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CASE REPORT

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# A remarkable patient – 40 years with probable multiple system atrophy (MSA)

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**Abstract** A 58-year-old woman with a 40-year history of very slowly progressive Multiple System Atrophy is described.

**Key words** multiple system atrophy · Shy-Drager syndrome · orthostatic hypotension

## Introduction

At the age of 18, this Japanese-American patient first noted that she could not dance quite as well as previously. Several months later, when she tried to take a modern dance course at the local university, she found that now, contrary to previous experience, she had become quite awkward. This sense of clumsiness gradually increased over the ensuing years, but did not prevent a normal and productive life. She had a successful pregnancy at the age of 25, but several months later definite orthostatic hypotension (OH) was first noted by her physician. Rather extensive investigation was performed in order to exclude postpartum pituitary hemorrhage: these tests, which included follicle-stimulating hormone and 17-hydroxycorticosteroid levels, were normal.

Three years later, when she was 28, she was referred to a neurologist for evaluation; blood pressure was noted as follows: supine 110/70; standing 40/0. Heart rate was 80 both supine and standing. Examination showed the following: deep tendon reflexes were absent, motor examination revealed normal bulk, tone and strength and there was no drift to the extended arms. However, on heel to shin test, there was marked abnormality on the right side, and somewhat better on the left. Rapid alternating movements were also performed somewhat slower in the hands than would have been appropriate for her age. On the finger and nose test, there was slowness noted, which was considered inappropriate for her age, although it was done accurately and without evidence of terminal tremor. The gait was markedly unsteady, and the patient was unable to walk tandem without falling to the right side. The Romberg test was positive and demonstrated a right-sided disequilibrium. Sensory examination revealed that vibratory sensation was present only at the level of the iliac crest on the right and at the rib margin on the left. She was unable to feel vibration at the wrist or the fingertip. The plantar responses were upgoing bilaterally.

Exhaustive laboratory investigation was performed and was considered normal. At this point, a diagnosis of Shy-Drager syndrome was suspected. Right-sided cardiac catheterization was normal. The valsalva maneuver was characterized by a drop in blood pressure and complete absence of a hypertensive overshoot or reflex bradycardia following the valsalva release. Infusion of norepinephrine was performed at 2 mg/liter; the concentration varied between 16–38 μg/kg/min. This resulted in a marked increase in both basal blood pressure and heart rate. The interpretation of this investigation was that there was a denervation sensitivity to infused norepinephrine.

The diagnosis of Shy-Drager syndrome was suspected clinically and the patient was started on 0.3 mg of 9-alpha fluorohydrocortisone in daily divided doses. She was followed by her regular physician until, at the age of 38, she was referred to the writer. At the time of my examination, she denied any related family history. Specif-

ically, there were no relatives with central nervous system disorders, including parkinsonism. Her major complaint was one of a clumsiness in walking around the house. She also felt that she could not walk without tipping over. She complained of dizziness on arising quickly but felt that this symptom had not changed for many years. Specifically, there were no bladder or anal sphincter disturbances and no apparent progression of her central nervous system symptoms. She, however, had developed recent hoarseness.

Blood pressure on examination initially was 130/70 supine and 70/? standing. The ventricular response was 96 beats/minute in both positions. The physical examination was otherwise unremarkable except for the persistent neurologic signs. She was taking 1.2 mg of 9-alpha fluorohydrocortisone daily in divided doses. Her serum potassium was consistently below 3 milliequivalents/liter.

She was referred to an otorhinolaryngolist, who confirmed the presence of bilateral vocal abductor cord paresis, supportive of the diagnosis of MSA (Shy-Drager syndrome).

During the years of follow-up, the patient has intermittently complained of very troubling gaseousness, belching, flatulence, and bloating. At times, these were her major symptoms. Her OH at present is being controlled on a dose of octreotide given subcutaneously by the patient of 0.05 mg/ml in a dosage of 0.3 ml (three times daily). She is no longer taking 9-alpha fluorohydrocortisone, midodrine or other pressor agents, principally because of side effects. Her physical condition has not changed very much. She has never shown any signs of dementia or parkinsonism. She still has profound OH, but obtains marked relief for two hours after each octreotide injection. She functions in a wheelchair for the rest of the time, and can walk with help around her house, but is strikingly ataxic. She travels with her husband to the mainland of the United States and has recently attended the wedding of her only daughter. Although she complains of chronic depression, she has done so for at least the past 15 years, and her current physician has noticed a gradual lifting of this mood over the past 10 years. Most recently, however, two episodes of laryngeal stridor necessitated acute intensive hospital care; a permanent tracheostomy was placed.

Recent magnetic resonance imaging disclosed moderate to advanced upper cerebellar atrophy on the axial T-2 view. The *hot cross bun* sign was not apparent.

On the saggital T-1 para midline cut, there was moderate to advanced lower cerebellar atrophy with enlarged sulci. The pons was considered normal. These changes were judged to be consistent with MSA (Figs. 1 and 2).

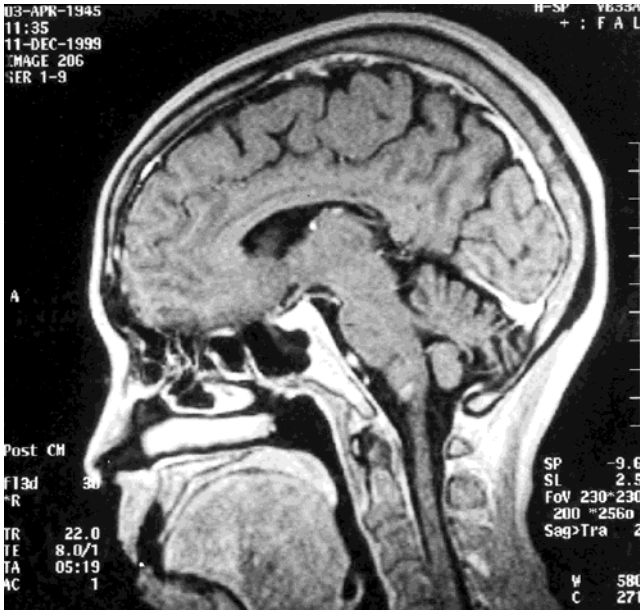


**Fig. 1** Magnetic resonance imaging procedure displaying moderate to advanced upper cerebellar atrophy (axial T-2 view)

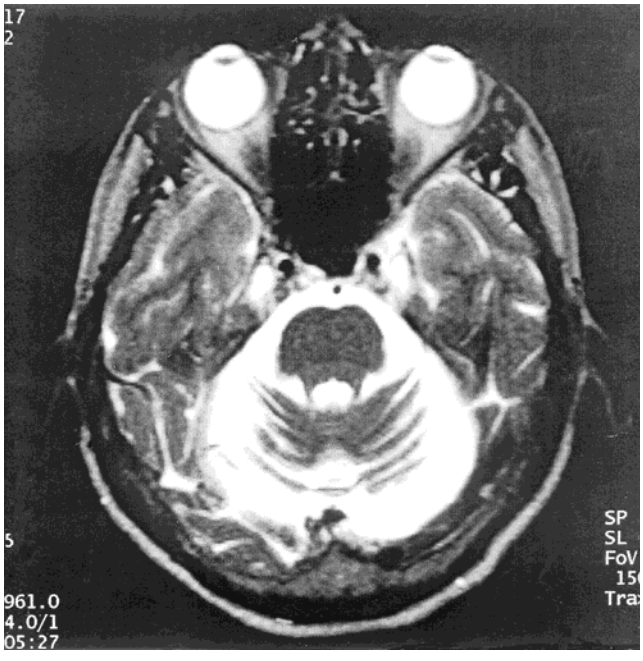


**Fig. 2** This cut demonstrates moderate to advanced lower cerebellar atrophy with enlarged sulci and a normal pons (saggital T-1 para midline view)

## Discussion

This patient is a straightforward illustration of MSA, except for one striking fact: she has survived until the age of 58 with extraordinarily slow progression of her neurologic disease. Her OH, although severe, is stable, and

she has responded to octreotide therapy for intermittent relief during the day. She tolerates systolic blood pressures of 70 without apparent symptoms. A myriad of other pressor agents were unsuccessful, and ultimately induced serious side effects.

She clearly represents a remarkable survival for this disease; in all reported series there is a mean life span of five to eight years from the onset of symptoms [1, 3]. If her complaints began at the age of 18, which seems likely, then she has survived 40 years, and 33 years when OH was confirmed at age 25.

One other aspect of her case history is striking: the onset of diagnosis was at age 25. Again, all reported series of MSA, as well as textbooks of autonomic disorders, describe this as a disease of later years with the average onset in the sixth decade of life.

Could this be a misdiagnosis? Definitive diagnosis of MSA must await neuropathologic confirmation; according to a consensus statement [2]. The absence of any suggestive family history is against a hereditary neurodegenerative disorder, but specific genetic testing was not performed. Also, the absence of deep tendon reflexes remains unexplained. In my opinion, however, the weight of evidence strongly supports a diagnosis of MSA.

This patient is noteworthy for at least two reasons: she presented with symptoms first appearing at the age of 18, with OH confirmed at age 25 and a diagnosis of MSA (Shy-Drager Syndrome) was made at age 28. She has survived until the age of 58 with this incurable and usually rapidly progressive disease.

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