

Letters

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Cerebral angiopathy and recurrent strokes following *Borrelia burgdorferi* infection

Sir: Neurological abnormalities are seen in 11 to 15% of *Borrelia burgdorferi* infection. We report a woman who developed an angiopathy with recurrent ischaemic events during 3 years following a tick bite, with *Borrelia burgdorferi* infection.

During spring 1983, this 40 year old woman noticed a tick bite under her left breast, followed by red lesions on the chest and limbs. One year later, she experienced headache associated with weakness and paraesthesia around the mouth and in the left hand. She also complained of vertigo and intermittent dysarthria. She received flunarizine (10 mg per day for 3 months) and the symptoms disappeared. In November 1985 she developed a left ataxic hemiparesis, and CT showed a hypodense area in the right lenticular nucleus suggesting infarction. As blood pressure was 170/120 mm Hg, amiloride and hydrochlorothiazide were introduced. The patient recovered within 4 weeks. Four months later, she complained of blurred vision with numbness in the hands. There was a slight left-sided hemiparesis. Treatment with atenolol (50 mg per day) was begun and the symptoms did not recur. In August 1986, she developed diplopia, confusion and a stumbling gait. The patient showed a skew deviation with the left eye down, superimposed microsaccadic movements on pursuit attempts to the left, and an abduction palsy in the left eye. There was a limitation of vertical gaze, particularly upward. The optokinetic nystagmus quick phase was decreased to the right. There was a slight left-side hemiparesis with increased tendon reflexes, without Babinski's sign. A mild ataxia was present in the left arm with dysdiadochokinesia. Sensory testing was normal. The patient was disoriented in time and place, and periods of irritability alternated with drowsiness. Comprehension and spontaneous speech were impaired. Writing and reading were also affected. There were no

apraxia. No meningeal signs were present and the remainder of the physical examination was normal. On CT scan, there was a bilateral hypodense area in the thalamus suggesting a paramedian infarct, and the old lesion in the right lenticular nucleus was still visible, without contrast enhancement (fig 1). The cerebrospinal fluid (CSF) contained 27.5 cells/mm³ with 82% lymphocytes and 9% plasmocytes. Protein 267 mg/dl IgG index = 2.13 (n < 0.6). Glucose = 3.2 mmol/l (peripheral blood glucose = 3.5 mmol/l). Oligoclonal bands were determined by agarose gel electrophoresis using concentrated CSF (Beckman Immunochemistry Systems). Titres of specific antibodies against *Borrelia burgdorferi* were determined in the CSF: IgM = 1/4, IgG = 1/128, and in the blood: IgM = 1/32, IgG = 1/256 (positive test: >1/32). Gram stain, routine culture and culture for acid fast bacilli and fungi were negative. Reagin tests to *Treponema pallidum* were negative in the CSF and blood. The right carotid arteriogram demonstrated segmental narrowing and obstruction of branches of middle and anterior cerebral arteries (fig 2). More distal branches of these arteries received collateral flow in a retrograde fashion via leptomeningeal anastomoses. The same lesions were present in the left side. The thalamic arteries were extremely narrowed bilaterally. The basilar artery and the right superior cerebellar artery (SCA) were small, and there were anastomoses between the SCA and the posterior inferior cerebellar artery, and between the anterior inferior cerebellar artery and leptomeningeal arteries. Labora-

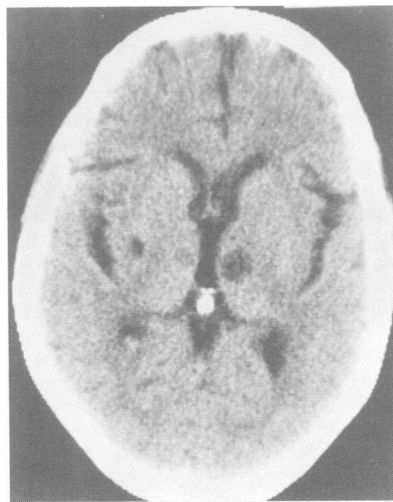


Fig 1 CT shows a hypodense area in the left thalamus and the old lesion in the right lenticular nucleus.

tory data showed a haemoglobin of 143 g/l and a white blood count of 9800 cell/mm³ with a normal differentiation. The ESR was 6 mm/h. The following tests were negative or normal: serum sodium, potassium, urea, glucose, SGOT, SGPT, alkaline phosphatase, gamma GT, serum protein and electrophoresis, IgA, IgG, IgM, Ig-K, Ig-λ, C3, C4, cryoglobulins, antinuclear antibody and anti-DNA, rheumatoid factors and Kweim test. Immune complexes were 7.1 (n < 5.6). The blood pressure was normal. A chest radiograph and an electrocardiogram showed no abnormality. A muscle biopsy (M vastus medialis) showed no abnormal fibres or vessels, but direct immunofluorescent studies of a skin biopsy specimen (thigh) revealed antibodies (IgG) in the basement membrane zone at the dermo-epidermal junction. Penicillin G (24 million units per day for 10 days) and prednisone (60 mg per day with tapering over 8 weeks) were begun. The neurological state improved within 3 weeks. The CSF showed 8.2 cells/mm³ with 92.5% lymphocytes and 1.5% plasmocytes. Protein 123 mg/dl, IgG index = 1.42. Glucose = 2.6 mmol/l (peripheral blood glucose = 3.4 mmol/l). Intrathecal synthesis of IgG and oligoclonal bands at electrophoresis. Clinical examination 3 months after the end of the treatment showed mild memory disorders and there was a relative palsy of the upward saccades. Specific antibodies against *Borrelia burgdorferi* were in the CSF: IgG = 1/8, and in the blood: IgG = 1/64. IgM were negative in the CSF and in the blood.

The relation between cerebral infarction and vasculitis due to infectious diseases prompted us to discuss the possible relation between a *Borrelia burgdorferi* infection and the development of ischaemic events associated with a diffuse cerebral angiopathy in our patient. During 3 years following the tick bite, repeated cerebrovascular accidents involving several vascular territories were observed. The CSF was typical with a lymphocytic pleocytosis, elevated protein, oligoclonal bands and IgG index. Specific antibodies against *Borrelia burgdorferi* were also present, compatible with an old infection.^{1,2} The cerebral angiopathy demonstrated on angiography has not been reported previously in *Borrelia burgdorferi* infections, probably because angiography is not performed currently in this condition, even when relapsing CNS dysfunction is present.³ In our case, the angiographic findings were similar to those observed in meningovascular syphilis or in several non-infectious arteritis.^{4,5} In our patient, there were neither findings suggesting arterial involvement outside the central nervous sys-



Fig 2 Right internal carotid arteriogram—lateral projection, subtraction film. Severe segmental narrowing or segmental occlusion of cortical arterial vessels (small curved arrows). Leptomeningeal anastomotic network (straight arrows).

tem nor any other generalised disease or drug abuse, and the clinical and laboratory data excluded other inflammatory or infectious diseases.^{4,5} Although no histological studies were obtained, it is possible that the vessel involvement seen at angiography represented an arteritis. There is a close similarity between *Borrelia burgdorferi* and *Treponema pallidum* with respect to their spirochaetal origins. Although the clinical picture is different, strokes secondary to meningovascular syphilis are often associated with prodromal disorders similar to those showed by our patient during the 3 years before the diagnosis was made.^{6,7} The pathogenesis of the angiopathy showed by our patient remains unclear. With antibiotic therapy, the earliest change in the CSF was a decrease of pleocytosis. The CSF is probably a better index of disease activity than antibody titres in the prognosis and evaluation of the patient after treatment. It is possible that the angiopathy observed in our

patient was the result of a direct spread of borrelias to the CNS vessels; likewise an obliterative endarteritis may develop in acquired syphilis. Alternatively, a vasculitis may be caused by immune mechanisms without the local presence of the infectious agent, in association with circulating immune complexes.^{3,8} The detection of such complexes in patients with postinfectious diseases and CNS vasculitis suggests that foreign antigens induce the formation of antigen-antibody complexes that damage the vascular endothelium.⁸ In our patient, deposits of antibodies were found in the skin and a slight elevation of circulating immune complexes was present. Recent reports^{7,9} and our study suggest that the clinical picture of chronic *Borrelia burgdorferi* infection needs to be enlarged to an angiopathic form. Because of the favourable response to treatment, one should consider the diagnosis of *Borrelia burgdorferi* angiopathy in unexplained stroke cases in areas with

endemic Lyme disease. We suggest that angiography should be performed in the patients with Lyme disease who suffer acute focal CNS events. We think that this diagnosis may be added to the other causes of cerebral infectious arteritis like pyogenic infections, tuberculosis, neurosyphilis and fungal infections.⁵

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