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CO-EXISTANCE OF TOXOPLASMOSIS AND NEUROBORRELIOSIS - A CASE REPORT

Katarzyna Gustaw, Katarzyna Bełtowska, Edyta Długosz

Department of Neurodegenerative Diseases, Institute of Agricultural Medicine, Lublin, Poland

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Abstract: The 53-year-old woman was initially diagnosed with multiple sclerosis, despite the fact that she did not really meet the clinical criteria. Her only symptoms were clumsiness and weakness of the right extremities. Being a veterinary research worker she had been exposed to infectious material. In 1995, she was diagnosed with ELISA as having toxoplasmosis and treated as such. In 2002, after the infectious, flu-like disease, she revealed arthritis and drowsiness, also with memory and language impairment. The patient continued to have symptoms consistent with previously examined clumsiness. She was diagnosed with Lyme via ELISA and PCR, and treated. She made a full recovery from acute symptoms. After a few months, neurological and neuropsychological examinations were performed. On the background of mild cognitive decline apraxia and difficulties of attention were noted as the main problems. A apraxia of the right hand complicated the patient's life and depreciated her quality of life. The patient underwent MRI examination. FSE, FAST and FLAIR sequences were made. The MRI demonstrated the appearance of several small hyperintense lesions in the white matter of the left and right frontal and left parietal lobe. These lesions were typical of the post-inflammatory leucoencephalopathy. Additionally, a ring-shaped, low-intensity lesion in the posterior part of the left parietal lobe was noticed. The lesion was 8 mm in diameter and described to be an old toxoplasmosis lesion. The patient had been treated and the symptoms consistent with Lyme disease resolved. Patient continues to have symptoms consistent with focal destruction of the parietal lobe. Over the past six months, she has not progressed and relapsed in a manner that is consistent with MS.

Address for correspondence: Dr n. med. Katarzyna Gustaw, Department of Neurodegenerative Diseases, Institute of Agricultural Medicine, Jaczewskiego 2, 20-090 Lublin, Poland. E-mail: kasiagu@yahoo.ca

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INTRODUCTION

Lyme disease, also called Lyme borreliosis, is a widely distributed multi-system disease caused by a tick transmitted spirochete *Borrelia burgdorferi*.

Lyme disease has now been shown to involve nearly every organ and organ system. The involvement of the central and peripheral nervous system has been widely documented. A broad range of neurological and psychiatric reactions have also been associated with Lyme disease [5, 8].

Chronic CNS involvement of Lyme neuroborreliosis may mimic any other inflammatory brain changes diseases, such as neurosyphilis, meningoencephalitis of viral, fungal or mycobacterial origin, brain tumour, autoimmune disease, stroke, or even Alzheimer's disease. The variable clinical manifestations have led to an awareness of neuroborreliosis as a imitator, especially in the case of multiple sclerosis [1, 8, 10].

Thus, neuroborreliosis must be considered in the differential diagnosis of numerous complaints, especially in those geographic areas where the spirochete is endemic.

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On the other hand, toxoplasmosis is a rare disease nowadays and is usually connected with immunodeficiency. Cerebral toxoplasmosis can possess many neurological conditions beyond focal neurological symptoms. Toxoplasmosis of the brain in immunodeficient patients can even mimic even Alzheimer disease [2, 3, 9]. Moreover, epileptic fits and hemiparesis, or other focal neurological signs commonly were associated with cerebral toxoplasmosis in AIDS patients [9].

It is suggested that toxoplasmosis infection or post-treatment immunodeficiency can also facilitate other infections.

According to the literature, this is a first report describing co-morbidity of cerebral toxoplasmosis and neuroborreliosis.

PATIENT

M.K., a 53-year-old woman and highly educated, was examined. She was right-handed, but when she noticed problems with that hand she began to use her left hand. She now claims to be left-handed.

She was examined with a 7-year history of clumsiness, weakness of the right extremities, and memory and language impairment. Being a veterinary research worker, she had been exposed to infectious material.

In 1995, the patient suffered from lymph nodes enlargement and fever.

She was diagnosed with ELISA as toxoplasmosis. After a routine treatment (Rovamycine and Fansidar) she was expected to make a full recovery. Her only complaint was clumsiness of the left extremities without any clear-cut picture of paresis (according to the history).

At the beginning of the year 2002, she suffered from an infectious flu-like disease. She revealed arthritis and drowsiness, with memory and language impairment. That patient continued to have symptoms consistent with previously examined clumsiness. She was initially suspected of and diagnosed with multiple sclerosis. According to the history, however, she did not really meet the clinical criteria for MS. Symptoms did not disappear after the treatment for MS. After a few weeks (2002), she was admitted to the Department of Occupational Biohazards Institute of Agricultural Medicine in Lublin. She underwent careful neurological examination as well as a careful history inquiry. She did not remember a tick-bite episode, but was being exposed to infectious material.

Finally, she was diagnosed with Lyme neuroborreliosis by ELISA and PCR. After 4-weeks treatment with cefalosporines intravenously, she recovered from arthritis, drowsiness and language impairment.

The patient, however, continues to have symptoms consistent with focal destruction of the parietal lobe.

It is important to note is that over the past 6 months she has not progressed or relapsed in a manner consistent with Multiple Sclerosis.

Thus, a careful neuropsychological examination was performed and neuroimaging (MRI) repeated.

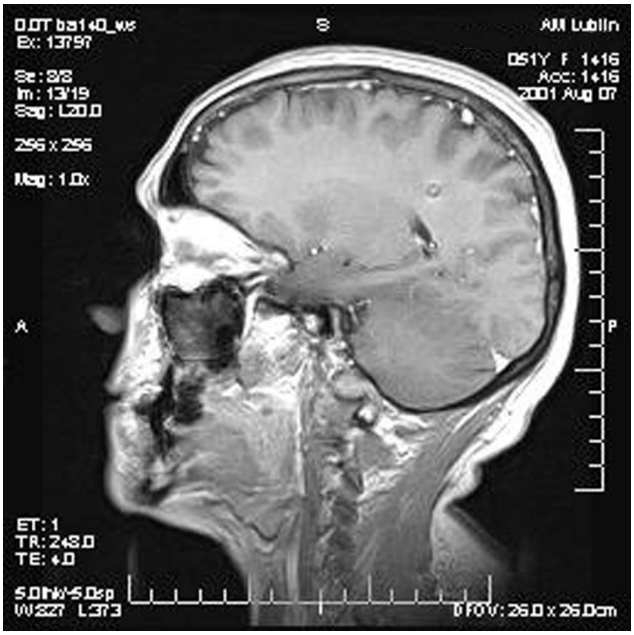

Figure 1. MRI of the brain of the patient showing the ring-shaped low-intensity lesion in the posterior parietal lobe, toxoplasmosis lesion.

MRI STUDY

The patient underwent a standard magnetic resonance imaging examination. FSE, FAST and FLAIR sequences were made to acquire T1 and T2-weighted images in axial, saggital, and transverse planes of the head (Fig. 1).

The MRI examination in the T2-weighted and FLAIR images demonstrated the appearance of several small hyperintense lesions in the white matter of the left frontal and left parietal lobe. A similar lesion was seen in the right frontal lobe. These lesions could have been considered rather typical for the post-inflammatory leucoencephalopathy. Additionally, the ring-shaped low-intensity lesion in the posterior part of the left parietal lobe, a little below the level of the lateral ventricles was observed. The lesion was 8 mm in diameter and did not enhanced after i.v. paramagnetic contrast medium administration. Based on this picture, an old toxoplasmosis lesion with calcifications was suspected. The cerebral ventricular system was symmetrical and not enlarged. The infratentorial structures were within normal limits.

It was concluded that the ring-shaped lesion could be a toxoplasmosis lesion, while the small hyperintense lesions could be the consequences of neuroborreliosis.

METHODS OF NEUROPSYCHOLOGICAL INVESTICATION

Neuropsychological diagnosis was performed twice within 6 months.

Standard battery of tests (Wechsler Inteligence Scale WAIS) - R, Benton Test, Rey'a Figure Test, ADAS, MMSE were used. Standard battery of test does not provide qualitative analyses of the structure of disorders, so experimental methods were also used.

Experimental methods were based on Łucki battery of tests and consists of: oral praxis, ideomotor praxis, ideational praxis and dynamic praxis (synchronization of hand movements).

RESULTS OF NEUROPSYCHOLOGICAL EXAMINATION

The results indicated that the level of intellectual skills of the patient was lower than average (II = 88, manifests lower than an average level of intellectual progress). The lowest results were assessed in arithmetic's. This suggested that she had problems with operations on the figural material. This lower then average score could have affected her thinking. The score on knowledge (knowledge, vocabulary) was also lower than average. The patient, however was aware of her problems, and was critical of the effects of her work on items.

Both transmission and reception activities of the speech were correct. Story speech was preserved. The dominant problem was a limited vocabulary. Patient's speech was hesitant and the patient had difficulty in finding the word in spontaneous speech, despite the fact that she was looking for very difficult words. The patient additionally had problems with attention. She could be distracted very easily. The patient correctly constructed items which needed generalization and abstractions (ex. classification).

Modest difficulties in calculation were noticed. Patient complained of writing difficulties; she could not write a sentence correctly or copy correctly. Despite problems with motor skill, she could write correctly with her left hand. Her drawing, however, was tremulous and micrographic.

Praxis seemed to be the most impaired function. The affected hand could not move on command. Patient's hand attempted unsuccessfully to perform movement, or was undertaken very slowly.

There was also disorder in ideational praxis. The patient was not able to demonstrate how to pray, how to brush teeth or how to salute. There were no disorders noticed, however, in oral praxis.

In the second investigation (after 6 months), improvement, especially within memory skills, was noticed. The patient made significant progress in developing strategies for remembering (from the interview and the observations).

DISCUSSION

There is substantial data in the literature which illustrate that months to years after initial infection, patients with borreliosis develop a subtle encelopathy characterized primarily by memory difficulty [12]. The same phenomenon following long periods of latent infection was described [12]. In addition, some of these patients exhibit peripheral sensory symptoms. For example, distal paresthesias or spinal radicullar pain were described [13]. These neurological abnormalities may occur in association with Lyme arthritis, or occur long after joint involvement has been resolved [13].

A few data have been published to characterize the memory disturbances of borreliosis encephalopathy. Steere *et al.*, [12] compared patients with this disorder to fibromyalgia and depressed patients using neuropsychological tests. Patients with borreliosis encephalopathy showed mild but statistically significant memory deficits in California Verbal Learning Tests and Wechsler Memory Scale. In contrast, the other 2 groups had normal test scores on memory, but abnormal on the tests that are more sensitive to somatic concerns, including anxiety and depression. In another study, the researchers compared the patients with Lyme disease to those with CSF abnormalities and those without. The patients with abnormal CSF analyses had significantly lower memory tests scores that the patients in the 2 control groups. Thus, it is possible to document the memory deficit in most patients with neuroborreliosis. These data are the evidence to prove the existence of borreliosis encephalopathy. These findings confirm that patients with neuroborreliosis can have active spirochetal infection in the white matter areas of the brain.

The other problem which occurred in the case of patients to be discussed is the growing body of evidence describing difficulties in diagnosis between neuro–borreliosis and multiple sclerosis.

There were data suggesting that *Borrelia* might have been involved in the etiology of MS [4].

This suggests the consideration of MS in the differential diagnosis of neuroborreliosis.

Because of age (41) and sex (female), 2 facts corresponding with multiple sclerosis, this diagnose was considered as well in the case of our patient.

After extensive differential diagnosis it was concluded, however, that she did not meet the clinical criteria for MS.

Multiple sclerosis is an autoimmune disease involving predominantly the white matter of the brain and spinal cord, and is one of the most common neurological disorders of younger adults and a substantial cause of lasting neurological disability [7].

Clinical pattern of multiple sclerosis have been defined by international consensus [6]. About 85% of patients initially experienced one or more relapses followed by complete or incomplete recovery. This clinical pattern is referred to as the relapsing-remitting phase. Over 10 years, roughly 50% of these patients will experience a transition to the secondary progressive phase, characterized by a gradually worsening disability, with or without superimposed relapses. About 10% of patients experienced a clinical course that is progressive from onset, primary progressive multiple sclerosis. The remaining 5% of patients experienced progressive disability from onset, later accompanied by one or more superimposed relapses; this pattern is referred to as progressive relapsing multiple sclerosis [6].

None of the above mentioned clinical patterns can be applied to the patient's experiences.

Moreover, the neuroimaging pictures did not meet MRI criteria for multiple sclerosis.

Although brain MR is abnormal in 95% of patients with clinically definite multiple sclerosis, the MRI alone cannot be a key factor in diagnostic procedures. For example MS plaque can mimic even neoplasm. On the other hand, lesion burden on T1 weighted images correlates well with clinical disability.

Key imaging findings, such as multiple perpendicular calloseptal hyperintensities and incomplete rim enhancement in MRI, are the best diagnostic clues to support clinical diagnosis of multiple sclerosis. Although iso- to hypodense changes with mild to moderate enhancement can be seen in CT, magnetic resonance imaging is crucial.

Acute multiple sclerosis demyelinating plaques are to mildly hypointense and hypointensity increases in initially demyelinated plaques while decreases in remyelinating lesions in T1 weighted images. Chronic lesions, however, in T1 weighted images usually have hypointense centres and with a mild hyperintense rim so-called lesion within a lesion appearance. In T2 weighted and FLAIR (saggital images are crucial) bilateral, asymmetric linear ovoid hyperintense lesions in corpus callosum, periventricular region (perpendicular to ventricles at calloseptal interface) are observed. Mostly, subcortical lesions are seen . In 10–20% of chronic MS cases, however, hypointense basal ganglia or (in 5%) cortical lesions are seen in T2WI and FLAIR. Perilesional edema can also be seen. There are characteristic changes in contrast-enhanced T1 weighted images. The other modality (MRS, DWI) findings differ with clinical type. The best recommendation for MS therefore is routine MR (sagittal FLAIR, coronal contrast enhanced T1WI).

In our patient no such a picture was observed, however. The MRI examination in the T2-weighted and FLAIR images demonstrated the appearance of several small hyperintense lesions in the white matter of the left frontal and left parietal lobe. A similar lesion was seen in the right frontal lobe.

These lesions could have been rather typical for the post-inflammatory leucoencephalopathy. The character of the changes observed in MRI corresponded well with the clinical picture of neuroborreliosis.

Moreover, unspecific *Borrelia* antibodies can be present in patients with demyeliniating processes. Not only *Borrelia* specific antibodies, however, can be seen in MS. CSF antibodies against other pathogens such as measles, rubella, VZV, mumps, HSV are present in MS [4].

Rehse-Kupper *et al.*[9] investigated unclassified MS patients with definite diagnosis for serum antibodies against *Ixodes ricinus Borrelia*, followed by CSF analysis, both by ELISA.

Their results did not support the hypothesis of a frequent etiologic role of *Borrelia* in MS.

Obviously, latent neuroborreliosis can be combined with MS serendipitously.

Thus, in order to differentiate neuroborreliosis from MS, the existence of a significant level of CSF antibodies in the beginning of the process, and normalization of the titer after specific therapy is needed.

Moreover regardless of the clinical picture, MS patients seropositive to *Borrelia* should be treated specifically with respect to latent *Borrelia* infection, especially when the patient has undergone immunosuppressive therapy.

CONCLUSIONS

To the best of our knowledge, this is the first case in the literature describing the coexistence of neurotoxoplasmosis and neuroborreliosis.

Chronic Lyme neuroinfection can cause mild cognitive decline of the patient. Chronic infection with toxoplasmosis can lead to immunodeficiency. It may be suggested that toxoplasmosis can facilitate Lyme infection, while any kind of focal neurological sign in an immunodeficient patient can suggest neurotoxoplasmosis.

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