Case Report

Cerebellar form of multiple system atrophy: A case report[☆],[☆☆]

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ABSTRACT

Multiple system atrophy is a form of synucleinopathy with an unknown etiology that causes progressive neurodegeneration. It may affect the cerebellum, autonomic nerves, and pyramidal and extrapyramidal systems. We present the case of a 51-year-old man who was hospitalized for recurrent balance problems and dizziness. Cranial magnetic resonance imaging showed the "hot cross bun" sign of the pons with major atrophy of the cerebellum. The cerebellar form of probable multiple system atrophy was the final diagnosis.

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Introduction

Multiple system atrophy (MSA) is a rare and progressive neurodegenerative disease that usually affects elderly people in their 50s and 60s [1]. MSA is frequently overlooked during clinical examinations because of its rarity, with a yearly incidence ranging from 0.1 to 3.0 per 100,000, depending on age and geographical region [2]. Recent investigations have linked MSA to aberrant accumulation of protein α-synuclein in the glial cytoplasm, but the specific cause of MSA remains unknown [3].

The disease is categorized into two subtypes based on the major clinical phenotype: the parkinsonian form of MSA (MSA-P) linked to striatonigral degeneration, and the cerebellar form of MSA (MSA-C) with olivopontocerebellar atrophy and prominent cerebellar characteristics [4]. MSA-P is more prevalent with clinical characteristics including rigidity, tremor, bradykinesia, and posture and balance abnormalities. Patients with MSA-C usually present with slurred speech, movement and coordination abnormalities, and vision and swallowing problems [5].

Patients with MSA can show neuroradiological abnormalities, including cerebellar and pons atrophy, degeneration of the lower brainstem, and hyperintensities in specific regions, such as the pons or putamen, identified on conventional magnetic resonance imaging (MRI) [6]. The prognosis of MSA is poor, with no effective treatment reported yet [7].
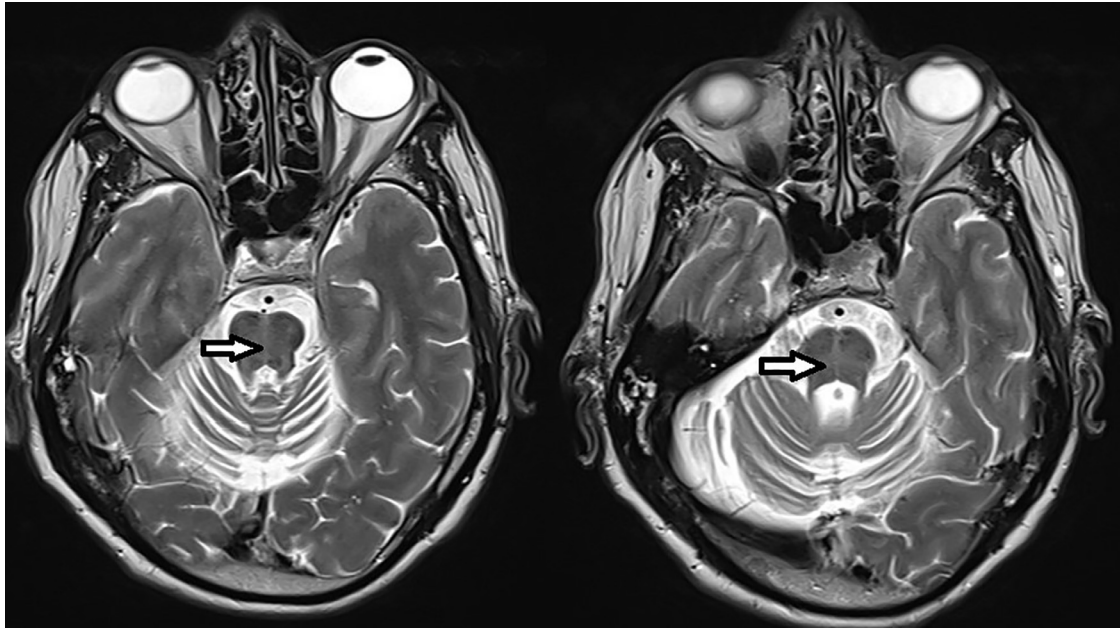

Fig. 1 – Cranial MRI on axial T2-weighted sequence showing a cruciform pattern of high intensity within the pons, indicating a hot cross bun sign (arrows).

Case report

A 51-year-old man was hospitalized in our neurological department after experiencing recurrent balance problems and dizziness. He has no medical history, with no family history of genetic disease or progressive neurological disorder, and has not used tobacco, alcohol, or long-term medication.

For two years, he exhibited progressive limb ataxia, gait disorder, urine problems, and orthostatic dizziness. The patient hadn't noticed any vision problems, trouble swallowing, or erectile dysfunction. There was no history of sleep disorders, memory loss, or cognitive decline.

On admission, the patient was conscious and well-oriented with normal vital signs. He had cerebellar dysarthria, gait ataxia, and a positive Romberg sign with multidirectional oscillations. Deep tendon reflexes were normal. The muscle strength scale was V, with normal sensitivity in all modalities. Babinski and Hoffman signs were negative. Movement coordination tests revealed dysmetria with dyschronometria. No rigidity, bradykinesia, or tremors were observed. The ocular movement test showed no nystagmus or ophthalmoplegia. The tilt test detected orthostatic hypotension after three minutes of standing.

Cerebral MRI on T2-weighted sequence showed a cruciform pattern of high intensity within the pons representing a "hot cross bun" sign (Fig. 1), with no signal abnormality in the basal ganglia (Fig. 2). On sagittal T1 and fluid-attenuated inversion recovery (FLAIR) sequences, there was an important atrophy of the cerebellum with enlargement of the fourth ventricle (Fig. 3). Positron emission tomography-computed tomography (PET-CT) revealed reduced metabolism in the cerebellar hemispheres compared with that in the cerebral hemispheres (Fig. 4).

Large paraclinical tests were negative (hemogram, serum thyroid hormone, serum electrolytes, renal and hepatic tests, blood alcohol level, vitamin B and E tests). Cerebrospinal analysis was normal. Computed tomography (CT) scan of the chest abdomen-pelvis was unremarkable. After diagnosis, the patient was assigned to physical and occupational therapy with fludrocortisone treatment for orthostatic hypotension.

Discussion

MSA is a progressive neurological disorder that mainly affects individuals with no gender predilection [4]. Although contact with pesticides, metal particles, and organic solvents is often assumed to be related to MSA, there are no confirmed environmental risk factors for the condition [8].

Alpha-synuclein glial cytoplasmic inclusions are believed to cause neuronal and oligodendrocyte malfunction, potentially leading to cellular degeneration in the cerebellum, inferior olives, and pons [9]. The exact process underlying the accumulation of alpha-synuclein is still unclear, but according to some studies, there may be a link between mutations in the GBA and COQ2 genes and a higher risk of MSA [10].

Based on the dominant symptom, MSA is classified into two variants: MSA-C, which has substantial cerebellar disorders, and MSA-P, which has significant parkinsonism [11].

The second consensus statement for the diagnosis of MSA in 2008 identified three clinical classifications: possible MSA, probable MSA, and definite MSA. Autopsy evidence of extensive α-synuclein-positive glial cytoplasmic inclusions and neurodegenerative alterations in the striatonigral or olivopontocerebellar area is necessary for a definitive MSA diagnosis. A probable MSA diagnosis is made when a disorder
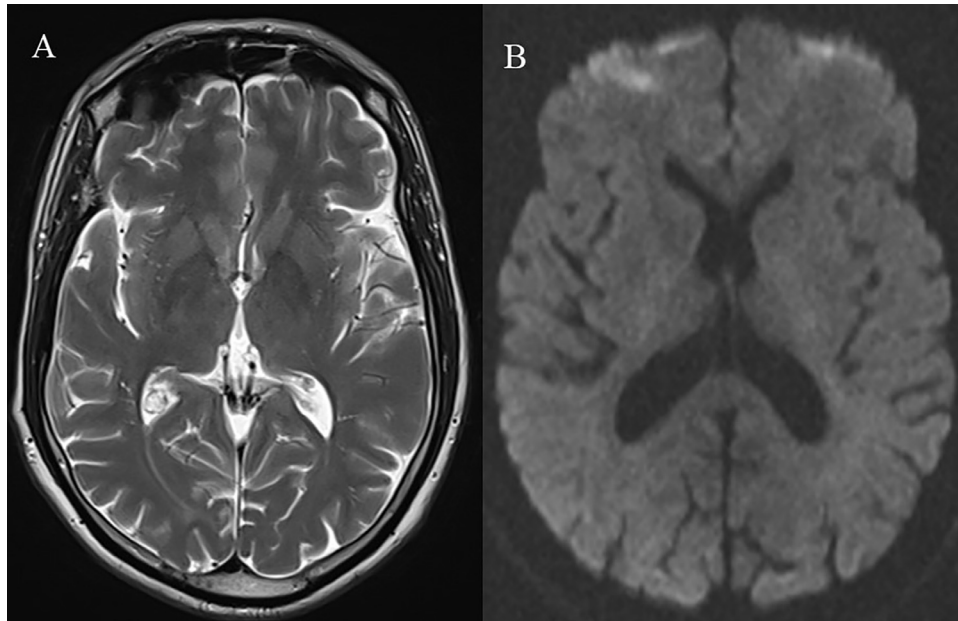
Fig. 2 – Cranial MRI on axial T2 (A) and DWI (B) sequences demonstrating no abnormalities in the basal ganglia.
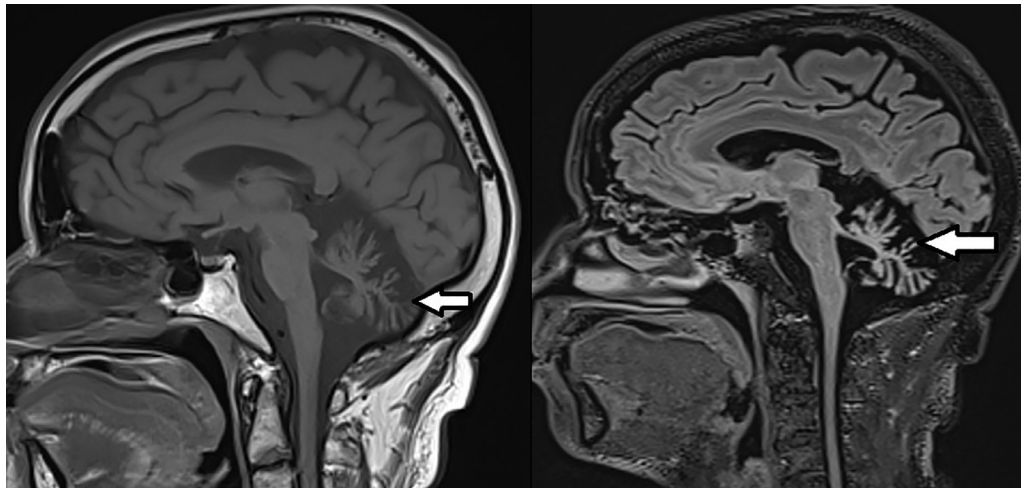

Fig. 3 – Cerebral MRI on sagittal T1 (A) and FLAIR (B) sequences showing major cerebellar atrophy (arrows) with dilatation of the fourth ventricle.

of the autonomic nervous system is paired with cerebellar ataxia (MSA-C) or insufficient levodopa-responsive parkinsonian syndrome (MSA-P). When autonomic dysfunction coexists with at least one red flag list item and either sporadic adult-onset parkinsonism (MSA-P) or cerebellar ataxia (MSA-C), it is considered a possible MSA diagnosis [4,12].

Our patient initiated the disease with clinical manifestations of cerebellar dysfunction, including gait ataxia, coordination disturbance, and cerebellar dysarthria, with no parkinsonism symptoms. These clinical signs increased gradually. The tilt test revealed orthostatic hypotension. Cerebral MRI demonstrated cerebellar atrophy with a classic "hot cross bun" sign. The progressive cerebellar disorder associated with auto-

nomic dysfunction and typical neuroimaging features of MSA-C lead to a probable diagnosis of MSA-C.

Cerebellar and brainstem degeneration is observed in MSA-C. The most distinctive feature of this condition is the hot cross bun T2/FLAIR hyperintensity pattern within the pons. This particular pattern has high specificity (96%) in MSA-C [13]. This indicates a preferential loss of myelinated transverse pontocerebellar axons and pontine neurons, whereas the craniocaudal corticospinal tracts remain intact [8].

Although the radiologic differential diagnosis of cerebellar diminution is wide, it usually covers more frequent conditions such as persistent alcohol consumption and chronic toxicity of Dilantin, which cause cerebellar flattering with no
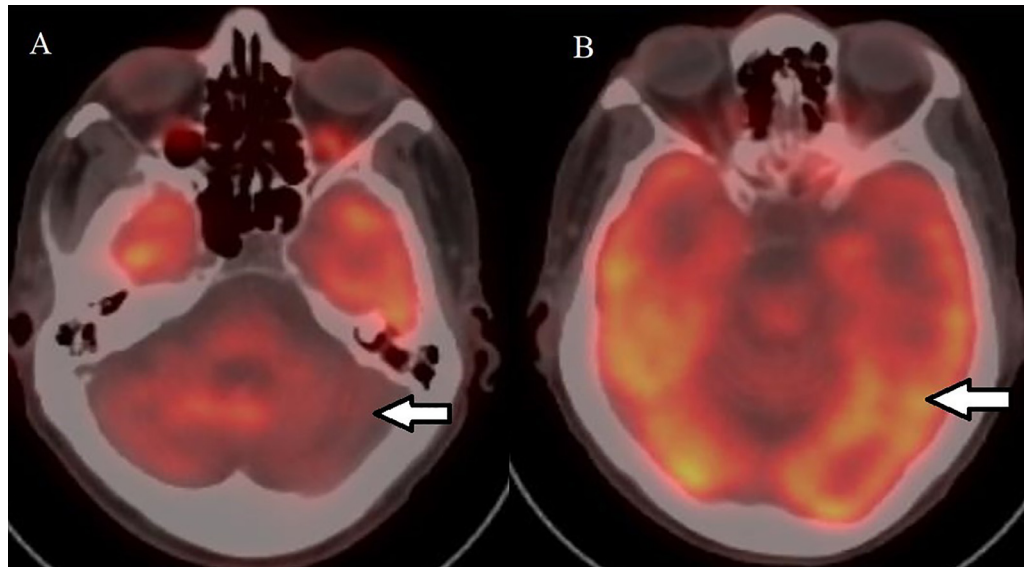
Fig. 4 – **PET-CT demonstrates reduced metabolism in bilateral cerebellar hemispheres (A) in comparison to the cerebral hemispheres (B) (arrows).**

cruciform sign or pontine atrophy [14]. Specifically, subtypes 2, 3, and 6 of spinocerebellar ataxia may be radiologically comparable to MSA-C, but genetic testing could distinguish the two entities. The hot cross bun sign may be observed in vasculitis or variant Creutzfeldt–Jakob disease. Vasculitis usually manifests as irregular vessel walls with zones of ischemia, whereas Creutzfeldt–Jakob disease presents with a typical pulvinar sign [15].

Regretfully, MSA-C has a poor prognosis, implying a gradual clinical decline over five to ten years [4]. The majority of therapy options include symptom management. For almost thirty percent of MSA patients, L-dopa is a successful option for parkinsonism symptoms; for MSA-C, physiotherapy is the optimal treatment. Symptoms, including orthostatic hypotension and depression, can be treated with drugs such as fludrocortisone and selective serotonin reuptake inhibitors. Future research on the use of autologous mesenchymal stem cells and recombinant human growth hormone to treat MSA should be conducted.

Conclusion

In conclusion, MSA represents a challenging and complex neurodegenerative disorder that poses significant clinical and diagnostic hurdles. We presented an unusual case of MSA-C with typical neuroradiological and clinical characteristics. MSA poses diagnostic challenges because of the overlap of symptoms with other neurological disorders, such as α- synucleinopathies and spinocerebellar ataxias. To obtain a correct diagnosis, clinical, MRI, and patient follow-up must be carefully coordinated.

Additional research on morphological and metabolic biomarkers in MSA with advancing therapeutic strategies tar-

geting α-synuclein aggregation and neuroinflammation is required.

Patient consent

I qualify as the corresponding author to this manuscript warrant that I have informed the patient of this scientific manuscript, and I confirm that I obtained his written and informed consent for the publication of this article.

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