MILD COGNITIVE DISORDER AS CLINICAL MANIFESTATION OF PITUITARY STALK NEUROSARCOIDOSIS: CASE REPORT

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SUMMARY – A case is presented of a 59-year-old male patient with a 5-year history of sarcoidosis. In the last half a year, deterioration of his intellectual abilities was noticed. Psychological testing detected a mild cognitive disorder. Laboratory diagnostics found a decreased level of testosterone and magnetic resonance imaging showed pituitary stalk neurosarcoidosis without any other pathomorphological substrate of cognitive impairment. This case indicates that neurosarcoidosis should be considered as a possible cause of mild cognitive disorder and, consequently, included in the International Classification of Mental and Behavioural Disorders.

Key words: Neurosarcoidosis; Pituitary gland; Cognition disorders

Introduction

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology. In 90% of patients, the disease affects the lungs, most commonly as bilateral lymphadenopathy. Sarcoidosis can also involve other organs such as lymph nodes, eyes, skin, heart, muscles, liver and brain1-14.

Neurosarcoidosis (central and peripheral) can be found in 5%-15% of patients with sarcoidosis, whereas central neurosarcoidosis occurs in about 5% of patients. Diagnosis of neurosarcoidosis is based on the clinical picture of sarcoidosis in other parts of the body (lung, liver, etc.), magnetic resonance imaging (MRI) of the brain, finding of angiotensin converting enzyme (ACE) in serum and liquor, and x-ray, but definitive diagnosis can only be made after biopsy14-20.

Previous research has shown that MRI helps in differentiating sarcoidosis from other brain diseases such as vasculitis, neoplasms (glioma, meningioma, metastases) and other granulomatous diseases. It is important to distinguish neurosarcoidosis from non-neoplastic diseases of the central nervous system, such as multiple sclerosis, stroke, pyogenic abscess, toxoplasmosis, tuberculosis, cysticercosis, fungal infections, syphilis, Behcet disease, radiation necrosis, venous thrombosis, but also manifestations of systemic lupus erythematosus, Henoch-Schönlein purpura, polyarthritis nodosa, Wegener’s granulomatosis, etc.20-23. In this case report, we describe a patient with pituitary stalk neurosarcoidosis, which presented itself as a mild cognitive disorder.

Case Report

A 59-year-old man diagnosed with lung sarcoidosis five years before was treated with corticosteroids during the first year and a half after the diagnosis, but in the last three and a half years he received no therapy. During the last 6 months, his family members and friends noticed that his thoughts were slowed down and that sometimes he had difficulties in remembering things. Therefore, he was referred for neurologi-
cal, neuroradiological and hormonal examination, as well as psychological testing. On clinical neurological examination, no motor deficit was found. Given the existing underlying disease, further diagnostic procedures were undertaken. Physical examination detected no enlarged lymph nodes, ACE in serum and liquor was increased; serum ACE was 127 IU/L (reference range: 8-51 IU/L) and ACE in the liquor finding was positive; computerized tomography (CT) of the chest showed lesions characteristic of sarcoidosis: bilateral enlarged hilar lymph nodes, enlarged hilar and mediastinal lymph nodes with peribronchovascular thickening and thickening of interlobular septa with nodal lesions connected to the pleura, consistent with the

Fig. 1. Axial chest computed tomography without contrast media administration showed enlarged hilar and mediastinal lymph nodes. Peribronchovascular and interlobar septa are thick with nodal lesions connected to the pleura, corresponding to the lymphoid type of distribution in parenchymal sarcoidosis. There are signs of fibrosis within the lower lung lobes (not seen in these images).

Fig. 2. Lung computerized tomography shows bilateral lymphadenopathy.

Fig. 3. Brain magnetic resonance image: coronal post contrast T1 weighted image demonstrating abnormally thickened pituitary stalk.

Fig. 4. Brain magnetic resonance image: on the sagittal post contrast T1 weighted image, abnormally thickened pituitary stalk is confirmed, with very tiny hypophysis pushed down and posteriorly by a mild suprasellar cerebrospinal fluid herniation.
lymphoid type of distribution in parenchymal sarcoidosis (Figs. 1 and 2).

Signs of initial fibrosis were found in the lower lung lobes (not shown in the images). CT of the neck was normal and showed no enlarged lymph nodes. Brain MRI revealed pituitary stalk neurosarcoidosis (Figs. 3 and 4).

Hormonal examination showed normal levels of T3, T4, TSH and growth hormone, whereas serum testosterone concentration was lowered (Table 1). Psychological examination detected psychomotor deterioration, memory losses and learning difficulties. Psychological testing showed a decrease in the efficacy in the tests of learning and remembering, as well as some cognitive deterioration. Visual-motor coordination and constructional functions were normal. Scores on the tests for solving complex visual-spatial tasks were within the acceptable limits, but with certain deviations indicative of cerebral dysfunction. Most prominent failures were detected in the tests of acquiring new verbal content, while memory functions were moderately affected. Verbal fluency tested by naming familiar objects was also subnormal. The speed of visual content processing was mildly to moderately decreased. Non-verbal memory was also somewhat below the average. Flexibility of thinking was reduced (Table 2). The above findings were indicative of a mild cognitive disorder. Six months after the therapeutic treatment, the findings partly normalized, and cognitive functions showed somewhat lesser deviations. Serum ACE was mildly raised and serum testosterone was mildly lowered. Neuropsychological tests showed signs of cognitive function improvements consistent with mild cognitive disorder.

<table>
<thead>
<tr>
<th>Serum hormone level</th>
<th>Serum hormone reference range</th>
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<tbody>
<tr>
<td>T3 2.1 mmol/L</td>
<td>1.3-3.6 mmol/L</td>
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<tr>
<td>T4 98 mmol/L</td>
<td>58-161 mmol/L</td>
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<tr>
<td>TSH 3.2 mIU/L</td>
<td>0.3-3.6 mIU/L</td>
</tr>
<tr>
<td>Growth hormone 4.8 mIU/L</td>
<td>&lt;10 mIU/L</td>
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<tr>
<td>Testosterone 2.8 nmol/L</td>
<td>4.6-21.7 nmol/L</td>
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Table 1. Hormone levels in the male patient with neurosarcoïdosis

Table 2. Neuropsychological tests in the male patient with neurosarcoïdosis

<table>
<thead>
<tr>
<th>Neuropsychological test</th>
<th>Test result</th>
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<tbody>
<tr>
<td>Memory losses</td>
<td></td>
</tr>
<tr>
<td>Learning difficulties</td>
<td></td>
</tr>
<tr>
<td>Test of learning and remembering</td>
<td>Decreased</td>
</tr>
<tr>
<td>Visual-motor coordination</td>
<td>Normal</td>
</tr>
<tr>
<td>Constructional functions</td>
<td>Normal</td>
</tr>
<tr>
<td>Complex visual-spatial tasks</td>
<td>Subnormal</td>
</tr>
<tr>
<td>New verbal content</td>
<td>Prominent failures</td>
</tr>
<tr>
<td>Memory functions</td>
<td>Moderately affected</td>
</tr>
<tr>
<td>Verbal fluency tested</td>
<td>Subnormal</td>
</tr>
<tr>
<td>Visual content processing</td>
<td>Decreased</td>
</tr>
<tr>
<td>Non-verbal memory</td>
<td>Somewhat below the average</td>
</tr>
<tr>
<td>Flexibility of thinking</td>
<td>Reduced</td>
</tr>
</tbody>
</table>

Discussion

A number of clinical manifestations of neurosarcoïdosis have been described. Primarily, one should differentiate between central and peripheral neurosarcoïdosis. Peripheral neurosarcoïdosis presents itself as polynuropathy, myopathy, multiple mononeuropathies, and also affects peripheral and cranial nerve roots. Central neurosarcoïdosis involves multiple or solitary supra- and infratentorial brain lesions, mostly in the hypothalamus and/or pituitary gland, pituitary stalk, basal ganglia, multiple lacunar infarctions, fourth ventricles, inflammatory lesions in the brain and spinal cord, dural and leptomeningeal enhancement, intracranial hemorrhage, pituitary tuberculoma, amygdala, anterior hippocampus, mesial temporal neocortex, medullary involvement, deep white matter, cerebral aqueduct with hydrocephalus, pons, spinal mass lesion, temporodorsal in the hemisphere and cranial nerves. ‘Aqueductal stenosis’ is commonly associated with psychosis and delirium in patients with neurosarcoïdosis.
Pituitary gland involvement caused by granulomatous changes in the hypothalamo-hypophyseal system results in hormonal disbalance, which is responsible for diabetes insipidus as well as for amenorrhea-galactorrhea with hypogonadotropic hypogonadism. Brain MRI reveals changes in the pituitary gland and especially in the pituitary stalk that is often thickened, which is quite characteristic of neurosarcoidosis. However, thickening of the pituitary stalk can occur in other diseases such as Langerhans cell histiocytosis and pituitary hypophysitis. This case report describes a man with visible changes in pituitary stalk, as detected by MRI, accompanied by the lowered level of testosterone and impairment of cognitive function, i.e. mild cognitive disorder consisting of concentration difficulties and some degree of memory and psychomotor deterioration.

The lowered level of testosterone can be explained by the pituitary stalk damage. The new, 10th, revision of the International Classification of Mental and Behavioural disorders (ICD-10) contains mild cognitive disorders. Mild cognitive disorder is diagnosed on the basis of neuroradiological and laboratory findings, and psychological testing, after all other possible causes have been ruled out.

Neuropsychological impairments (psychomotor slowing, weakened memory, etc.) in mild cognitive disorder are not confirmed by morphological substrates in the brain detected by the neuroradiological diagnostics (CT and MRI). Definitive diagnosis of neurosarcoidosis in our patient was made on the basis of lung x-ray, ACE in serum and liquor, neuroradiological examination and psychological testing which, together with clinical symptoms, indicated mild cognitive disorder. In our patient, neurosarcoidosis of the pituitary stalk could explain the lowered level of testosterone, but could not be associated with cognitive impairments. In the case presented, we found no morphological substrate that could explain the mild cognitive disorder. Prüter et al. have previously described a mild cognitive disorder with no clear morphological substrate found on MRI in a woman with sarcoidosis, which they explained by meningitis caused by neurosarcoidosis. In our case, there were no signs of meningitis or any other inflammatory process in the central nervous system during the course of illness. Prüter et al. state that neurosarcoidosis in most cases occurs as a subacute form of sarcoidosis. Obviously, in our case neurosarcoidosis developed in a subacute phase, when bilateral hilar lymphadenopathy was in regression.

In the male patient, pituitary stalk neurosarcoidosis resulted in a lowered level of testosterone, whereas hyperprolactinemia and amenorrhea are described in female patients. Similar to the previously described case, mild cognitive disorder found in our patient did not have a clear morphological substrate. Studies have shown that in most of the patients with mild cognitive disorder caused by other etiological factors there is no clear pathomorphological substrate detectable by standard neuroradiological diagnostics. An exception is MRI 3T, which allows recognizing some differences in comparison to control group.

In conclusion, pituitary stalk neurosarcoidosis in men can present itself with a low level of testosterone, but also as a mild cognitive disorder. Since this is the second case of mild cognitive disorder reported in patients with neurosarcoidosis, we suggest that neurosarcoidosis should be considered as a possible cause of mild cognitive disorder and, consequently, included in the International Classification of Mental and Behavioural Disorders.

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Sažetak

BLAŽI KOGNITIVNI POREMEĆAJ KAO KLINIČKA MANIFESTACIJA NEUROSARKOIDOZE LIJEVKA HIPOFIZE: PRIKAZ SLUČAJA

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Prikazuje se slučaj 59-godišnjeg bolesnika s 5-godišnjom povijesću bolesti sarkoidoze. U posljednjih pola godine pri-
mjetno je bilo slabljenje njegovih intelektualnih sposobnosti. Psihološkim testiranjem otkriven je blaži spoznajni pore-
mećaj. Laboratorijskom dijagnostikom utvrđena je snižena razina testosterona, dok je magnetska rezonancija pokazala
neurosarkoidozu lijevka hipofize bez ikakvog drugog patomorfološkog supstrata kognitivnog poremećaja. Ovaj slučaj po-
kazuje da neurosarkoidozu treba uzeti u obzir kao mogući uzrok blažeg spoznajnog poremećaja, pa bi je trebalo uvrstiti u
Međunarodnu klasifikaciju psihičkih bolesti i bolesti ponašanja.

Ključne riječi: Neurosarkoidoza; Hipofiza; Kognitivni poremećaji