreliosis has to be included in the differential diagnosis of non cardioembolic ischaemic stroke in the young, even in the absence of commemoration of tick bite or *erythema chronicum migrans*. Blood and CSF analysis are mandatory for confirming the diagnosis.

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