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CASE REPORT

I. Piccolo · G. Thiella · R. Sterzi · N. Colombo · C.A. Defanti

Chorea as a symptom of neuroborreliosis: a case study

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Abstract *Borrelia burgdorferi* (Bb) can cause a large number of neurological symptoms. Although extrapyramidal disturbances are rare (representing less than 2% of all neurological complications), diffuse choreic dyskinesias have been described during the course of mild encephalitis. The data published in the literature suggest that there are clinical and neurological analogies between neuroborreliosis and multiple sclerosis (MS). The presence of specific anti-Bb antibodies in cerebrospinal fluid is a discriminating factor that allows a diagnosis of neuroborreliosis to be made. We describe the case of a patient with Lyme disease, characterised by widespread chorea and behavioural disturbances. Emphasis is placed on the atypical onset and evolution, the difficulties encountered in formulating a diagnosis, and the uncertainties concerning the pathophysiology and clinical/neuroradiological correlations of the disease.

Key words Lyme disease · Neuroborreliosis · Chorea · Sporadic chorea

I. Piccolo (✉) · R. Sterzi · C.A. Defanti
Division of Neurology
Hospital Niguarda Ca' Granda
Piazza Ospedale Maggiore 3, I-20162 Milan, Italy

G. Thiella
Rizzi Division of Medicine
Hospital Niguarda Ca' Granda, Milan, Italy

N. Colombo
Neuroradiology Service
Hospital Niguarda Ca' Granda, Milan, Italy

Introduction

Borrelia burgdorferi (Bb), the cause of Lyme disease, can provoke a wide variety of neurological manifestations including meningitis, neuritis of the cranial nerves, encephalomyelitis and radiculoneuritis [1-5]. Its clinical severity varies from rapidly onsetting forms with severe focal neurological signs *ab initio*, to mild and fleeting forms; in some cases, the disease only gives rise to a moderate confusional state [6, 7]. Chronic progressive encephalopathy due to *Borrelia* is a rare condition [2, 3, 5]. In some cases, the magnetic resonance (MR) picture is characterised by multiple bilateral periventricular focal lesions that are similar to the plaques observed in patients with multiple sclerosis (MS), but the two can be distinguished by the presence of anti-*Borrelia* antibodies in cerebrospinal fluid [3, 8]. Movement disorders are rare in patients with Lyme disease, although choreic dyskinesias have been observed during the course of mild encephalitis [9, 10].

We describe a case of Lyme disease with an atypical onset, a chronic and progressive evolution, and unusual symptomatology (widespread chorea, behavioural disturbances and a confusional state).

Case report

A 45-year-old woman was seen in our Casualty Department on 28 June 1996 because of the onset of behavioural disturbances and confusional episodes during the month of January, and the subsequent appearance of involuntary choreic movements that had lasted for some months. Her family history included a deceased brother who suffered from depression and possibly committed suicide, another brother attending a psychosocial centre, and a chronically depressed mother who had died at the age of 79 years. The patient had been examined twice in the Casualty Department during the previous months

because of episodes involving a loss of consciousness, but was discharged on both occasions because the results of clinical and instrumental examinations were negative. After undergoing brain computerised axial tomography (CAT), she was admitted to the Division of Neurology because of suspected Huntington's chorea.

The patient had never taken neuroleptic or narcotic drugs, and was not an alcoholic. Objectively, she appeared to be disoriented in time and space, and had little critical or judicial awareness of the disease. She could remain still and walk. Although she appeared to be bradykinetic and hypotonic in global terms, she also presented diffuse choreic dyskinesia in the four limbs and trunk. Her deep reflexes were normal, and she had bilateral glabella, nasal and palmomental reflexes. Her Mini-Mental State Examination (MMSE) score was 16/30. As the patient manifested severe mental confusion, agitation and multiple aggressiveness, she was transferred to the Division of Psychiatry on 2 July where a Wechsler Adult Intelligence Scale (WAIS) revealed an Intelligence Quotient (IQ) of 65, with a deterioration index of 65%.

Neuroleptic therapy was initiated with haloperidol 15 drops t.i.d. (4.5 mg), followed by intramuscular tiapride (100 mg/d). Her behavioural disturbances improved, but the patient remained confused and her choreic movements unchanged. After having discontinued neuroleptic therapy, she returned to the Neurological Department on 18 July 1996. The results of a genetic test for Huntington's chorea and pallido-hemiballismus atrophy were negative (15 repeated low allele and 18 high allele CAG triplets). The results of routine hematological and lues serological tests were normal, except for the fact that the level of sideremia was at the lower limit of the norm (41 µg/dl); her ferritin level was normal, as were the levels of antistreptolysin, C reactive protein, rheumatoid factor and complement fractions. The search for anti-nDNA, anti-nuclear, anti-mitochondrial and anti-phospholipid antibodies was negative; there were no cryoglobulins and the patient was negative for lupus anticoagulant. The levels of the free fractions of thyroxine, triiodothyronine and thyroid stimulating hormone (TSH) were normal. There were no anti-HIV (human immunodeficiency virus) antibodies. Cupremia, cupruria and ceruloplasmin levels were normal. The search for acanthocytes on a peripheral blood smear was negative. Chest X-ray, electrocardiogram (ECG) and the evoked potentials of the trunk were normal. Electroencephalogram (EEG) revealed diffuse slow spiked-wave abnormalities in brief bouffées in both hemispheres.

Brain magnetic resonance (MR) (11 July 1996) documented a slight diffuse peritrigonal hyperintensity in proton density and T2-weighted images, with some small and more markedly hyperintense areas (Fig. 1a-d); the T2-weighted images also showed a slight decrease in the signal from both putamens (Fig. 1b, d).

On the basis of the hypothesis of an infective and/or demyelinating cause, a lumbar puncture was performed for the purpose of cerebrospinal fluid (CSF) analysis. Cytochemical examination of the CSF revealed a slight increase in protein content, the presence of seven cell elements (lymphomonocytes), and normal glycorrhachia. Isoelectrofocussing showed oligoclonal bands. Bacterioscopic and culture tests (aerobes and mycetes), herpes virus Polymerase Chain Reaction (PCR), Mycobacterium Tubercolosis (BK) and mycobacteria examinations were performed, as well as the antibody battery for viral and bacterial agents (Table 1). Only the IgG anti-*Borrelia* antibodies tested using the IgG IgM Lyme VIDAS-ELFA method proved to be significantly positive: IgG index 2.1 (negative value <0.75) with a CSF:serum level >1. The other antibody tests were negative.

On the basis of the CSF results, antibiotic treatment with intravenous ceftriaxone 2 g b.i.d. was started on 2 August 1996, and led to a progressive improvement in cognitive function and the dyskinesia. After about two weeks of antibiotic therapy, the patient became lucid and collaborative, and the results of a neurological examination were normal.

The restoration of her memory capacities allowed a partial reconstruction of a number of significant anamnestic events relating to the disease. She remembered having experienced an erythematous and pruritic skin rash on her neck towards the end of the previous year, which spontaneously regressed after a period of a few weeks. Her memory of the subsequent period was fragmentary, but she did say that the two episodes of loss of consciousness that had led to her being treated in the Casualty Department had been preceded by hyposthenia in her right arm.

Her MMSE score on 29 August 1996 was 26/30, thus documenting the recovery of her intellectual capacities.

After the disappearance of the anti-*Borrelia* antibodies from the CSF, the antibiotic treatment was discontinued and the patient was discharged from hospital on 10 September 1996. One month later, the results of an outpatient neurological examination were normal. Brain MR imaging revealed that, although the small areas with an altered signal in the left peritrigonal white matter remained substantially unchanged, those in the right hemisphere were less apparent. The putamen signals were essentially the same (Fig. 2).

Discussion

The diagnostic picture of this case was highly complex and required considerable investigation not only because of the absence of the anamnestic and objective characteristics typical of Lyme disease, but also because its unusual syndromic presentation involved behavioural disturbances and chorea: the patient did not have any of the signs or symptoms of the first phases of the disease [11]. The *a posteriori* discovery of the prodromic appearance of a possible erythematous skin lesion is objectively weak and certainly not conclusive.

The clinical association of behavioural disturbances, chorea and a positive family history of psychiatric diseases

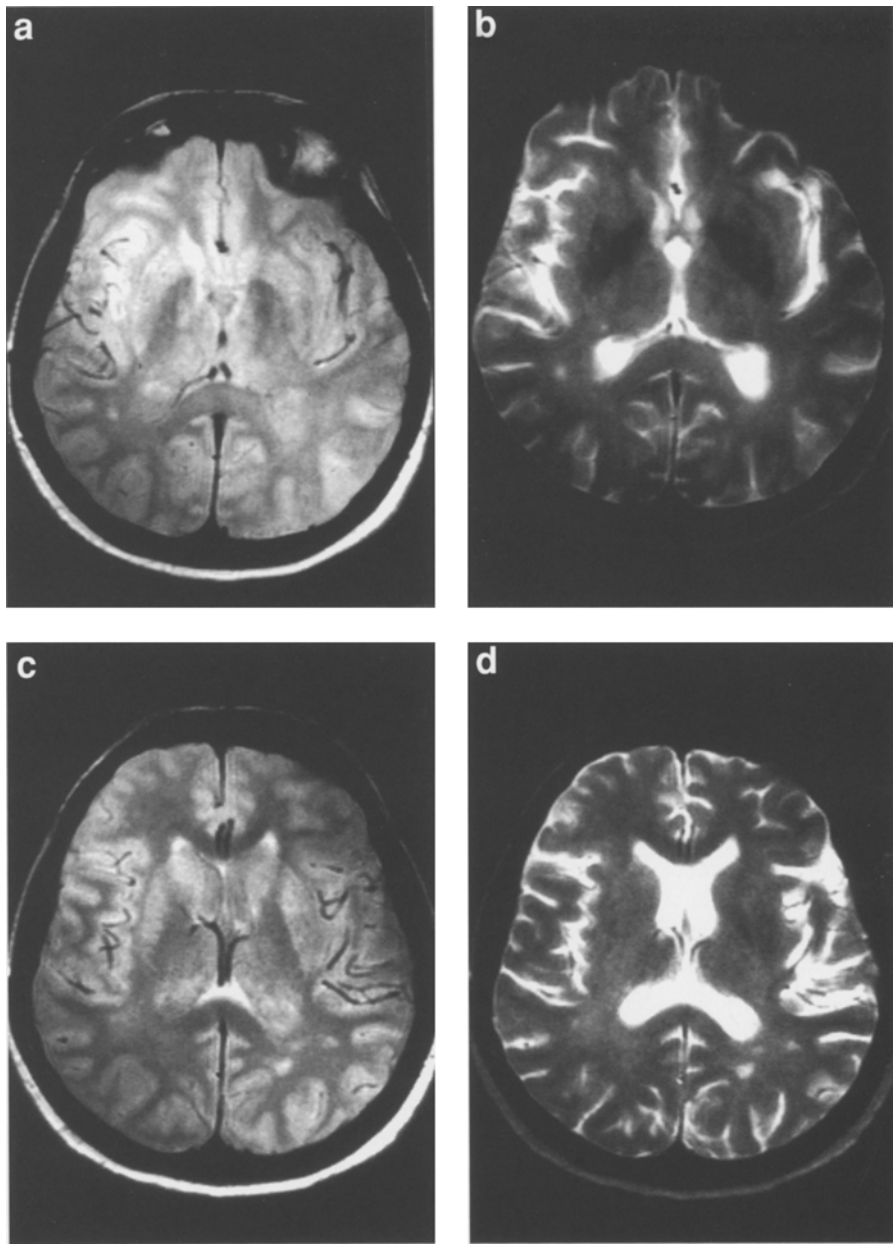

Fig. 1a-d *PD-weighted **a**, **c** and T2-weighted **b**, **d** axial MR images.* Both sequences show small areas with an altered signal in the peritrigonal white matter on both sides, where there is also slight diffuse hyperintensivity. There is a decreased signal in both putamens on the T2-weighted images

led us to suspect the presence of Huntington's disease, but this was excluded by the results of the genetic test. The normality of copper metabolism made it possible to exclude Wilson's disease, and the absence of peripheral blood acanthocytes excluded neuroacanthocytosis.

The subsequent investigations were therefore aimed at establishing whether or not this was a case of sporadic chorea. An iatrogenic origin was excluded on the basis of the fact that the patient had never taken any drugs that act on the central nervous system, and there was no evidence of alcohol or narcotic abuse.

The most well-known cause of secondary chorea is Sydenham's disease, which occurs in 10%-20% of patients with rheumatic fever. It is currently thought that rheumatic fever is correlated with an auto-immune mechanism that is triggered by an infection sustained by group A streptococci. The literature contains descriptions of IgG antibodies that cross-react with neuronal cytoplasmatic antigens of the caudate and subthalamic nuclei [12], whereas MR studies have documented the selective involvement of the basal ganglia [13]. Sydenham's chorea could be excluded in our patient because she had a negative anti-streptolysine titre and did not satisfy the criteria of Jones [14].

The clinical characteristics of the patient, and the negative results obtained from the use of the panel of antibodies related to auto-immune diseases, excluded the possibility of chorea due to systemic lupus erythematosus, nodular polyarthritis, necrotising vasculitis or a disease due to antiphospholipid antibodies. HIV infection was excluded on the grounds of the absence of HIV-antibodies.

Table 1 CSF laboratory examinations

Examination	25 July 1996	2 September 1996
Appearance	Limpid	–
Colour	Colourless	–
Glucose (mg/dL)	55	–
Proteins (mg/dL)	137 (nv, 13.4-23.7)	–
Albumin (mg/dL)	49	–
IgG globulin (mg/dL)	42 (nv, 0.6-6.1)	–
No. of elements/mm^3	7	–
Cytology	Lymphomonocytes	–
Bacterioscopy	Negative	–
Cultural examination (aerobes and mycetes)	Negative	Negative
Oligoclonal bands	Positive	Positive
Antisera		
- *Borrelia burgdorferi* IgG	2.1 (nv, <0.9)	Negative
- *Borrelia burgdorferi* IgM	0.1	Negative
- *Borrelia burgdorferi* CSF/serum	1.2	–
- *Chlamydia trachomatis* IgG/IgA	Negative	–
- *Cryptococcus*	Negative	–
- Toxoplasma IgG/IgM (IU/mL)	<4, negative	–
- CMV IgG/IgM (EU/mL)	<0.1, negative	<0.1, negative
- EBV IgG/IgM (EU/mL)	0.2, negative	0.1, negative
- HSV1 IgG (EU/mL)	0.2	0.2
- HSV2 IgG/IgM (EU/mL)	0.1, negative	0.1, negative
- Varicella-Zoster IgG/IgM (EU/mL)	0.1, negative	0.1, negative

nv, normal value; *CMV*, Cytomegalovirus; *EBV*, Ebstein-Barr virus; *HSV*, Herpes simplex virus

It is known that the clinical and neuroradiological presentation of neuroborreliosis and multiple sclerosis are similar [3], and some studies have led to the hypothesis that there may be a causal and pathogenetic correlation between Lyme disease and multiple sclerosis [6, 15]. In the case of our patient, MR imaging revealed multiple alterations in the signal derived from the peritrigonal white matter that were similar in appearance to those of the demyelination plaques observed in MS patients. It is now well established that the intrathecal production of antibodies specific for Bb

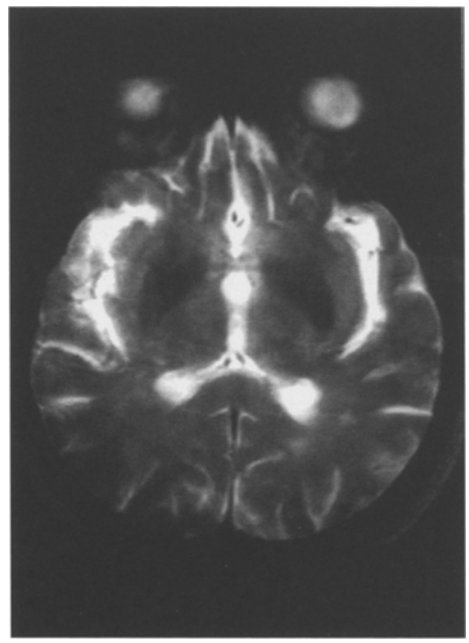

Fig. 2 Follow-up MR examination. T2-weighted axial image at a level comparable with that of Figs. 1a and b. The area of right peritrigonal hyperintensity has almost completely disappeared (compare with Fig. 1b)

distinguishes the two pathologies, and makes it possible to formulate a diagnosis of neuroborreliosis [6]. In our case, which is atypical in terms of the clinical symptoms indicative of Lyme disease, the laboratory findings are suggestive of the intrathecal production of anti-*Borrelia* antibodies and its normalisation after antibiotic therapy with ceftriaxone.

Although the estimated specifity of the ELFA method used by us is 98.7%, the limitations of a diagnosis exclusively based on microbiological data are well known. It is therefore important to underline the clinical response to therapy, particularly because the diagnosis of Lyme disease is prevalently clinical [16-19].

The affinity of the demyelinating MR picture that characterises both neuroborreliosis and multiple sclerosis is highly suggestive, and allows some considerations to be made concerning possible anatomic/clinical correlations in the case of movement disorders. This is particularly true of the choreas that may appear in patients with multiple sclerosis and in those affected by Lyme disease.

Extrapyramidal disturbances are rare in patients with borreliosis and have been described in less than 2% of those suffering from neurological disturbances [9]. The literature does not include any report of MR or anatomopathological findings concerning chorea in patients with neuroborreliosis but, in the case of patients with MS, the results of anatomical studies seem to indicate that the pathological basis of movement disturbances may be an impairment of the myelinated fibres contained in the striatum, pallidum and thalamus [20]. Three cases of chorea during the course of multiple sclerosis have been reported in which the alterations observed in the MR signal were localised to the basal ganglia or striatum [21].

Bearing in mind the limitations of laboratory examinations, our diagnostic conclusions are mainly based on the response to therapy, which is certainly in favour of a diagnosis of neuroborreliosis: ceftriaxone resolved the confusional state and the chorea, restored cognitive function, eliminated the CSF antibodies and partially resolved the neuroradiological picture.

Sommario *La "Borrelia burgdorferi" (Bb) può causare numerosi sintomi neurologici. Benché i disturbi extrapiramidali siano rari, meno del 2% di tutte le complicanze neurologiche, sono descritte discinesie coreiche diffuse in corso di lievi encefaliti. I dati della letteratura suggeriscono analogie cliniche e neuroradiologiche tra neuroborreliosi e sclerosi multipla (SM); il riscontro di anticorpi specifici per la Bb nel liquor discrimina le due entità patologiche e consente la diagnosi di neuroborreliosi. Descriviamo un caso di malattia di Lyme, caratterizzato da corea diffusa e disturbi comportamentali. Si sottolineano l'esordio e l'evoluzione atipici, la difficoltà dell'iter diagnostico, le incertezze sulla fisiopatologia e sulle correlazioni clinico-neuroradiologiche.*

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