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Untreated neuroborreliosis: Bannwarth's syndrome evolving into acute schizophrenia-like psychosis

A case report

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Summary. In general, meningopolyradiculitis (Bannwarth's syndrome, stage 2 of neuroborreliosis) follows a predictable monophasic self-limiting course. In contrast, we report the case of a patient with an untreated meningopolyradiculitis which evolved into acute schizophrenia-like psychosis due to persistent infection with *Borrelia burgdorferi*. The psychosis resolved within 1 week of treatment with ceftriaxone. This case shows that the usually benign monophasic meningopolyradiculitis may progress to severe CNS complications, which may have implications on current pathophysiological beliefs.

Key words: Neuroborreliosis – Persistent infection – Schizophrenia-like psychosis

Introduction

Meningitis, cranial neuritis and meningopolyradiculitis (Bannwarth's syndrome) are the most common and well-known forms of nervous system infections due to *Borrelia burgdorferi* (stage 2 of infection). Rather little is known about the involvement of the central nervous system (stage 3 of disease), which presents with non-specific neurological and psyschiatric features [1,10]. Mechanisms leading to stage 3 remain unclear. Furthermore, it is unknown whether the second and third stage represent different immunological responses to *Borrelia burgdorferi* or if stage 3 develops from stage 2. We present a patient suffering from both stages within 6 months.

Case report

In April 1989 a 54-year-old academic suffered from acute neck stiffness and burning pain radiating to the head and shoulders which he described as "entrapment of a nerve". Symptoms were worse during the night. Furthermore he noted a moderate left-sided facial weakness which occurred in parallel with the onset of pain and completely resolved after 1 week. His medical history was uneventful; several tick bites had been noted in autumn 1988. As the radiograph of the cervical spine revealed no abnormalities, his physician diagnosed "cervicobrachialgia". Massage of the neck and shoulders was administered without effect. During the following weeks the pain decreased but fatigue accompanied by slowly increasing loss of concentration developed, which made it impossible for him to continue his profession. In September 1989 he first noticed that his thoughts were influenced by persons from the television and radio. He suffered from sleep disturbances and felt incapable of thinking. On admission to our hospital 1 week later the patient was fully orientated, presenting with parathymia, incoherence of thoughts, forced thinking, thought blocking, delusion of persecution and reference. Neurological examination, routine blood tests, and radiographs of the chest showed no abnormalities. The EEG revealed moderate slowing. In view of the patient's age and the first manifestation of psychosis, lumbar puncture was performed on 6 October 1989. The results are shown in Tables 1 and 2. Because of the initial cerebrospinal fluid (CSF) findings antituberculous treatment was started but acid fast bacilli staining, tuberculostearic acid and cultures for *Mycobacterium tuberculosis* were negative. Despite the combined administration of chemotherapeutic and neuroleptic treatment the patient's clinical condition remained unchanged. Computed tomography (CT) and magnetic resonance tomography (MRI) of the brain were normal. One week

Table 1. Time-course of cerebrospinal fluid (CSF) cell count and protein. CC, Cell count/µl; TP, total protein (mg/100 ml); Ig, antibody species (mg/100 ml; (% a), percent of autochthonous antibody production in the CSF; oIB, oligoclonal banding; Pl, plasma

Date	CC	TP	IgG (% a)	IgM (% a)	IgA (% a)	oIB (CSF)	oIB (Pl)
6 October 1989	100	92	66 (70)	0	7 (20)	+	–
27 October 1989	61	120	38 (70)	0	4 (20)	+	–
23 November 1989	17	108	33 (70)	0	3 (40)	+	–
10 January 1990	7	97	26 (70)	0	3 (45)	+	+
5 March 1990	4	48	14 (45)	0	2 (30)	+	+

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Table 2. Time-course of *Borrelia burgdorferi* antibody titres in the CSF and plasma (Pl). IFT, Immunofluorescence test *(titration limit of 1:5);* EIA, enzyme immunoadsorbent test (units/l); G, IgG; M, IgM; CPI, *Borrelia burgdorferi*-specific CSF: plasma index of IgG. This index was calculated by: (total IgG plasma: CSF) × (specific IgG CSF: plasma)

Date	CSF IFT(G)	Pl IFT(G)	CSF IFT(M)	Pl IFT(M)	CSF EIA(G)	Pl EIA(G)	CPl IFT(G)	CPl EIA(G)
6 October 1989	1:256	1:512	1:5	1: 8	266	424	6.2	7.7
27 October 1989	1:128	1:512	1:5	1: 8	183	411	7.8	9.3
23 November 1989	1:128	1:512	1:5	1: 8	204	689	8.8	10.1
10 January 1990	1:128	1:256	1:5	1:16	20	356	15.1	1.8
5 March 1990	1: 64	1:128	1:5	1: 8	11	187	14.8	0.9

after the initial lumbar puncture the following CSF results led to the initiation of antibiotic treatment with ceftriaxone (2g/day, at least 2 months): increased antibody titres aginst *B. burgdorferi*, a significantly elevated IgG CSF-plasma index [CPI IFT(G) = 7.7; normal range below 2, see Table 2]. Two western blots, which were performed on CSF and plasma samples at 2 different days (6 October 1989 and 27 October 1989), revealed positive results concerning the following antigen compounds of *B. burgdorferi*: 94, 60, 41, 30 and 21 kDa. Furthermore, the following diseases could be excluded: cryptococcosis, sarcoidosis, toxoplasmosis, infections with *Treponema pallidum*, HIV, arboviruses, candida, parasites and meningeosis. In addition, blood examinations of the immune system (immune electrophoresis, complement C3c, C3d, C4, C2) were normal. After initiation of ceftriaxone treatment a rapid resolution of psychotic symptoms followed which completely disappeared after 1 week, but left the patient in a moderate organic psychosyndrome which lasted until discharge 5 months later. The CSF follow-up is given Tables 1 and 2.

Discussion

CNS manifestations of stage 3 infection due to *B. burgdorferi* may present with various neuropsychiatric symptoms [10]. According to the criteria of Ackermann et al. [1] our patient's diagnosis was confirmed by the course of the elevated IgG CSF: serum index, the positive western blot and the course of the antibody titres. With ceftriaxone treatment the CSF cell count rapidly declined, whereas CSF protein only moderately decreased. A significant decrease of CSF IgG antibody titres against *B. burgdorferi* was detected 5 months after antibiotic treatment. This case report reveals two interesting aspects. First, the patient presented with an acute schizophrenia-like psychosis indistinguishable from "endogenous" schizophrenia as there were no neurological (focal or meningitic) signs. Because CT and MRI could not detect focal lesions a diffuse affection of the brain rather than cerebral vasculitis can be assumed. The dramatic improvement with ceftriaxone suggests an underlying encephalitis due to direct bacterial invasion. However, in contrast to "endogenous" schizophrenia the patient passed into a moderate organic psychosyndrome. Secondly, 6 months before the onset of psychosis the patient suffered from acute neck stiffness, headache, unilateral facial weakness and radiating pain after a history of tick bites. These classical symptoms of meningopolyradiculitis (Bannwarth's syndrome) were misdiagnosed and the patient received physical therapy. Independent of antibiotic treatment most authors view Bannwarth's syndrome as a self-limiting benign clinical entity [2,6,8]. This is in contrast to our patient's course of disease, which does not support the view that neuroborreliosis presenting as Bannwarth's syndrome is always a monophasic illness. Lately, however, there have been reports of patients with signs of both stages (meningitis, encephalopathy) in parallel [12]. Our patient continously progressed from Bannwarth's syndrome through cognitive difficulties to the acute pyschosis. This seems to argue against a possible re-infection with *B. burgdorferi*. It is likely that cognitive difficulties reflect active CNS infection, which has recently been described by Halperin et al. [4]. As CT and MRI were normal and the symptoms promptly responded to ceftriaxone, this clinical course can be attributed to a progressive spread of bacteria. This is in accordance with the experimental observation that *B. burgdorferi* infection tends not to focal aggregates but is rather randomly distributed [3].

It would be great interest to know in which patient the infection may lead to stage 2 or stage 3 or which patients are liable to suffer from both stages. One way to answer this would be to compare the morphological changes of stage 2 and 3 with the differing mechanisms of the immune regulation. Regarding this aspect the current literature is inconclusive. Histopathological changes which could give important clues are sparse. The acute stages are thought to be due to a direct vascular inflammatory response to the bacteria [9]. In the development of stage 3, pathological immune response (cross-reacting IgM antibodies, [13]), demyelinization, autoimmune vasculitis and direct bacterial encephalitis [10] have been postulated. On the other hand, the investigation of components of the immune system such as HLA antigens has produced diverging results. Pflueger et al. [11] suggested that HLA DR 2 and 3 are associated with a lower incidence of severe courses limiting the inflammatory process (monophasic meningopolyradiculitis, Bannwarth's syndrome). In contrast, Kristoferitsch et al. [7] reported that HLA DR 2 antigens direct the course of *Borrelia* infection towards its chronic forms. Thus in neuroborreliosis these unequivocal views currently leave immunoregulatory aspects open. In our patient, in the absence of gross immunological abnormalities the question of other explanations of this clinical course arises. As European and North American *Borrelia* strains are known to cause different clinical features, one reasonable possibility is infection with a further strain exhibiting different immunogenetic properties. Our observation led us to conclude

that despite the often prevailing view of Bannwarth's syndrome as a monophasic illness an adequate antibiotic treatment is needed to prevent the development of stage 3. Furthermore, as some authors have suggested [5,10], in certain cases especially with progressive courses additional immunosuppressive treatment may be required.

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