MULTIPLE SYSTEM ATROPHY: DIAGNOSTIC AND TREATMENT CHALLENGES: A CASE REPORT

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S u m m a r y. Multiple System Atrophy (MSA) is a rare, fatal, primary α-synucleinopathy that leads to multisystem neurodegeneration. MSA is the second most common form of atypical parkinsonism, after progressive supranuclear palsy. MSA is characterized by the occurrence of parkinsonian, cerebellar and autonomic symptoms of varying severity. Basing on the severity of cerebellar and parkinsonian symptoms two types of MSA are mainly distinguished: MSA-P (dominating parkinsonism) and MSA-C (predominance of cerebellar ataxia). The aim of the study is to present diagnostic and clinical problems in patients with MSA. This report presents a 50-year-old female patient suffering from worsening balance disorders, speech difficulties, head tremor, tremor of upper limbs, lower limbs muscle strength loss, paresis and ataxia of the lower limbs, memory disorders and psychomotor slowness, who was admitted to the Department of Neurology. MSA-C was diagnosed on the basis of the interview and additional tests. The prognosis in both types of MSA is poor, causative treatment is unknown and the survival time in most cases is 6-9 years.
K e y w o r d s: multiple system atrophy, multiple system atrophy with predominance of cerebellar ataxia, cross bun sign.

INTRODUCTION

Multiple System Atrophy (MSA) is a rare, fatal, primary α-synucleinopathy that leads to multisystem neurodegeneration [1, 2, 3, 4]. α-synucleinopathies are diseases characterized by the abnormal accumulation of α-synuclein aggregates in nerve fibers, glial cells and neurons [4, 5, 6, 7]. MSA is characterized by the occurrence of parkinsonian, cerebellar and autonomic symptoms, these symptoms may occur with varying severity [1, 2, 8, 9]. Basing on the severity of cerebellar and parkinsonian symptoms two types of MSA are mainly distinguished: MSA-P (superiority of parkinsonism) and MSA-C (predominance of cerebellar ataxia). Some scientists, however, distinguish the third subtype of MSA: MSA-A, in which the dysfunction of the autonomic system prevails [10]. There are no significant differences in the median survival time between MSA-P and MSA-C [1, 11]. The survival time in most cases is 6-9 years [12]. MSA occurs most often after the age of 50, mainly in the sixth decade of life. It's a rare disease with an incidence of 3:100 000 [3, 13, 14, 15]. Researchers believe that these statistics are understated due to MSA being undiagnosed or misdiagnosed.

MATERIALS, METHODS AND AIM

The present article reviews scientific reports on MSA. In the study we report a case of 50-year-old female patient who was admitted to the Department of Neurology. On the basis of the interview and additional tests, MSA-C was diagnosed.

CASE REPORT

This report presents a 50-year-old female patient suffering from worsening balance disorders, speech difficulties, head tremor, tremor of upper limbs, lower limbs muscle strength loss, paresis and ataxia of the lower limbs, memory disorders and psychomotor slowness, who was admitted to the Department of Neurology. The patient also reported that 3 years earlier she experienced an episode of the loss of muscle strength and sensation

from the lower limbs followed by fall, after which the mentioned symptoms disappeared immediately. Past medical history revealed hyperthyroidism and depression (she was no longer taking antidepressants). The patient suffered from emotional lability. She had difficulty urination and suffered from frequent urinary tract infections. In 2016, the patient was hospitalized, and diagnosed with a transient cerebral insufficiency. Patient underwent appendectomy 30 years ago, excision of Bartholin's gland in 1992, and uterine polyp in 2015. The patient mentioned that her brother was suffering from similar symptoms.

During hospitalization in the Department of Neurology, neurological examination was performed. It revealed dysarthria, adiadochokinesis, intentional and positional tremor of the upper limbs, head tremor, slight paresis and ataxia of the lower limbs and excessive myotatic reflexes in the limbs. In addition, the patient reported urgency of urinary incontinence and dysphagia. A series of additional tests were performed. The magnetic resonance imaging scan of the head showed the presence of atrophic changes in the cerebellum and brainstem with atrophic flattening of the abdominal surface of the pons with typical MSA-C 'hot cross bun sign', however no focal lesions were found. Electromyography revealed a slight degree of sensory-motor neuropathy of the right peroneal nerve and a tendency to generalized depletion during stress test record with a predominance of changes in the right lower limb. Two EEG examinations were carried out with an interval of 4 days, which showed slight irregularities in the form of alpha waves in the temporal area, distinguished from the background signal, while the basic signal was normal. A control transcranial and carotid arteries USG with Doppler function was also performed. However, it did not show any pathologies within these vessels. The analysis of blood and cerebrospinal fluid did not reveal significant abnormalities. A lower urinary tract infection was diagnosed, which could be linked to the urinary disorders reported by the patient. During the entire period of hospitalization, the patient's condition remained stable. On the basis of the interview and additional tests, multiple system atrophy with cerebellar ataxia (MSA-C) was diagnosed. The patient was discharged home in a good general condition, neurologically unchanged from the time of admission, and a referral to the Center of Daily Rehabilitation and Speech Therapy Clinic was issued. The following outpatient symptomatic treatment was prescribed: betahistine, thiethylperazine to reduce the severity of balance disorders, pridinol to decrease extrapyramidal symptoms, opipramol a tricyclic antidepressant, furazidine for lower urinary tract infection, and amantadine to increase secretion of dopamine in the striatum to reduce the intensity of parkinsonian symptoms such as tremor.

DISCUSSION

Diagnosis of MSA

In 2010, the European MSA Study Group (EMSA) analyzed data from 9 European countries and Israel. This study showed that parkinsonian symptoms occurred in 87% of patients with MSA. Bradykinesia was accompanied by rigidity in 93% of patients, 69% of patients suffered from dysarthria. Furthermore, this study showed that postural instability occurred in 89% of patients, tremor affected 33% of patients, and freezing of gait in 38% of patients with MSA. In the EMSA study, ataxia occurred in 64% of patients. 78% of patients with MSA suffered from limb ataxia, and 86% from gait ataxia. Autonomic disorders occurred in 99% of patients, including mainly urinary symptoms (83%) and orthostatic dysregulation (75%). Erectile dysfunction was reported in 84% of male patients [16]. In addition, MSA patients have other symptoms that include pyramidal signs (abnormal plantar reflex, generalized hyperreflexia), stridor, dysphagia, sleep apnea, rapid eye movement, sleep disorder, depression, hallucinations, delusions. Up to 75% of MSA patients may present cognitive impairment, patients may also feel pain, most often in lower limb. [1,2,16]. Patients with MSA frequently experience painful sensations [17].

The Second MSA Consensus distinguishes: MSA-P in which parkinsonism is the most discernible in the clinical picture and MSA-C in which the cerebellar syndrome dominates [8]. Some scientists, however, distinguish a third subtype of MSA, i.e. MSA-A, in which the dysfunction of the autonomic system prevails [10]. MSA is characterized by the occurrence of parkinsonian, cerebellar and autonomic symptoms, these symptoms may occur with varying severity [1, 2, 8, 9]. In the present study we report a case of a 50-year-old female patient suffering from parkinsonian (head tremor, tremor of upper limbs, psychomotor slowness, memory disorders), cerebellar (a failure of muscular coordination), and autonomic symptoms like difficulty urination and frequent urinary tract

infections. This report presents a female patient suffering from MSA with dominating cerebellar syndrome like balance disorders, muscular coordination failure and motor impairment. Neurological examination revealed ataxia of the lower limbs and speech difficulties.

In clinical practice, MRI is used to diagnose MSA. The MRI scan of the brain in patients with MSA-C often shows atrophy of the cerebellum, middle cerebellar peduncles and the brainstem. The MRI scan of our patient patient showed atrophic changes in the cerebellum and brainstem. 'Hot cross bun sign' typical of MSA-C was also found. In patients with MSA-P, changes are detected in the putamen, e.g. 'putaminal rim sign' [18, 19, 20].

Treatment of MSA

There is no causative treatment, and therapy is based on the alleviation of clinical symptoms. Levodopa is used to treat parkinsonism. According to a study conducted in the USA, a beneficial response to levodopa administration occurs in 51.6% of patients. In the presented case of the 50-year-old female patient amantadine was prescribed to increase the secretion of dopamine in the striatum, and to reduce the intensity of parkinsonian symptoms such as tremor. The patient had extrapyramidal symptoms. In order to decrease extrapyramidal symptoms, pridinol was introduced. The cerebellar symptoms are resistant to symptomatic treatment [1, 2, 21]. The following symptomatic treatment was prescribed for the reported patient: betahistine, to increase neurotransmitter secretion in the central nervous system (CNS) and reduce the severity of balance disorders, and thiethylperazine to reduce the balance disorders. The patient had difficulty urination and frequent urinary tract infections, therefore the patient was given furazidine. A tricyclic andidepressant opipramol was prescribed for emotional lability and reduced mood. Orthostatic hypotension was treated using midodrine, fludrocortisone, pyridostigmine and norepinephrine [22].

Currently, there are no known methods of causative treatment of proven efficiency. Only therapies aimed at alleviating symptoms accompanying the disease are used, however, they do not have any influence on the rapid progression of the disease, which leads to disability and death within 6-9 years from diagnosis. There are many ongoing trials aimed at developing a treatment targeted to slow, or even prevent the process of depositing α-synuclein in the CNS cells. Main potential therapeutic targets and examples of tested drugs and methods include blocking α-synuclein from reaching oligodendroglia e.g. sertraline, paroxetine; blocking α-synuclein aggregation e.g. rifampicin, nonsteroidal anti-inflammatory drugs e.g. lithium, nocodazole; providing neuroprotection e.g. riluzol, rasagiline, fluoxetine, autologous mesenchymal stem cells therapy (MSC), and decreasing neuroinflammatory response e.g. minocycline, intravenous immunoglobulins (IVIG) [23]. The administration of a new drug that could be used to treat MSA, i.e. IVIG brought improvement in 7 patients after a 6-month treatment [24]. Another therapy proved to be effective is MSC. Good results were obtained by administering MSCs to patients with MSA-C. In these patients, the progression of the disease was slowed. However, these studies were conducted on a very small groups of patients and require verification [25, 26]. All of the above treatment options have shown potential effectiveness, during molecular studies, reducing damage caused by α-synuclein deposits, however, only selective serotonin reuptake inhibitor, autologous MSC and IVIG have shown promising results in clinical trials. Well-planned and extensive clinical trials are still required [22]. Non-pharmacological approaches are also recommended, including avoiding overheating, heavy meals, proper hydration, avoiding alcohol, using elastic stockings, higher than torso position of the head during sleep, salting food, elimination of previously used antihypertensive drugs. Rehabilitation, physiotherapy, anti-fall exercises, orthostatic syncopes prophylaxis are also recommended. In the case of speech and swallowing disorders, speech therapist's help is advisable. In the case of severe movement disorders with posture instability, it is advisable to use rehabilitation equipment, including crutches, walkers and wheelchairs. It is essential not to forget about providing psychotherapy and depression treatment. [12, 27]

CONCLUSIONS

MSA is a rare, fatal, primary α-synucleinopathy that leads to multisystem neurodegeneration. Clinically differentiating multiple system atrophy and other similar neurodegenerative disorders may be challenging in all stages of the disease [7, 9]. In MSA-C, 'hot cross bun sign' can be seen on MRI scans. Currently, there are not known methods of causative treatment of proven efficiency. Only therapies aimed at alleviating symptoms accompanying the disease are used,

however, they do not have any influence on the progression of the disease. The prognosis in MSA is poor with 6-9-year survival. International collaboration could be useful in understanding the pathogenesis in MSA. There are many ongoing trials aimed at establishing a treatment targeted to slow or even prevent the disease. Well-planned and extensive clinical trials are still required to unambiguously confirm the efficacy and suitability of MSA therapy [23]. Non-pharmacological approaches are also recommended, including avoiding overheating and alcohol. Rehabilitation, physiotherapy, speech therapy and psychotherapy are also important.

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