SYPHILIS OF THE CENTRAL NERVOUS SYSTEM AS A CAUSE OF COGNITIVE IMPAIRMENT AT YOUNGER AGE, DIAGNOSTIC DIFFICULTIES

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ABSTRACT

Cognitive impairment in young patients requires special attention and accurate differential diagnosis. Vascular, metabolic, infectious, genetic, autoimmune and neurodegenerative causes should be taken into consideration. During last decades there has been rise in the number of cases of syphilis amongst infectious diseases, which if not treated could affect central nervous system. A 30 - year old man was admitted to the Alzheimer's Unit of Neurology Department in order to diagnose memory impairment. Three months earlier the patient was hospitalized in a Psychiatric Department due to acute psychotic disorders. This was the first psychotic episode. His family psychiatric and cognitive disorders history was unremarkable. At the time of admission the MMSE score was 26/30 points. Brain MRI revealed extensive cortical and subcortical atrophy, gliosis in temporal lobes. Cerebrospinal fluid analysis showed cytosis 15 cells / ul, protein level of 118 mg / dl and glucose level 45 mg/dl. HSV IgM and IgG antibodies were negative. Positive results for syphilis were obtained in serum and cerebrospinal fluid. The treatment was implemented, control visits were performed after 3 and 12 months. The first symptoms of neurosyphilis could present with psychotic disorders and cognitive impairment. Magnetic resonance imaging can suggest herpetic etiology therefore it is important not only to perform virological tests, but also serology tests for syphilis.

Keywords: neurosyphilis, dementia, cognitive impairment, encephalitis

INTRODUCTION

Cognitive impairment in young age, particularly in patients aged 40 or less is rare, that is why it requires an increased vigilance in diagnostics. Various vascular, metabolic, infectious, genetic, autoimmune, neurodegenerative and neoplastic causes must be taken
into consideration. In patients with early onset dementia, magnetic resonance imaging (MRI) is mandatory as it would exclude brain tumor and assess cortical and subcortical atrophy. The full panel of blood tests is taken to exclude metabolic reasons of dementia. The diagnostics is supplemented by cerebrospinal fluid (CSF) analysis to assess inflammatory etiology and concentration of β-amyloid and tau protein. When familial Alzheimer's disease is suspected genetic testing should be performed. Syphilis can cause dementia, usually a few or more than 10 years after the patient become infected. Neurosyphilis develops in approximately 10% of patients, if the disease isn't treated. Syphilis may however affect central nervous system (CNS) at any time in the course of infection, even in early stages because Treponema pallidum penetrates CNS already in the primary syphilis. The most common forms of the neurosyphilis are asymptomatic syphilis, meningeal syphilis and vascular syphilis. Asymptomatic syphilis is diagnosed based on the results of serological tests and cerebrospinal fluid analysis in which cytosis is more than 5 cells / uL and MRI scans may show increased intensity of meninges. Symptoms of meningeal syphilis are similar to the symptoms of viral meningitis. They include fever, headache, malaise and a nuchal rigidity. These symptoms are usually observed within one year of the primary infection. CSF shows increased cytosis (several hundred cells/ul), elevated protein level and decreased glucose level. In vascular syphilis the symptoms may be similar to stroke depending on the location of the foci of cerebral infarction. These symptoms occur between 5-30 years of the primary infection. Progressive paralysis is a form of syphilis tarda and may occur about 10-25 years after the infection. This form is characterized by dementia, psychotic disorders and in final stages can lead to tetraplegia. Penicillin administered intravenously is the treatment of choice in the neurosyphilis. Doxycycline or ceftriaxone is the second line of treatment.

CASE STUDY

A 30 - year old man was admitted to the Alzheimer's Unit of Neurology Department due to memory impairment. Three months before admission to the Department he experienced an acute psychotic incident without symptoms of schizophrenia. This was the first psychotic episode. The patient was hospitalized in a psychiatric ward for a month, at that time first symptoms of cognitive impairment were noticed. He had secondary education, the history of chronic diseases was unremarkable, there was no family history of dementia. The patient claimed that for many years he had one sexual partner. There was no skin or mucous membranes pathological changes at the time of examination or in the past. Neurological examination revealed asymmetry of the palpebral fissures P <L, increased deep tendon reflexes P> L, bilateral Rossolimo sign, bilateral positive palmomental sign. The MMSE (Mini–Mental State Examination) score was 26/30 points (deficits in calculation and recall), the patient had difficulties with clock drawing test, Figure 1. The neuropsychological assessment showed high generalized cognitive impairment, CDR 0.5/1. Brain MRI revealed extensive cortical and subcortical atrophy in supratentorial position. The atrophy involved especially both temporal lobes with right side predominance (Figure 2). Moreover MRI scan demonstrated subcortical gliosis (high intensity signal in T2-weighted images) in mesial, anterior parts of temporal lobes and in both insular areas (Figure 3). Asymmetry and asynchrony were registered in
electroencephalogram (EEG), the basic activity was irregular, too slow in correlation with age. Standard laboratory tests showed no abnormalities (hematology, electrolytes,

Figure 1. Clock drawing test on admission.

Figure 2. MRI of the brain on admission. T2-weighted images in the axial plane show atrophy within both temporal lobes (2a, 2b).
Figure 3. MRI of the brain on admission. Areas of gliosis in the subcortical location within the insulas (Figure 3a, 3b) and in the antero-basal parts of the temporal lobes (Figure 3c, 3d) on T2-weighted images in the axial plane.
transaminases, TSH, vitamin B12, folic acid, renal parameters). The serum tests for HBV, HCV and HIV were negative. CSF analysis showed increased cytosis 15 cells / ul (98% of mononuclear cells), protein level of 118 mg / dl and glucose level 45 mg/dl. Levels of β- amyloid, total tau and phosphorylated tau in CSF were normal. Based on the result of cerebrospinal fluid analysis and MRI, viral (herpetic) encephalitis was suspected. Acyclovir therapy was empirically initiated, the outcome of virological testing was expected. In the meantime positive results for syphilis were achieved: Venereal Disease Research Laboratory test (VDRL) at 1:256 titers in serum, 1:32 titers in CSF and positive fluorescent treponemal antibody absorption (FTA-ABS) test. HSV IgM and IgG were negative, acyclovir was discontinued, penicillin intravenously was included. Dermatological, ophtalmological and internal assessment was performed to exclude systemic syphilis. Additional tests (echocardiogram, ultrasound of the abdomen) ruled out symptomatic syphilis of other organs. After 3 months deficits in neurological examination didn't change. MMSE score was 23/30 due to deficits in writing, calculation and recall. In the EEG asymmetry and asynchrony were registered but the basic activity improved. Parameters of CSF also improved, cytosis was 4 cells / ul, protein 52 mg /dl and glucose 53 mg /dl. Results for syphilis remained positive but VDRL- and FTA- test titers were significantly lower, Table 1. MRI scans showed smaller areas of gliosis, no new pathological foci in the brain were found (Figure 4).

Table 1. Titers of antibodies for individual visits.

<table>
<thead>
<tr>
<th>Visit</th>
<th>Test</th>
<th>Serum</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>VISIT 1</td>
<td>VDRL</td>
<td>1:256</td>
<td>1:32</td>
</tr>
<tr>
<td></td>
<td>FTA</td>
<td>1:32000</td>
<td>1:24000</td>
</tr>
<tr>
<td>VISIT 2 AFTER 3 MONTHS</td>
<td>VDRL</td>
<td>1:128</td>
<td>1:16</td>
</tr>
<tr>
<td></td>
<td>FTA</td>
<td>1:1600</td>
<td>1:1200</td>
</tr>
<tr>
<td>VISIT 3 AFTER ONE YEAR</td>
<td>VDRL</td>
<td>1:64</td>
<td>1:8</td>
</tr>
<tr>
<td></td>
<td>FTA</td>
<td>1:800</td>
<td>1:600</td>
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Figure 4. MRI after 3 months. Partial regression of the areas of gliosis within the insulas (Figure 4a, 4b) and antero-basal parts of the temporal lobes (Figure 4c, 4d) on T2-weighted images in the axial plane.
Figure 5. Clock drawing test after a year.

Figure 6. Performance on 10 – word list of Auditory – Verbal Learning Test (raw score) conducted at the first examination and 12 months later.

The second follow-up was performed after one year. Deficits in neurological examination didn't change. MMSE score was 27/30 (difficulties with calculation). There was significant improvement in the clock drawing test (Figure 5) and in neuropsychological examination, which is illustrated by comparison chart of performance on 10 – word list of Auditory – Verbal Learning Test conducted at the first examination and the 12 months later (Figure 6), CDR still 0.5/1. The result of CSF was normal (cytosis 1 cell/ul, protein 36 mg/dl, glucose 55 mg/dl). VDRL and FTA titers both in serum and in CSF were lower.
in comparison to previous results (Table 1). Changes in descending after encephalitis in MRI were revealed. The patient returned to work but he is still monitored by Venerological Outpatient Clinic and Department of Neurology.

**DISCUSSION**

In differential diagnosis of cognitive impairment infectious etiology should be taken into consideration. Infection of Treponema pallidum plays in this case keys role. VDRL screening in young patients with no family history of dementia is very important. Areas of hyperintensity in T2-weighted images in mesial parts of temporal lobes may occur in Herpes simplex encephalitis, limbic encephalitis and also in neurosyphilis. It may cause cognitive and psychotic disorders. There has been no reports of neurosyphilis mimicking herpetic encephalitis on MRI in the Polish patients. However about twenty cases with similar changes on MRI in patients with neurosyphilis were already described in previous studies. In these cases the time from the onset of symptoms to the diagnosis was usually a few months (maximal 2 years). Cognitive disorders which are characteristic for progressive paralysis may occur earlier, even two years after infection of Treponema pallidum. MRI may also reveal hippocampal atrophy, which was present in our case. Hippocampal atrophy requires differentiation with Alzheimer's disease (in young age particularly with familial Alzheimer's disease). After diagnosis and initiation of therapy, control visits are necessary and should be scheduled after a few months and then after a year. It allows clinical and radiological assessment of treatment's effects as well as serological control. If the antibody titer (VDRL, FTA) increases, antibiotic course should be implemented again. The prognosis is good with early diagnosis and appropriate treatment. Accurate differential diagnosis in young patient with cognitive impairment is mandatory. Early initiation of antibiotic therapy may prevent severe intellectual disability.

**COMPETING INTERESTS**

The authors declare that the authors have no competing interest.

**REFERENCES**