

Short report

Polyneuritis cranialis associated with *Borrelia burgdorferi*

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SUMMARY Three patients with classical idiopathic polyneuritis cranialis, in whom no other aetiology could be detected, were examined serologically, by means of indirect immunofluorescence test, for antibodies (IgM and IgG) against *Borrelia burgdorferi*, the aetiological agent of Lyme disease. In each case polyneuritis cranialis was caused by infection with *Borrelia burgdorferi*. Therapy with penicillin proved to be effective.

The term polyneuritis cranialis has been applied to an inflammatory lesion of cranial nerves within the skull, sometimes following osteomyelitis of the skull or basal meningitis (for example tuberculosis). It must be distinguished from neoplastic infiltration of the meninges and multiple cranial nerve involvement seen in sarcoidosis or other granulomatous meningitides, such as syphilis and torulosis¹ and from Melkersson's syndrome.² A small percentage of cases remain unexplained as idiopathic.³ The neurological aspects of Lyme disease include, beside radiculoneuritis and encephalitis, involvement of cranial nerves or neuritis cranialis.⁴ The aetiological agent of Lyme disease has been finally identified by Burgdorfer *et al*⁵ as a spirochete, subsequently named in 1984 *Borrelia burgdorferi*,⁶ which is transmitted by the bite of tick or tabanidae.

We present three cases of typical polyneuritis cranialis associated with *Borrelia burgdorferi* without any involvement of peripheral nerves of nerve roots, or any involvement of the brain.

Patients and methods

The patients were examined neurologically, by electroencephalogram, contrast medium enhanced CT and radiography of the skull with particular respect on the base and nasal sinuses. CSF was examined in the usual way, including immunoglobulins, serum/CSF ratios of immunoglobulins^{7,8} and CSF electrophoresis.

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The serological examinations were performed at the Hygiene-Institute of the University of Vienna by means of indirect immunofluorescence test (IIFT).

Case reports

Case 1, a female, aged 39 yr, was in good health until 26 October, 1983, when she noticed a rightsided facial paresis. On 31 October, 1983 an additional leftsided facial paresis lead to admission at our department. There was no history of insect bite (for example tabanidae), nor did she recall an erythema chronicum migrans, an arthritis or any cardiac problems. Neurological examination showed an almost complete bilateral peripheral facial paresis with impairment of taste. No other abnormal neurological signs could be detected. There was no neck stiffness. A lumbar puncture was performed and repeated several times. CSF showed lymphocytic pleocytosis and markedly raised IgG-, IgA- and IgM indices thus indicating intrathecal immunoglobulin-production. CSF electrophoresis showed oligoclonal bands. Culture of CSF for pathogenic organisms, including acid fast bacilli yielded no result. Intraperitoneal inoculation into guinea-pigs did not confirm the suspected diagnosis of basal meningitis due to tuberculosis. Contrast medium enhanced CT scan and skull radiographs were normal as was the EEG.

Complementfixation reactions to neurotropic viruses were negative on several occasions. Antinuclear factor and cryoglobulins were also negative. Electrophoresis showed a mild elevation of α_2 globulins (13,5%). Electrocardiogram (ECG) was completely normal. Radiography of the thorax showed no abnormality, particularly no signs of pulmonary tuberculosis or sarcoidosis. Tine Test was negative and *Treponema pallidum* haemagglutination test was non reactive. All routine laboratory serum findings were within normal limits. ENT examination revealed no abnormality.

Basal meningitis due to *Mycobacterium tuberculosis* was nevertheless suspected and antituberculosis treatment with INH 600 mg, myambutol 1600 mg and rifampicin 600 mg daily was initiated. Pyridoxin 50 mg daily was added. Within 1 week the bilateral facial paresis showed signs of remission until full recovery was reached about 3 weeks after starting this treatment, whereas the CSF findings remained abnormal for more than 3½ months.

By late spring 1984 the facilities of determination of antibodies (IgG and IgM) against *B burgdorferi* by means of indirect immunofluorescence test became available to us. Only by September were we able to examine the patients' serum and CSF for these antibodies; the results are listed below. Immediately, the antituberculous drugs were stopped and a 2 week's course of penicillin G (5×10^6 units iv four times daily) was started. The positive effect of this therapy onto the serological titres can clearly be seen:

	IgM		IgG	
	Serum	CSF	Serum	CSF
19 Sept 1984	1:64	1:2	1:2048	1:4
4 Oct 1984	1:16		1:2048	
6 Nov 1984	neg		1:128	

It should be noted that the patient had no neurological symptoms at all since the episode of bilateral facial palsy, nor had she been bitten by ticks or tabanidae during the previous year.

Case 2, a male aged 43 yr was bitten by a tick early in July 1982. 2 weeks later he noticed erythema around the tick-bite, which spread, and was diagnosed as erythema chronicum migrans. On 6 August 1982 he developed left sided V, VI and VII cranial nerve pareses. Lumbar CSF show mild lymphocytic pleocytosis and raised IgG index. Culture of CSF for pathogenic organisms including acid fast bacilli were negative; intraperitoneal inoculation of CSF into susceptible animals did not yield any result. Contrast medium enhanced CT scan, skull radiographs, EEG, ECG, thoracic radiographs and all routine serum parameters were normal. *Treponema pallidum* haemagglutination test was non reactive. The diagnosis of polyneuritis cranialis of unknown origin was established, basal meningitis due to tuberculosis, sarcoidosis, or syphilis fairly certainly being excluded. Complement fixation reactions to neurotropic viruses did not indicate any recent viral infection. The patient was treated with prednisolone, 40 mg daily. Within 2½ weeks time the cranial nerve pareses subsided completely. After having diagnosed the case 1 this year, this patient's serum was examined for antibodies (IgM and IgG) against *B burgdorferi*; the results (IgM 1:16, IgG 1:64) proved the diagnosis of Lyme disease. On exact questioning the patient gave no history of tick bite or any disease in the years following his episode of polyneuritis cranialis, after the tickbite in July-August 1982.

Case 3, a female aged 29 yr she was in good health until early September 1984. Three weeks earlier she had been bitten by a tick without subsequent erythema. The first

neurological symptoms were impairment of hearing (left side) and double vision when looking into the distance. Neurological examination on 3 October 1984, revealed a trigeminal lesion on the rightside, bilateral involvement of the abducens nerves, hypacusis in the left ear and mild right sided IX cranial nerve palsy. No other neurological abnormalities were detected. Lumbar CSF revealed only mild pleocytosis and a borderline IgG index. Culture of CSF did not grow any pathogens. EEG, contrast-medium enhanced CT scan, skull radiographs and cerebral angiography were all normal. Serum electrophoresis showed slightly elevated α_2 globulin fraction (11.4%). Cryoglobulins and antinuclear factor test were negative. ECG, chest radiograph, and all routine laboratory findings were normal. *Treponema pallidum* haemagglutination test was non reactive. Repeated complement fixation tests for neurotropic viruses excluded recent infection. The serum was examined repeatedly for antibodies (IgG and IgM) against *B burgdorferi* by means of indirect immunofluorescence test, the results proving a recent infection by this organism:

	IgM		IgG	
	Serum	CSF	Serum	CSF
3 Oct 1984	1:64	neg	negative	
24 Oct 1984	1:64		1:128	
18 Nov 1984	1:128		1:64	
17 Dec 1984	1:64		1:32	
2 Jan 1984	1:16		1:32	

Thus the diagnosis polyneuritis cranialis due to infection by *B burgdorferi* was clearly established. Because of a known allergy to penicillin, tetracyclin (500 mg qid) was given for a period of 2½ weeks. Neither the neurological symptoms nor the serological findings did show any improvement; only when latamoxef (1.5 g bid intravenously for 2 weeks) was given, was a response observed, both serologically and clinically, leading eventually to partial improvement of the cranial nerve involvement.

Discussion

Tick transmitted Lyme disease as described by many authors^{4,9,10} is a multi-organ disease involving skin, joints, heart muscle and central nervous system. In Europe a chronic lymphocytic meningo-radculitis is known as Garin-Bujadoux or Bannwarth's syndrome.^{11,12} Only very recently was the spirochetal aetiology of Lyme disease recognised by Burgdorfer *et al*⁵ and a similar or the same pathogenetic agent was subsequently suspected by Ryberg *et al*¹³ for Bannwarth's syndrome, who suggested it was a neurological variety of Lyme disease.¹⁴

The signs are those of meningoradiculoneuritis. Reik and Meyerhoff stressed the involvement of various cranial nerves together with encephalitis, radiculitis and/or neuritis.^{4,9} As with other manifestations of *B burgdorferi* infection (for example

erythema chronicum migrans) the neurological symptoms tend to resolve spontaneously,^{9,10} but their course is markedly shortened and long term complications can be prevented by antibiotic therapy, described below.¹⁵

Our three patients suffered from polyneuritis cranialis without radiculitis, peripheral neuritis or encephalitis. Two had a history of tickbite, one of erythema chronicum migrans. There are no other parameters which would be typical for Lyme disease, except that all three showed a highly elevated level of antibodies (IgG and IgM) against *B burgdorferi* (by means of indirect immunofluorescence test) indicating infection with the organism which is known to cause Lyme disease.

When osteomyelitis of the base of the skull, basal meningitis (for example tuberculous), diabetes mellitus, neoplastic infiltration of the meninges and multiple cranial nerve involvement seen in sarcoidosis or other granulomatous meningitides (such as syphilis, torulosis) can be excluded, an infection by *B burgdorferi* is to be suspected as the cause of polyneuritis cranialis, as in the three patients described here. The bilateral facial paresis of case 1 resolved within a period of three weeks without specific antibiotic therapy; a feature observed frequently in Lyme disease.^{9,10} Whether the improvement of the deficits of case 2 were due to corticosteroid therapy, is not proved. However, before the detection of *B burgdorferi* as the aetiological agent of Lyme disease, corticosteroid therapy has been recommended for lymphocytic meningoradiculitis.⁴

Nevertheless the main implication of diagnosing polyneuritis cranialis as being caused by *B burgdorferi* is the readily availability of therapy for this condition. Penicillin G, 20×10^6 , IU per day for 2 weeks has proved to be very effective.¹⁵ Case 1, although without neurological deficit at the time of penicillin therapy showed a dramatic serological response. Case 3, known to be allergic to penicillin, was given tetracyclin, without clinical or serological response within 2½ weeks. Only when she was given latamoxef iv (1,5 gbid for 2 weeks) did the cranial nerve pareses show partial improvement, corresponding to the decreasing serological titre. Three weeks after the completion of moxalactam therapy, partial left sided VI and VIII palsies still remained. The conclusion is that tetracycline is not effective in treating neurological complications of

Lyme disease, whereas, like penicillin, latamoxef seems to influence positively its course.

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