Neurosyphilis with dementia and bilateral hippocampal atrophy on brain magnetic resonance imaging

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Key words: neurosyphilis; dementia; hippocampal atrophy; Alzheimer’s disease; MRI
Abstract

**Background:** This article reports a rare case of active neurosyphilis in a 33 years old man with mild to moderate dementia and marked hippocampal atrophy, mimicking early onset Alzheimer’s disease. Few number of cases have so far described bilateral hippocampal atrophy mimicking Alzheimer’s disease in neurosyphilis.

**Case presentation:** The clinical feature is characterized by a progressive cognitive decline and behavioral changes for the last 18 months. Neuropsychological examination revealed mild to moderate dementia (MMSE=16) with impaired memory, and attention, and executive dysfunction. Pyramidal, and extrapyramidal signs, as well as dysarthria and impairment in coordination were documented. Brain magnetic resonance imaging showed cortical atrophy with noticeable bilateral hippocampal atrophy. The diagnosis of active neurosyphilis was based on positive results of Venereal Disease Research Laboratory test/Treponema Pallidum Hemagglutination reactions in blood and cerebrospinal fluid samples. In addition, cerebrospinal fluid analysis showed pleocytosis and elevated protein levels. High dosage of intravenous penicillin therapy was administered. During the follow up that was taken after 6 months, the clinical signs, neuropsychological examinations, and cerebrospinal fluid samples showed improvement.

**Conclusion:** This case underlines the importance of early diagnosis of neurosyphilis. The results suggest that neurosyphilis should be considered when magnetic resonance imaging results indicate mesiotemporal abnormalities and hippocampal atrophy. Neurosyphilis is a treatable condition which needs early aggressive antibiotic therapy.

**Keywords:** Neurosyphilis; Dementia; Hippocampal Atrophy; Alzheimer’s Disease; MRI
Background

Neurosyphilis results from infection of the brain, meninges or spinal cord by Treponema Pallidum and develops in about 25%–40% of persons who are not treated for syphilis. After the appearance of acquired immunodeficiency syndrome (AIDS) in 1981, the occurrence of neurosyphilis in human immunodeficiency virus (HIV) infection is the reason for the increased number of new cases in developed countries. The disease is treatable with antibiotics however, early diagnosis and treatment is critical. Making the diagnosis is often difficult with the wide variety of CNS manifestations of neurosyphilis, both clinically and on neuroimages. The clinical presentations of neurosyphilis are extremely diverse and, for practical purposes, can be divided into early and late neurosyphilis. The clinical picture of meningovascular syphilis may be associated with focal neurological signs of cerebral arteritis [1,2].

Cognitive decline is one of the late syphilis manifestations. However, mild cognitive impairment could be observed in early stages of neurosyphilis [3]. Imaging findings of meningovascular syphilis, the most common form of neurosyphilis, include cortical and subcortical infarcts, cortical atrophy, hydrocephalus, leptomeningeal enhancement associated with a clinical meningitis, and arteritis. The arteritis is of two forms; Heubner arteritis, which is the more common form, affecting the medium and large arteries, and the Nissl-Alzheimer form, which affects the small arteries and arterioles. Other manifestations of meningovascular syphilis include leptomeningeal and cerebral gummas [1, 4,5,6].

Few case reports presented mesiotemporal abnormalities in neurosyphilis [7]. This article reports a rare case of active neurosyphilis in a 33 years old man with mild to moderate dementia and marked hippocampal atrophy, mimicking early onset Alzheimer’s disease (EOAD).

Case presentation

We present a case of a 33 years old man who attended Neurological Clinic at University Hospital Alexandrovska because of progressive attention and memory impairments as well as apathy, anxiety and irritability reported by family members. Eighteen months earlier his brother noticed that he is confused, forgetful and is not able to manage with his professional activities as a construction worker. He became apathetic, irritable and more verbally aggressive. Our patient is a low educated
individual with poor written language and simple arithmetic abilities but a good worker being able to carry out everyday activities.

Neuropsychological assessments were performed by means of general cognitive functioning scale (Mini Mental State Examination, MMSE), and tests for attention, memory, language and executive functions evaluation (see table 1). He had definitely lost the general time (year, seson, month, day and date) however, he showed to be relatively conscious of the orientation around him. Memory examinations revealed severe verbal learning impairment with very low ability to retain new information. He also had difficulties with remembering autobiographical and personal data. His verbal communication was relatively spared, with mild anomia and low categorical fluency. Severe dysexecutive syndrome was also documented (with very low coding and letter fluency). Keeping the patient’s premorbid cognitive status in mind, neuropsychological assessment revealed mild to moderate dementia (MMSE=16).

There was no history of skin lesions or symptom of Argyll-Robertson, his pupillary reflexes were preserved, and the pupils constricted in response to light and accommodation. Pyramidal, extrapyramidal signs, dysarthria and impairment in coordination were documented. Laboratory workups including a complete blood count and differential, serum electrolytes and glucose, liver and renal function tests, thyroid function tests, serum B12 and folate levels were normal. In addition, cerebrospinal fluid (CSF) analysis showed pleocytosis, elevated protein levels, and positive oligoclonal band. Cerebrospinal fluid was clear with 1 x 10⁶/l erythrocytes, 39 x 10⁶/l leucocytes (82% lymphocytes, 16% monocytes) and protein of 0.88g/l. The diagnosis of active neurosyphilis was based on positive results of Venereal Disease Research Laboratory test/Treponema pallidum. hemagglutination assay (VDRL/TPHA) reactions in blood and CSF samples (serum-VDRL 1:128, serum-TPHA 1:2560, CSF-VDRL 1:64, CSF-TPHA 1:640). The serum and CSF test for HIV was negative. Magnetic resonance imaging (MRI) of brain demonstrated moderate cortical and marked hippocampal atrophy.

No adverse reactions were observed upon receiving a course of intravenous Penicillin G 5x5000000 UI/daily for 20 days.

During the follow up examination at 6 month, the clinical signs and neuropsychological findings showed slight improvement in general cognitive functioning. The MMSE was done 6 months after the treatment scored 19 (see table
1). Improvement were also noticed in the activities of daily living assessment and behavioural disturbances. The patient’s CSF protein level was 0.55 g/L, with $1 \times 10^6$/l leucocytes, and VDRL testing of CSF yielded positive results.

Table 1 about here

Discussion

A case of active neurosyphilis has been presented with dementia, behavior changes and rare bilateral hippocampal atrophy mimicking EOAD. A few reports have described the mesiotemporal involvement in neurosyphilis. There are several reports with unilateral or bilateral asymmetrical mesiotemporal T2 hyperintense lesions on MRI images of the brain in neurosyphilis. This is especially important considering that the clinical presentation of neurosyphilis may also seemingly mimic that of herpes simplex encephalitis or paraneoplastic limbic encephalitis [5,7,8,9,10].

The cause of the mesial temporal T2-weighted hyperintensity is not clear. To our knowledge, there is no pathological study on mesial temporal hyperintensity on T2 weighted image in neurosyphilis patients. It is suggested that the signal changes represent a combination of edema and gliosis. The edema component itself most likely have multiple causes. In meningitis, there are changes in the meningeal and cerebral capillaries, with a possible increase in the permeability of the blood-brain barrier, leading to a vasogenic edema component. There may also be some cytotoxic edema and interstitial edema component, inflammation, meningovasculitis, or microglial hypertrophy [5,7].

There is no reliable marker to predict the outcome in patients with neurosyphilis after treatment. The duration the illness takes to become symptomatic and the delay in therapeutic intervention are important factors for preventing further progression of disease. Cases with reversible high signal T2 lesions in the mesial temporal region had also been reported [11,12,13]. The presence of edema is further suggested by the imaging improvement which were noticed consequent to antibiotic therapy. The residual T2 hyperintense lesion might have a vasculitic origin. The presence of gliosis may be present secondary to infection-induced small-vessel ischemic changes.
In our patient, the cognitive and behavioral symptoms, the neuropsychological profile and MRI data and the early age at onset were compatible with a diagnosis of probable EOAD. Moreover, focal neurological abnormalities could be present in a rare case of EOAD [14]. However, the serological tests were performed because of the young age and focal neurological abnormalities.

Neurosyphilis is associated with cognitive decline and progressive dementia. Nevertheless few numbers of cases have been described mimicking Alzheimer’s disease radiologically. In one of the four cases reported by Zifko et al., MRI showed atrophy and gliosis over bilateral hippocampi [15]. Another patient reported by Van Eijsden et al. [16] presented cognitive and behavioral symptoms with MRI scan of medial temporal lobe atrophy equivalent to the highest degree of atrophy on a visual rating scale, mimicking EOAD. Our patient showed similar neuropsychological and neuroimaging features with the described case. Both cases had AD like neuropsychological profile and high degree of medial temporal atrophy. In addition, our patient had focal neurological signs (pyramidal and extrapyramidal signs). CSF abnormalities in both cases showed pleocytosis and elevated protein levels. The follow-up examination showed improvement in neuropsychological results after treatment in both cases.

It is not clear why atrophy occurs in the medial temporal regions is not clear. One explanation is that initial infection causes inflammatory T2 hyperintensity, which with no treatment might disappear at a later stage when the tissues undergo irreversible atrophy [16]. Another explanation may be the emergence of a secondary atrophy due to dysfunction in the diffuse cerebral cortex, as the medial temporal regions have connections with the cerebral association areas, including the frontal, temporal, and parietal lobes.

This is the first case report of a Bulgarian patient with neurosyphilis, showing progressive cognitive and behavioral changes with bilateral cortical and hippocampal atrophy mimicking EOAD.
Conclusion

The temporal lobe imaging abnormalities suggest the necessity of adding neurosyphilis in differential diagnosis of medial temporal lobe T2 hyperintensities (herpes simplex encephalitis or paraneoplastic limbic encephalitis) and mesiotemporal atrophy (Alzheimer’s disease). Reversible MRI lesions in patients with neurosyphilis after treatment correlate to clinical improvement, which should alert the physicians that early diagnosis and aggressive treatment are worthwhile.

List of abbreviations used

Acquired immunodeficiency syndrome (AIDS)
Human immunodeficiency virus (HIV)
Central nervous system (CNS)
Early onset Alzheimer’s disease (EOAD)
Mini Mental State Examination (MMSE)
Cerebrospinal Fluid (CSF)
Venereal Disease Research Laboratory test - Treponema Pallidum. Hemagglutination Assay (VDRL-TPHA)
Magnetic Resonance Imaging (MRI)

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.
Authors' contributions

All authors participated in the care of the described patient. SM and MR were major contributors in writing the manuscript. MT, TS, LP and OG collected the data and helped to draft the manuscript. LT critically revised the content of this manuscript. All authors have read and approved the final version of the manuscript.

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References


Figure 1 - Magnetic Resonance Imaging (MRI) of the brain.

A/ Axial fluid attenuated inversion recovery (FLAIR)
B/ Sagittal fluid attenuated inversion recovery (FLAIR)
C/ Coronal 3D -T1-TFE
D/Coronal T2WI – TSE
All images are showing marked diffuse loss of brain parenchyma including mesiotemporal atrophy.
Note that there are no areas of increased signal intensity in the FLAIR and T2W images.
### Table 1 - Neuropsychological follow-up

<table>
<thead>
<tr>
<th>Neuropsychological assessment</th>
<th>I examination</th>
<th>II examination – after 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td><strong>Verbal memory (10 words)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Immediat recall</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Recognition</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VF (animal)</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>BNT</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><strong>Attention/executive function</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit symbol</td>
<td>8 (2 mistakes)</td>
<td>10 (1 mistake)</td>
</tr>
<tr>
<td>VF (M)</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

MMSE - Mini Mental State Examination; BNT – Boston Naming Test; VF (animal) – number of animals produced for 1 min; VF (M) – number of words beginning with letter “M” for 1 min;