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A Case of Reversible Dementia? Dementia vs Delirium in Lyme Disease

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Lyme disease is an uncommon cause of reversible dementia. A 75-year-old male patient, with a personal history of mild memory deficit, was admitted to Alzheimer's Disease Care Unit due to hallucinations, confusion and aggressive behavior that are unresponsive to antipsychotic therapy. A computed tomography (CT) scan of the brain was negative, while blood exams showed a rise in inflammatory parameters. A complete screening of infective diseases showed a positive serology for *Borrelia burgdorferi*, confirmed at Western blot. Even though the patient refused cerebrospinal fluid (CSF) exam, the brilliant clinical improvement after the appropriate antimicrobial therapy is strongly suggestive for a diagnosis of neuroborreliosis. This case report underlines the importance of a diagnostic approach to dementia, as to find out and treat the reversible causes.

Key Words: Neuroborreliosis, Dementia, Lyme disease, Delirium, Cognitive impairment

INTRODUCTION

The causes of cognitive impairment are multiple and not always clearly identifiable. As a consequence, the diagnostic process is often challenging. Cognitive impairment is usually seen as a condition destined to worsen and end in dementia, but a significant proportion of cases can be reversible. In this context, an accurate and timely identification of the underlying disease is critical. The present report has described a case of cognitive impairment (and possible delirium) due to neuroborreliosis.

CASE REPORT

A 75-year-old man was admitted to our Alzheimer's Disease Care Unit of the Institute Golgi (Abbiategrasso, Italy) after having been discharged from a local hospital 2 weeks before with the diagnosis of "cognitive impairment, deficit of memory, and poor capacity of criticism compatible with degenerative disease."

The patient was a multilingual interpreter with a high school degree who loved walking in the countryside with its dog. His medical history included smoking habits, hyperlipidemia, an undocumented history of chest pain, and previous hospitalization for self-injurious behavior in affective psychosis.

At the recent hospital admission, his wife also reported that the patient had experienced knee pain for approximately a month, which had been treated with local infiltration without significant benefit. The pain worsened and tended to migrate to other joints. The woman said the patient had also been presenting with a mild memory deficit and ideomotor slowdown for the past couple of years. No mental confusion, aggression, or irritability was reported at home. The patient had preserved autonomy in the activities of daily living (ADLs) and most instrumental activities of daily living (IADLs).

During the previous hospital stay, brain computed tomography (CT) was performed. The examination showed slight enlargement of the ventricular system, an increased amount of peripheral cerebrospinal fluid (CSF), chronic vascular leukoencephalopathy, and signs of chronic inflammation in the left sphenoid sinus and some ethmoid cells. Blood test results were within normal ranges, except for increased indices of inflammation. The patient gradually be-

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came confused and disoriented over time. He started presenting with hallucinations and aggressive behavior, requiring antipsychotic therapy and physical restraints to reduce the risk of self-injury.

Electroencephalography (EEG) was also performed, and and pathological anomalies could be excluded by the results of EEG. A neurologist was consulted for this purpose. He had described the presence of a confusional state of indeterminate genesis, recommending magnetic resonance imaging (MRI). However, this examination did not provide any relevant information. Viral and autoimmune causes on blood samples were also investigated, and the results were all negative. The urine culture test results were negative. Because of the persistence of elevated levels of inflammatory markers, empiric therapy with ceftriaxone was administered for approximately a week, without substantial benefits.

Before the hospital discharge, a second evaluation by the neurologist was conducted, classifying the case as "compatible with degenerative disease" with the subsequent referring of the patient to our center.

Upon admission, the patient was confused and disoriented. He experienced delusional ideas and persistent hallucinations. Wandering, aggressive behavior, and urinary incontinence were reported. Insomnia was another critical and hard-to-manage symptom. Migrant arthritis and acrodermatitis were also documented.

The Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) scale, Barthel Index, and Tinetti scale scores were 22/30, 3/5, 35/100, and 7/28, respectively. The Comprehensive Geriatric Assessment showed frailty, functional dependence, and the worst outcomes in geriatric patients.

The Neuropsychiatric Inventory (NPI) underlined the presence of delusional ideas, hallucinations, irritability, depression, apathy, insomnia, and aberrant motor behavior objectives, with a final score of 80/144. The neuropsychological tests confirmed space, time, and self-disorientation. Memory loss and executive and attentional deficits were identified, along with the aforementioned symptoms. Aspects of aphasia (i.e., anomias and circumlocutions) were also described. A subsequent EEG was negative for epileptic anomalies. Clopixol, olanzapine, promazine, rivastigmine, and bromazepam were ineffective in controlling the symptoms.

Therefore, the diagnosis of dementia had been inconsistent. The negative findings of the instrumental tests and the fact that the patient, before hospitalization, was completely autonomous in the ADLs and IADLs, had no behavioral disorder, and only presented with a minimal memory disorder pushed toward the formulation of an alternative hypothesis.

Because arthritis was present, we excluded all infective causes not previously tested, including *Borrelia burgdorferi*. The patient tested positive for Lyme antibodies. Western blotting confirmed this result; however, the patient and his family refused CSF sampling.

Antibiotic treatment was initiated with intravenous ceftriaxone (2 g twice daily for 21 days). A cycle of low-dose prednisone was also administered to alleviate arthritis symptoms, and positive results were obtained. At the end of the antibiotic therapy, as the levels of inflammatory biomarkers remained elevated and neutrophilia was still present, oral doxycycline (200 mg/day for 7 days) was administered. Quetiapine was also administered for a short period to acutely control the hallucinations, after which it was discontinued.

Soon after 6–7 days of antibiotic therapy, delusional symptoms and hallucinations were attenuated, and insomnia improved. Urinary incontinence was completely resolved.

Clinical and neuropsychological evaluations at discharge revealed improved orientation (in space, time, and self), regression of delusional thoughts, and non-disturbing complaints of hopelessness. The behavioral profile also improved, with a reduction in agitation, aggression, and depression. The language was more fluent and communicative.

The memory loss and executive deficits persisted. However, the attentional deficit was attenuated compared with that before antibiotic therapy. The MMSE, CDR scale, NPI, Barthel Index, and Tinetti scale scores were 29/30, 2/5, 14/144, 62/100, and 25/28, respectively.

The informed consent for the publication of the case report was obtained.

DISCUSSION

A detailed analysis, focused on premorbid assessment, is the first step in understanding early symptoms and their subsequent progression. The acute onset of cognitive symptoms and rapid deterioration of the behavioral profile in an autonomous person without a diagnosis of dementia or behavioral disorders should lead to the hypothesis that an inflammatory or infectious disease affects the central nervous system (e.g., meningitis, neurosyphilis, and Lyme disease).[1] This case report underlines the importance for geriatricians that old age and progressing cognitive decline do not always conclude for dementia.

First, we excluded bacterial and viral meningitis because the patient had no fever or typical symptoms (e.g., neck stiffness or focal neurologic deficits). In addition, the blood culture results were negative. We then explored the possibility of limbic encephalitis; however, the lack of a specific pattern in the examinations (i.e., MRI and immunological blood test screening) reduced the likelihood of the hypothesis.[2] We also hypothesized Creutzfeldt–Jakob

disease. However, the lack of ataxia and myoclonus and absence of signs on MRI and EEG reduced this possibility.[3] We could have conducted a CSF analysis to exclude this hypothesis; however, this was not possible.[4] Finally, a common infectious pathogenesis of the osteoarticular signs/symptoms and neurological manifestations was considered. As syphilis had already been excluded, the blood samples were analyzed for human immunodeficiency virus (negative result) and Lyme disease (positive result).

The patient confirmed a tick bite approximately 6 months before the beginning of the arthritis and could not exclude the possibility of other similar events, as he used to walk in the countryside. Migrant erythema, the first clinical sign of Lyme disease, was not observed. In contrast, the beginning of joint involvement, another typical sign of Lyme disease, was clearly evident. No clear cardiac condition or gait disturbance was reported in the patient's medical history, which sometimes occurs in Lyme disease.[2,5,6]

As for neurological symptoms, they particularly altered the cognitive and behavioral profile without signs of early neurological disorders, such as Bannwarth syndrome. The rapid onset of neurological conditions, hallucinations, delusional ideas, wandering, and aggressive behavior seemed to be associated with the manifestations of encephalitis in late neuroborreliosis.[7]

The major limitation of our case was the unavailability of CSF testing,[7,8] which could have further supported our diagnosis.[9] Accordingly, we reformulated the diagnosis of "delirium in Lyme disease." Finally, it is noteworthy that the lack of information about other comorbid conditions that can cause cognitive decline, except for a mild memory deficit and ideomotor slowdown over the past couple of years, does not exclude the possibility of pre-existing early mild cognitive impairment.

Therefore, a follow-up visit was organized for the patient at a local dementia and cognitive disorder outpatient clinic.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, CS, CP; Data curation, CC, TEP, MC; Investigation, CC, CS, CP, TEP; Methodology, CC, CS, CP, TEP; Project administration, CC, CS, CP, TEP; Supervision, CC, TEP, MC; Writing-original draft, CS, CP; Writing-review & editing, CS, CP.

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