Neuroborreliosis in an HIV-1 Positive Patient

R. Černý, L. Machala, M. Bojar, H. Rozsypal, D. Pícha

Abstract
Simultaneous co-infections of Borrelia burgdorferi sensu lato and HIV-1 are rare events, with only six published cases. A case of acute neuroborreliosis with facial palsy, meningoradiculitis (Bannwarth's syndrome) in an HIV-1 positive individual is described. Diagnosis was confirmed by Western immunoblot analysis of serum and CSF and by proof of intrathecal production of antibodies against B. garinii. The patient was successfully treated with cefotaxime. In all published HIV+ cases, the course of borreliosis did not differ from that of the HIV negative population and the prognosis in properly treated patients was good.

Introduction
Although both Lyme borreliosis (LB) and HIV-1 infection are common diseases, only six cases of LB/HIV co-infection have been — to our knowledge — published, three out of them with neurological manifestation [1–6]. LB is the most frequent neuroinfection in the Czech Republic, followed by the European tick-borne encephalitis (ETBE). LB represents a multiorgan illness with frequent impairment of the central nervous system, with a yearly incidence 50–55/100,000 cases. The occurrence of HIV-1 infection remains low in the Czech Republic with a yearly incidence of 0.6/100,000 cases [7]. The case of an HIV-infected man who developed an acute borreliosis starting with erythema migrans, followed by a facial palsy and meningoradiculitis with a favorable outcome is described.

Case Report
Our patient is a 46-year-old man with a 16-year history of HIV-1 infection (CDC classification A2). He decided to stop the antiretroviral treatment in the year 2000, because his immunological and virological parameters were stable and favorable over the long term. He came in July 2002 to the out-patient department with a sudden onset of fever, arthralgias and multiple macular erythema on both forearms. These symptoms were resolved within 6 days by symptomatic treatment only. Two weeks later he complained about left facial palsy. The Bell’s sign was positive with 4-mm lagopthalmos. No taste or sensation disturbances were noted; the patient was afebrile and without irritation of meninges. He was admitted because of shooting pain in the cervical spine and left shoulder followed by facial palsy progressing within 48 h to plegia. No fever or other systemic symptoms were observed. EEG and computer tomography of the brain were normal.

Laboratory tests results: CD4+ T-lymphocytes 426/μl, IRI 0.27, viral load < 400 HIV RNA copies/ml (Roche Amplicor). CSF: protein 3.02 g/l (0.2–0.5 g/l), glucose 2.2 mmol/l (2.2–4.2 mmol/l) and mononuclear pleocytosis 416 cells/μl. CSF serology: IgM ELISA against HSV 1and 2, VZV and CMV negative, PCR HSV 1 negative, VDRL negative. Blood serology: VDRL negative, highly positive IgG and negative IgM against ETBE (the patient had never been vaccinated against ETBE).

Serology for LB: on July 31, 2002 high titers IgG and IgM (ELISA, TestLine, Brno, Czech Republic) both in serum and CSF. Western immunoblotting (WB) against B. garinii (Bio-Western, Praha, Czech Republic) was positive both in serum and CSF. Upon follow-up on November 24, 2003, the IgM titer in the serum was borderline and the IgG titer was negative. WB against B. garinii was negative. CSF was not examined. Serum IgG was 21.52 g/l, serum albumin 39.29 g/l, CSF IgG 814.8 mg/l and CSF albumin 1244.0 mg/l. The value of IgG index was 1.2 (ratio of IgG quotient 37.86·10–3 to the albumin quotient 31.66·10–3; positive if > 0.7), which confirmed the intrathecal IgG production [8]. The intrathecal production of specific antibodies was further proved by high specific antibody index = 4.76. This index is calculated as the ratio of specific IgG antiborrelial antibody CSF/serum index to the global IgG CSF/serum index (positive > 1.5) [9, 10].

Treatment with IV cefotaxime (2 g TID for 21 days) was started on day 7 of hospitalization. On this therapy radicular pain quickly disappeared and facial palsy improved substantially. Only a moderate facial weakness was present upon discharge – the Bell’s sign was negative, lagopthalmos 1 mm, forehead wrinkle and teeth showed a half range of mobility, platysma contraction was visible. Six months later only subtle signs were observed — a
slight hypokinesia of the left face when speaking. There was no relapse of LB symptoms during 2 years of follow-up.

Discussion
Despite the high incidence of both infections, the occurrence of LB/HIV co-infection remains extremely low. This fact is still to be elucidated, but a possible explanation could be found in the different epidemiology of these infections. LB is primarily a rural or suburban disease, whereas HIV is prevalingly an urban infection [3]. Also, considering that many symptoms of both infections are overlapping (e.g. lymphadenopathy, skin and neurologic manifestation), underreporting of LB in HIV+ patients seems possible [11].

Our patient had lived for many years in a log-house in a forest area in central Bohemia with a high occurrence of both LB and ETBE. Clinical presentation was characteristic for an early disseminated stage of LB. Combination of neurological symptoms and CSF findings is typical for Gariñ–Bujadoux–Bannwarth syndrome, which represents common form of neuroborreliosis in Central Europe.

From all up to now published cases of LB/HIV co-infection (four in Europe and two in USA), three were with neurologic involvement [2–4]. Erythema migrans (EM) was found in all European cases and in one American case. Neither skin nor neurologic symptoms were observed only in one case with an isolated LB arthritis [6]. In two European cases only prolonged atypical skin manifestation was observed [1, 5]. Three cases with the neurologic involvement included: lumbar radiculitis [4], meningoencephalitis [2] and meningoencephalitis with bilateral facial palsy [3]. In all these cases the neurologic symptoms were preceded by extensive skin manifestations – as in our case.

Standard diagnosis of LB is based on presence of both clinical symptoms and antiborrelial serum antibodies. The HIV infection with impaired immunity may significantly modify the serological response to LB infection. Both false positive and negative results of screening tests for LB (indirect immunofluorescence and ELISA) were observed in HIV+ persons [12, 13]. Diagnosis is verified by WB. The intrathecal production of LB antibodies, which is generally required for the diagnosis of neuroborreliosis, is confirmed by positive CSF/serum antibody index; the value found in the presented case was high [9]. In our patient, the concentrations of IgG and IgM antibodies at the onset of the disease both in serum and CSF were high, and WB was also positive in both serum and CSF.

Control serologic examinations after 16 months were negative with the exception of slight positivity of ELISA IgM, which can be explained by common non-specific antibody reaction (WB negative). Rapid decline of specific IgG antibodies is not frequent, but possible in the early disseminated borreliosis and is considered as a sign of borrelia eradication. In our case this could be also corroborated by the moderate immunodeficiency caused by HIV infection [12, 14].

The treatment of LB is based on administration of antibiotics; early skin forms may be treated either with oral doxycycline or amoxicillin; for treatment of neuroborreliosis, it is generally recommended iv administration of penicillin or third-generation cephalosporins [15]. All patients with neuroborreliosis, our case included, were successfully treated with third-generation cephalosporins administered iv.

Two cases with dermatological manifestation were successfully cured by oral tetracyclines only [1, 5]. On the contrary, a short treatment with azithromycin for 5 days in the case of Dudle et al. [2], did not prevent progression to neuroborreliosis in an HIV+ patient with low immune status (250/µl CD4+ T-lymphocytes) and an early local form of borreliosis.

Our case is in good correspondence with the above mentioned reports, particularly with the case of Garcia-Monco et al. [3] – meningoencephalitis and facial palsy with a good outcome in a moderately immunocompromised patient.

The simultaneous LB/HIV co-infection remains a rare event, despite the high occurrence of both infections. The clinical course of neuroborreliosis in HIV+ patients, even with severe immunodeficiency, does not differ from the course in most patients with LB, but due to the overlap of many similar symptoms, LB in HIV+ patients can escape the correct diagnosis. Serologic screening tests for LB may be unreliable and in all clinically suspected cases the diagnosis of LB should be verified by WB.

Clinicians in endemic areas should be aware of the nonfrequent LB/HIV co-infection in order not to miss a treatable infection.

Acknowledgment
This work was supported by MH grant No. 5673/3 and Research Program Grant of the Ministry of Education and Sports No. 111300003.

References