Radiology Case Reports 18 (2023) 3192–3195

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Multiple system atrophy associated with Meige syndrome: A rare case report ☆

*Jiaji Liang, MD, Xi He, MD, Jinqiang Lu, MD**

Department of Plastic Surgery, The First Affiliated Hospital of Jinan University, Guangzhou, China

ARTICLE INFO

Article history:
Received 11 January 2023
Revised 27 April 2023
Accepted 28 April 2023

Keywords:
Multiple system atrophy
Meige syndrome
Mesenchymal stem cells
Botulinum toxin type A

ABSTRACT

Multiple system atrophy (MSA) is a rare form of adult-onset α-synucleinopathy. Meige syndrome, identified as bilateral blepharospasm and oromandibular dystonia, is a type of focal dystonic movement disorder. This case report aims to highlight the clinical features of multiple system atrophy associated with Meige syndrome in a patient. Additionally, we aim to provide the treatment experience in a patient with Meige syndrome as this is an extremely rare clinical case.

Introduction

Multiple system atrophy (MSA) is a progressive neurodegenerative disease with rapid progression and poor prognosis. The term was first proposed in 1969. The estimated prevalence of MSA is 2-5 cases per 100,000 population. It mainly involves the extrapyramidal system, the autonomic nervous system, and the cerebellar system [1]. The main clinical features of MSA are autonomic failure, including urogenital dysfunction or orthostatic hypotension, akinetic-rigid Parkinsonism, and cerebellar ataxia. The combination of neuroimaging and autonomic nerve function tests is helpful for the early identification of MSA and other neurodegenerative diseases [2].

Meige syndrome is a clinically rare neurological disease and a type of segmental dystonia. It is also called orbital-mandibular dystonia syndrome which mainly causes various forms of dystonia in the eyelids, facial muscles, mandible, and neck muscles. Generally, it is more common in middle-aged and elderly people. Bilateral blepharospasm and oromandibular dystonia are the 2 major clinical characteristics of this disease. It is divided into primary and secondary Meige syndromes according to distinct clinical manifestations and etiologies. The pathogenesis of Meige syndrome may be associated with the dysfunction of gamma-aminobutyric acid neurons, cholinergic hyperactivity, dopamine receptor hypersensitivity, or dopaminergic transmitter imbalance [3].

Case presentation

The patient, a 59-year-old male, had urinary frequency and increased micturition times without obvious induction for 5 years. He was admitted to our hospital because of urinary frequency accompanied by dizziness and unsteady walking

☆ Competing Interests: The authors have declared that no competing interests exist.

* Corresponding author.
E-mail addresses: liangjiaji20@stu2020.jnu.edu.cn (J. Liang), withhope@163.com (X. He), blues200@163.com (J. Lu).

https://doi.org/10.1016/j.radcr.2023.04.055

while he was standing or walking. Furthermore, the patient gradually seemed to shout and kick in his sleep at night. The patient was diagnosed with OPCA. L-dopa, buspirone, memantine, and citicoline were prescribed regularly for treatment. Additionally, umbilical cord-derived mesenchymal stem cells (1×10^6 cells/kg) were injected into the spinal canal of the patient 4 times since the inception of illness. The patient's symptoms were significantly improved.

The patient gradually had difficulty in opening his eyes since last year. His eyelids would close involuntarily during frown, bitter smile, or "grimace" like abnormal actions. This was especially pronounced when he was emotional or nervous. As the eyelids closed involuntarily, the patient had to force them open. On many occasions, the patient found it exceedingly difficult to open his eyes when he tried harder.

The abnormal findings on physical examination were as follows: the patient had severe dysarthria, bilateral orbicularis muscle contracted involuntarily, and his eyes blinked involuntarily. Bilateral superficial and deep sensibility were normal. Although the limb strength was normal, hypermyotonia was observed. The right side was distinct from the left side. The right side of the upper limb had static tremor, and the bilateral finger-to-nose and heel-knee-tibia tests revealed instability and inaccuracy. Rapid alternating movement coordination was poor. The left biceps reflex hyperreflexia and electropositive bilateral Babinski signs were positive. Madopar, buspirone, memantine, and citicoline were discontinued after admission and the symptoms were improved by intrathecal injection of UC-MSCs (1×10^6 cells /kg). Subsequently, the patient was treated with botulinum toxin type A injections. The patient achieved partial remission.

Discussion

The major manifestation of MSA-C is ataxia [4]. Previous studies have shown that buspirone can be used to improve ataxia in patients with MSA, but the effect is not satisfactory [5]. L-dopa can be used as the first-line treatment for parkinsonian symptoms in patients with MSA, and approximately 30 % of patients may benefit from this drug. The daily dose can reach 2 g/d [6]. Dopamine agonists and amantadine (up to 300 mg daily) are also available alternatives. However, deep brain stimulation is not recommended for patients with MSA [7,8]. If patients have dystonia, botulinum toxin A injection is recommended as benzodiazepines and anticholinergic drugs may increase the risk of apnea and aggravate cognitive impairment in patients with MSA [6]. The medications used for MSA have been summarized in Table 1 [9]. Intrathecal injection of UC-MSC therapy is safe and can improve the clinical symptoms of patients to a considerable extent. Multicourse treatment is helpful to further improve the neurological function of most patients and delay the disease progression [10].

The most widely accepted hypothesis of Meige syndrome is GABAergic neuron hypofunction and dopaminergic or cholinergic hyperactivity. Functional magnetic resonance imaging (fMRI) has shown decreased activation of the primary motor cortex (Brodmann Area 4) and premotor cortex (Brodmann Area 6) in patients with Meige syndrome. These may be the areas responsible for blepharospasm. Brain imaging identifies grey matter volume reduction in the cerebellum, superior frontal gyrus, insular cortex, and calcarine fissure in patients with oromandibular dystonia [11]. Treatment options include botulinum toxin A injections, drug interventions, and deep brain stimulation (DBS). Medications include anticholinergic agents, GABA sensitizers, anti-epileptics, and various psychoactive drugs. These drugs act on GABAergic or cholinergic neurons [12]. Botulinum A injection has shown promising results and is reserved for patients who are poorly responsive to oral medication or have side effects from these medications. However, with the treatment process, the dose of botulinum toxin type A needs to be gradually increased. Moreover, some patients can produce neutralizing antibodies, thereby resulting in treatment resistance [13,14]. Deep brain stimulation (DBS) of the globus pallidus interna (GPi), which belongs to the surgical domain, has proven to be an effective treatment method for this disease. In addition, double-sided DBS is superior to 1-sided DBS. According to research by a Japanese group, double-sided DBS for the development of related symptoms has improved by more than 80%. At the same time, damage to the globus pallidus is supposed to be an alternative measure, which will have an acceptable therapeutic effect [15].

Multiple system atrophy associated with Meige syndrome is a rare situation. The diagnosis of MSA with Meige syndrome is based on a combination of clinical features and imaging studies. Both are indispensable as no clinical features or imaging studies are conclusive. These considerations are particularly important because some evidence is often normal or equivocal in early disease conditions.

Table 1 – Symptomatic treatment strategies for MSA.

Symptoms	Treatment options
Ataxia	Buspirone, Physiotherapy
Parkinsonian symptoms	L-Dopa, Dopamine agonists, Amantadine
Dysmyotonia(Blepharospasm)	Botulism A
Postural hypotension	Fludrocortisone, Midodrine
Urgency of urination, Urinary incontinence	Anticholinergics, Botulism A
Urinary Retention	Tamsulosin, Prazosin
Rapid eye movement sleep behavior disorder	Melatonin, Clonazepam

Conclusions

Multiple system atrophy associated with Meige syndrome in the same person is a rare case that has not been reported yet. Both the medical history and clinical manifestations are to be considered for accurate diagnosis in such cases. Thus, as per our treatment experience, local injection of botulinum toxin type A and intrathecal injection of UC-MSCs are safe and effective treatments of choice.

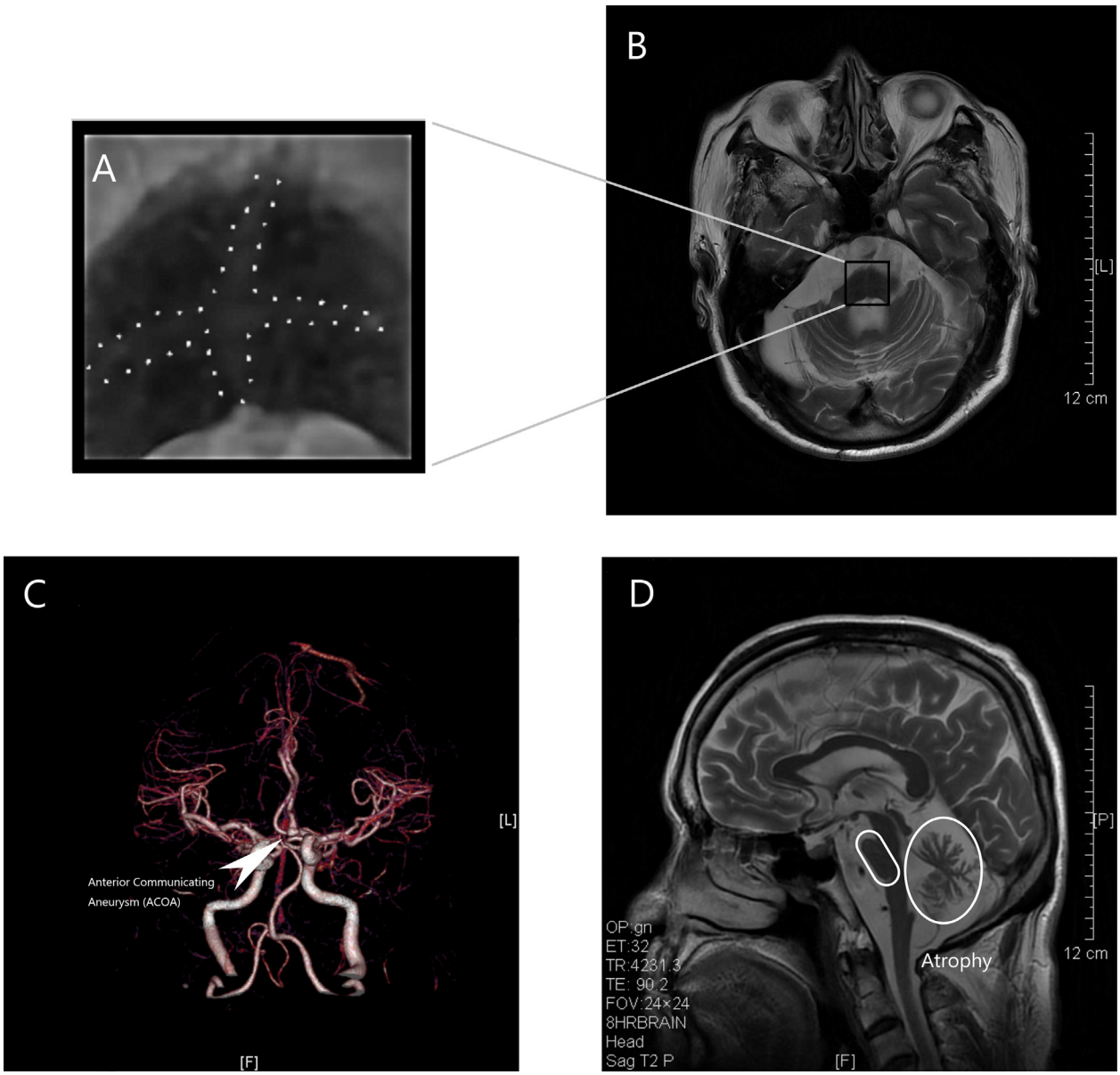

Fig. 1 – Head MR+CTA examination indications: The "hot cross bun sign" can be seen in mesocephalon (A and B). There was arterial aneurysm in anterior communicating artery (C). Mesocephalon and epencephalon exist atrophy obviously (D).

Patient consent

The patient provided informed consent for publication of his case details and any accompanying images. Institutional Approval was taken to publish the case report.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2023.04.055.

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