

NEUROLOGICAL AND PSYCHOLOGICAL SYMPTOMS AFTER THE SEVERE ACUTE NEUROBORRELIOSIS

Katarzyna Gustaw¹, Katarzyna Beltowska², Marta Makara Studzińska³¹Outpatients Neurological Department, Institute of Agricultural Medicine, Lublin, Poland²Department of Public Health, Institute of Agricultural Medicine, Lublin, Poland³Department of Medical Sociology, Institute of Sociology, Maria Curie-Skłodowska University, Lublin, Poland

Gustaw K, Beltowska K, Makara Studzińska M: Neurological and psychological symptoms after the severe acute neuroborreliosis. *Ann Agric Environ Med* 2001, **8**, 91–94.

Abstract: The purpose of this study was to delineate distant neurological and neuropsychological effects of severe neuroborreliosis. A group of 33 patients (12 men and 21 women) were selected for the study. Every patient had suffered from severe meningitis, meningoencephalitis or meningopolyradiculoneuritis due to neuroborreliosis in the chronic form of the illness. Standardised medical interview, physical examination and a series of neuropsychological tests (WAIS-R, BDI, BENTON-BENDER, DUM) were performed. In the clinical history, 36.4% of the patients complained of headache, 27.3% of subjective memory distortions; 33.3% of the patients suffered from sleeplessness. The neurological examination showed that 36.4% of the patients experienced such cerebellum integrity disturbances as abnormalities in gait and coordination or even mild ataxia. 21.2% of the patients experienced dysfunction in the proprioceptive pathways, 9% asymmetry in deep tendon reflexes (DTR's), 27.3% disturbances in the sensory responses. The examination showed, however, no muscular strength abnormalities. Half of the patients had slight depression. Psychological tests indicated that 21.2% of the patients had problems in thinking process and experienced memory impairment. 36.4% of the patients had significant organic damage in the central nervous system. The results of this study suggest the existence of long-lasting consequences of acute neuroborreliosis, which can significantly influence the quality of life of patients.

Address for correspondence: Katarzyna Gustaw, MD, PhD, Outpatients Neurological Department, Institute of Agricultural Medicine, Jaczewskiego 2, P.O. Box 185, 20-950 Lublin, Poland. E-mail: gustaw@galen.imw.lublin.pl

Key words: neuroborreliosis, meningitis, encephalopathy, cerebellum disturbances, neuropsychological tests.

INTRODUCTION

In the literature [1, 9, 12, 13], Lyme borreliosis is classified as having early and late infections. The most obvious criterion of an early infection with *B. burgdorferi* is erythema migrans (EM), but this is present only in about 40-60% of patients [9, 17]. After EM, the Bannwarth syndrome (meningitis, radiculoneuritis, cranial nerve palsies) represents the second most common clinical manifestation of acute *Borrelia* infection, especially in Europe.

Meningitis hardly ever affects adult Europeans; it is rather noted in children [1, 2]. It is reported that neurological symptoms associated with acute meningitis and polyradiculoneuritis have a good prognosis [1, 7, 15, 17]. On the other hand, it has been reported that chronic neuroborreliosis (involvement of the CNS) does not remit spontaneously. Moreover, it tends not to respond well to a specific treatment [8, 12, 18]. The symptoms usually begin to subside only after several weeks or months, and the improvements are less visible in patients with a longer duration of neurological deficits. It has also been reported

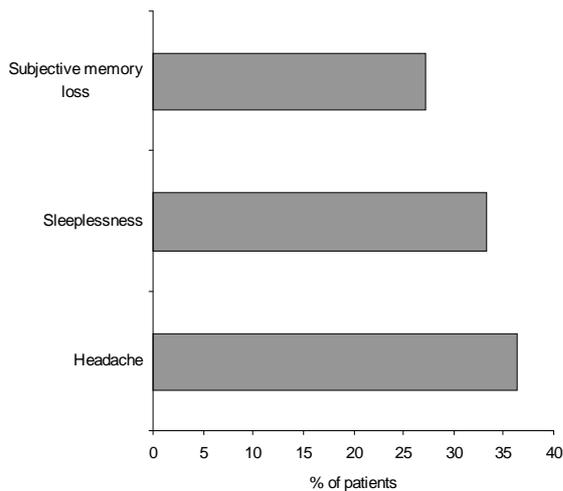


Figure 1. Characteristic changes in clinical history.

that a small percentage of Lyme borreliosis patients develop mild to moderate encephalopathic symptoms months or years after diagnosis and treatment [12, 20]. Moreover, a chronic fatigue syndrome, memory loss, sleep disturbance, and depression as consequences of Lyme disease are widely suggested [22]. However, the etiology of this syndrome still remains unclear [19, 21].

According to the clinical history of the patients diagnosed and treated in the Institute of Agricultural Medicine, distant effects of neuroborreliosis are often noted. The purpose of this study was to delineate and assess distant neurological and neuropsychological effects of acute neuroborreliosis in the chronic form of the illness.

PATIENTS

The Institute of Agricultural Medicine database was used to find a group of patients who suffered from acute neuroborreliosis in the time period 1995-1998. A group of 33 patients (12 men and 21 women of average age 44.2) were selected for the study.

According to the clinical history, the diagnosis of acute neuroborreliosis was based on: a history of tick bite, typical clinical presentation of meningitis, lumbar puncture results (detection of lymphocytic pleocytosis), and positive results of ELISA test for the presence of anti-*Borrelia* IgM and IgG antibodies in the serum and CSF samples. In all the samples, levels of IgM and IgG antibodies were significantly high, being above 21 BBU (Bellco Biomedica Units) per 1 ml. All the patients experienced moderate intensity headache, fever, meningism, nausea, retching and dizziness. It should be underlined that all the patients were hospitalized and treated with antibiotics therapy for a long period of time. None of the patients showed clinical symptoms when discharged from hospital after treatment. The patients under 20 and over 65 were excluded from the study, as the results might have been influenced by genetically transmitted neurological

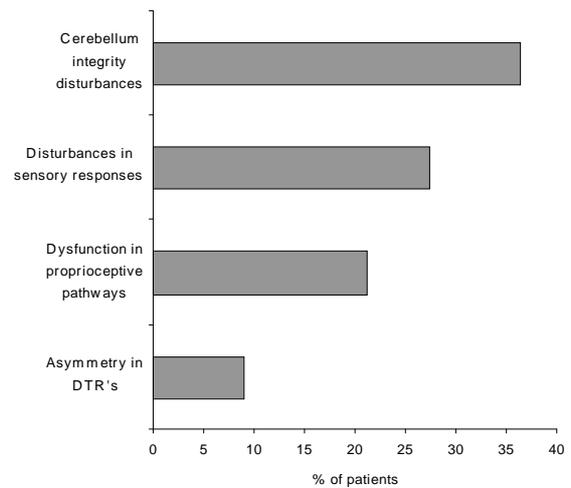


Figure 2. Results of neurological investigation.

diseases (before the age of 20) or neurodegenerative processes, especially dementia (after 65).

METHODS

Standardised medical interview, physical examination and a battery of neuropsychological tests were used in this study.

WAIR-S was performed to assess cognitive areas of intelligence, information processing speed, novelty problem solving and executive functioning, short-term and intermediate memory, as well as acquisition of new information and data [25].

BDI-BECK depression inventory was used to reveal mood disorders, especially depression [4].

DUM test was performed to assess memory impairment [26].

BENTON and BENDER tests were used to diagnose definite damage in the central nervous system functioning [5, 6].

RESULTS

In the clinical history, 36.4% of the patients complained of headache and 27.3% of subjective memory loss. In addition, in 33.3% cases sleeplessness was also frequently experienced (Fig. 1). The most common abnormalities in the neurological examination (36.4% of the patients) were cerebellum integrity disturbances - such as abnormalities in gait and coordination, or even mild ataxia (Fig. 2). 21.2% of the patients showed dysfunction in the proprioceptive pathways. A few patients (9%) showed asymmetry in deep tendon reflexes (DTR's), while 27.3% of the patients had disturbances in sensory responses (Fig. 2).

Psychological tests indicated that half of the patients had slight depression in BDI (Beck Depression Inventory) (Fig. 3). 21.2% of the patients experienced distorted

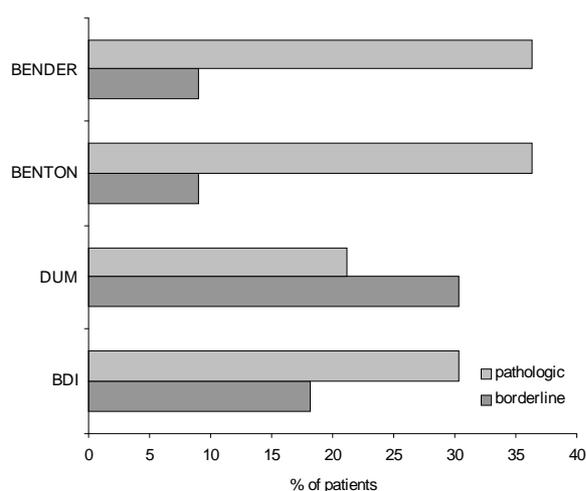


Figure 3. Results of psychological tests.

thinking process and memory impairment in DUM test (Fig. 3). 36.4% of the patients had significant organic damage in the central nervous system, as assessed by BENTON and BENDER tests (Fig. 3).

The above-mentioned disturbances seem to be the direct consequences of acute neuroborreliosis.

DISCUSSION

Various neurological conditions were reported in the late stage of Lyme disease, such as blindness, epileptic seizures, extrapyramidal disorders, amyotrophic lateral sclerosis. Chronic infection with *Borrelia burgdorferi* may take the form of dementia or even PSP [10]. Chronic progressive sensory ataxic neuropathy was also reported as being the consequence of neuroborreliosis [11]. Gait disturbances, deep and superficial sensory loss without deep tendon reflexes were also reported [11].

The results of our study confirm the existence of cerebellum disturbances in the course of neuroborreliosis, despite the lack of morphological cerebellum abnormalities which have not been found even in sophisticated radiological evaluation. The cerebellar ataxia and subsequent mental deterioration were previously described by Kobayashi *et al.* [14] as symptoms of Lyme neuroborreliosis. Moreover, in the above-mentioned study spongiform changes, neuronal cell loss, and microglial activation were described as Lyme neuroborreliosis' characteristic pathological features. The authors pointed to dentate and olivary nucleus lesions caused by *B. burgdorferi* as being the origin of the ataxia symptoms. Mental deterioration was attributed to the cortical and thalamic lesions. Moreover, *B. burgdorferi* can cause focal inflammatory change in the central nervous tissues, being a kind of an encephalitic form of Lyme neuroborreliosis [14].

Another case of a patient with clinical features of subacute cerebellitis, positive test for *Borrelia burgdorferi*

antibodies in CSF, and negative brain magnetic resonance imaging, was described by Neurophytides *et al.* [16].

Currently, it is suggested that all cases of subacute cerebellitis should be considered as potential neuroborreliosis, especially since *B. burgdorferi* shows a particular tendency to colonise infratentorial structures, especially the cerebellum.

A growing body of evidence also indicates the occurrence of depressive syndrome or fibromyalgic complaints after neuroborreliosis, despite initially successful antibiotic therapy eliminating its acute symptoms. However, fibromyalgia (or chronic fatigue syndrome) tends to produce more disabling symptoms in comparison with neuroborreliosis [22, 24]. A disturbance of the body's ability to recover after a severe illness is often present in fibromyalgia cases [22]. As depicted in our study, depressive syndromes also confirm the literature data. Moreover, we have noticed significant damage in the central nervous system functioning, thinking process, and memory disturbances. As the data concerning these subjects are limited [1, 3, 18, 20, 23] and since most of them are only case reports, a more detailed neuropsychological study is needed to describe the origin of functional disturbances.

The present study draws attention to the fact that despite initially successful antibiotics therapy, neuroborreliosis can often have late neurological and psychological outcomes, which significantly influence the quality of the patients' life.

REFERENCES

- Adams WV, Rose CD, Eppes SC, Klein JD: Cognitive effects of Lyme disease in children: a 4 year follow up study. *J Rheumatol* 1999, **26**, 1190-1194.
- Adams WV, Rose CD, Eppes SC, Klein JD: Long-term cognitive effects of Lyme disease in children. *Appl Neuropsychol* 1999, **6**, 39-45.
- Barr WB, Rastogi R, Ravdin L, Hilton E: Relations among indexes of memory disturbance and depression in patients with Lyme borreliosis. *Appl Neuropsychol* 1999, **6**, 12-18.
- Beck AT, Beamesderfer A: Assessment of depression: the depression inventory. Psychological measurements in psychopharmacology. *Modern Problems of Pharmacopsychiatry*, 1974, **7**, 151-169.
- Bender L: *Instructions for the Use of Visual-Motor Gestalt Test*. American Orthopsychiatric Association, New York 1946.
- Benton Sivan A: *Test Pamięci Wzrokowej Bentona*. Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego, Warszawa 1996.
- Cimperman J, Maraspin V, Lotric Furlan S, Ruzic Sabljic E, Strle F: Lyme meningitis: a one-year follow up controlled study. *Wien Klin Wochenschr* 1999, **111**, 961-963.
- Elkins LE, Pollina DA, Scheffer SR, Krupp LB: Psychological states and neuropsychological performances in chronic Lyme disease. *Appl Neuropsychol* 1999, **6**, 19-26.
- Estanislao LB, Pachner AR: Spirochetal infection of the nervous system. *Neurol Clin* 1999, **17**, 783-800.
- Garcia Moreno JM, Izquierdo G, Chacon J, Angulo S, Borobio M.: Neuroborreliosis in a patient with progressive supranuclear paralysis. An association or the cause? *Rev Neurol* 1997, **25**, 119-121.
- Hirabayashi H, Hamano H, Ohnuki Y, Nitta M, Shinohara Y: Inflammatory sensory ataxic neuropathy presenting with alternating skew deviation on lateral gaze: a case report. *Rinsho Shinkeigaku* 1997, **37**, 937-939.
- Kaplan RF, Jones Woodward L, Workman K, Steere AC, Logigian EL, Meadows ME: Neuropsychological deficits in Lyme

disease patients with and without other evidence of central nervous system pathology. *Appl Neuropsychol* 1999, **6**, 3-11.

13. Kindstrand E, Nilsson BY, Hovmark A, Nennesmo I, Pirskanen R, Solders G, Asbrink E: Polyneuropathy in late Lyme borreliosis - a clinical, neurophysiological and morphological description. *Acta Neurol Scand* 2000, **101**, 47-52.

14. Kobayashi K, Mizukoshi C, Aoki T, Muramori F, Hayashi M, Miyazu K, Koshino Y, Ohta M, Nakanishi I, Yamaguchi N: Borrelia burgdorferi-seropositive chronic encephalomyelopathy: Lyme neuroborreliosis? An autopsy report. *Dement Geriatr Cogn Disord* 1997, **8**, 384-390.

15. Murakami I, Hara H, Shigeto H, Yamada T, Isogai E, Kira J: A case of Lyme disease with the triad of neurologic manifestations (meningitis, radiculoneuritis, facial nerve palsy) and dermatitis of the nail roots. *Rinsho Shinkeigaku* 1999, **39**, 570-572.

16. Neophytides A, Khan S, Louie E: Subacute cerebellitis in Lyme disease. *Int J Clin Pract* 1997, **51**, 523-524.

17. Pfister HW: Diagnosis and therapy of Lyme neuroborreliosis. *Ther Umsch* 1999, **56**, 664-669.

18. Pollina DA, Sliwinski M, Squires NK, Krupp LB: Cognitive processing speed in Lyme disease. *Neuropsychiatry Neuropsychol Behav Neurol* 1999, **12**, 72-78.

19. Prasad A, Sankar D: Overdiagnosis and overtreatment of Lyme neuroborreliosis are preventable. *Postgrad Med J* 1999, **75**, 650-656.

20. Primavera A, Gazzola P, De Maria AF: Neuropsychological deficits in neuroborreliosis [letter]. *Neurology* 1999, **53**, 895-896.

21. Schutzer SE, Natelson BH: Absence of Borrelia burgdorferi-specific immune complexes in chronic fatigue syndrome. *Neurology* 1999, **53**, 1340-1341.

22. Shadick NA, Phillips CB, Sangha O, Logigian EL, Kaplan RF, Wright EA, Fossil AH, Fossil K, Berardi V, Lew RA, Liang MH: Musculoskeletal and neurologic outcomes in patients with previously treated Lyme disease. *Ann Intern Med* 1999, **31**, 919-926.

23. Svetina C, Barr WB, Rastogi R, Hilton E: The neuropsychological examination of naming in Lyme borreliosis. *Appl Neuropsychol* 1999, **6**, 33-38.

24. Treib J, Grauer MT, Haass A, Langenbach J, Holzer G, Woessner R: Chronic fatigue syndrome in patients with Lyme borreliosis. *Eur Neurol* 2000, **43**, 107-109.

25. Wechsler D: A standardized memory scale for clinical use. *J Psychol* 1945, **19**, 87-95.

26. Weidlich S, Lamberti G: *DUM. Diagnozowanie Uszkodzeń Mózgu*. Wydawnictwo ERDA, Warszawa 1997.