A Case of Multisystem Degeneration of the Autonomic Nervous System

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Introduction:

Shy-Drager Syndrome (SDS), now called Multiple System Atrophy (MSA) is a rare, degenerative neurological disorder that affects autonomic, pyramidal, parkinsonian, and cerebellar functions [1]. This condition was initially classified in 1960 for cases of hypotension of unknown etiology from neurologic disorder. Depending on predominant clinical features, MSA is categorized as MSA-P for parkinsonian and MSA-C for cerebellar. Brain atrophy, primarily on the cerebellum, pons, and putamen, is the anatomical hallmark of MSA [2].

Several hypotheses have been proposed for the etiology of MSA, but its exact cause is yet to be discovered. Pathology ranges from intracellular alpha-synuclein accumulation to mitochondrial dysfunction and inflammation. In contrast to Parkinson's disease, which has an accumulation of alpha-synuclein intracellularly, alpha-synuclein accumulates in oligodendrocytes in MSA [2]. Several areas of the CNS are found to have neuronal loss and gliosis. Aggregates of misfolded alpha-synuclein in oligodendrocytes are the hallmark of MSA [3].

MSA usually manifests in the sixth decade of life with the incidence rate approximated between 0.6 - 0.7 per 100,000 people each year. Geographic distribution is observed for each subtype. Japan has largely MSA-C cases, while Western countries mostly have MSA-P [2].

Case Presentation:

Our patient was a 60-year-old African American male with a past medical history significant for Shy-Drager Syndrome, Benign Prostatic Hyperplasia (BPH), Vitamin D deficiency, sickle cell, seizures, asthma, CKD Stage 2, and hypertension. He had been residing in a nursing home for about 10 months. The patient was being followed by the medical team for his monthly visit at the nursing home. During a follow-up visit, he noted: "neck stiffness when straining to defecate".

The neck stiffness was associated with constipation and bowel movements, described as pellet-like in small amounts. He was prescribed a stool softener but refused as he was afraid of incontinence episodes. He was also prescribed a muscle relaxant for neck pain but refused it because he thought this medication would cause his rectal sphincter to relax and lead to incontinence episodes. He also reported nighttime urinary incontinence. As for his BPH, he was being followed by a Urology team; the Prostate-Specific Antigen (PSA) checked roughly 1 month prior was within normal limits. He also reported chronic right shoulder pain, without improvement seen with physical therapy. He noted a history of trauma when a motor vehicle hit him and dragged him across the road approximately 10 years ago. At that time, he was told that his shoulder could not be fixed because he had nerve damage in the area.

The patient mentioned multiple episodes of lightheadedness and dizzy spells when standing and straining. In the past, this has resulted in multiple falls and seizures that were determined to be caused by hypotension. He follows up with a cardiologist for these episodes of bradycardia and syncope. A recent cardiology visit about 2 months prior for profound dysautonomia and orthostatic hypotension which resulted in falls and syncopal episodes. He endorses fluctuations of blood pressure with elevations as high as 170/110 mmHg. Per his Cardiology team, he had not tolerated any scheduled antihypertensive regimens due to low blood pressure fluctuations, as low as 80/50 mmHg. Hydralazine was offered to him on an as-needed basis for episodes of systolic blood pressure greater than 160 mmHg. They recommended further evaluation at a dysautonomia center or by neurology at a tertiary care center. These episodes of syncope and seizures had led to many hospitalizations. About 2 years ago during a hospitalization for seizures and syncope, a CT scan of the head was done that showed chronic cerebellar atrophy without any evidence of acute stroke, hemorrhage, hydrocephalus, or mass. Neurology was consulted at that time and the patient was placed on Levetiracetam (Keppra) 500 mg tablet twice daily for seizures. The patient did not follow up with the neurologist thereafter.

The patient's current medications include Polyethylene glycol (MiraLAX) for constipation, vitamin D supplements, Bisacodyl 10 mg for when the patient has not opened bowels in 4 days, Hydralazine 25 mg as needed for elevated systolic blood pressure, Magnesium Hydroxide for constipation at bedtime, Acetaminophen 325 mg for pain as needed, Finasteride 5 mg QD, fleet enema, Albuterol Sulfate as needed for asthma, Carboxymethylcellulose Sodium ophthalmic gel for dry eyes.

Discussion:

Diagnosis:

MSA is primarily a clinical diagnosis and great care should be taken to differentiate it from other, more common neurological disorders. Classically, the disease presents with two variants: MSA-P which presents with primarily parkinsonian features, and MSA-C which presents primarily with cerebellar features [4]. An important feature distinguishing MSA from purely parkinsonian or cerebellar pathological processes is concurrent autonomic dysfunction, most frequently manifesting as orthostatic hypotension or urinary incontinence. In practical terms, the concurrent presence of autonomic dysfunction with signs of parkinsonian or cerebellar degeneration should alert the clinician to the possibility of a diagnosis of MSA.

For these reasons, history and complete neurologic examination are central in the diagnosis of SDS. Accurate timing should be elicited from the history since SDS begins at an earlier age and progresses more rapidly when compared to Parkinson's disease; this would be a strong differential diagnosis for our patient.

Also, it should be noted, that SDS presents with ambulatory dysfunction and risk for falls. Tilt table tests can be done to confirm autonomic instability, such as orthostatic hypotension. Additionally, levodopa response assessment could distinguish Parkinson's Disease (PD) from SDS. Excellent response is associated with the former and poor and un-sustained response is for the latter [5]. Since urological symptoms are often present as well, it may be helpful to elicit a history of urinary urgency, frequency, nocturia, and urge incontinence. A Point of Care Ultrasound (POCUS) bladder scan may also be helpful in eliciting post-void residual.

Although not strictly necessary for diagnostic purposes, imaging can help confirm the diagnosis of MSA. A sensitive but not specific finding for MSA on MRI is the “hot-cross bun sign,” a cross-shaped hyperintensity visualized on T2-weighted pontine axial imaging which is said to resemble the pastry traditionally on Good Friday in much of the Anglosphere [6]. Imaging can also help confirm the diagnosis of MSA by demonstrating atrophy of the olivopontocerebellar system (MSA-C) or the striatonigral system (MSA-P).

Treatment:
The treatment for SDS is mainly symptomatic management, as there is no currently recognized definitive cure for the underlying cause of the condition [7]. Consequently, clinicians should work closely with the patient to identify symptoms most responsible for patient distress and take steps to alleviate them directly.

Parkinsonian symptoms can be treated in much the same way as Parkinsonism, primarily through the use of dopamine agonists such as Levodopa. Levodopa is used primarily as a diagnostic way to differentiate SDS from PD; for those with probable SDS, MSA patients may respond better to Levodopa than when not on it, especially if diagnosed with the MSA-P variant [8]. More so, the role of dopamine agonists are limited. Patients who do not respond to Levodopa would unlikely respond to dopamine agonists.

Botulinum toxin can be used for focal dystonia associated with the disease. For urologic symptoms such as overactive bladder, lifestyle modification such as reducing consumption of caffeine at night or fluids at bedtime is reinforced. A beta adrenergic-3 agonist, such as Mirabegron, can be used if the former fails. For urinary retention, self-catheterization can be performed as needed if there is residual volume of more than 100 mL. For autonomic dysfunction with wide swings in blood pressure, Midodrine can be used to improve blood pressure. More conservative measures such as compression stockings or careful control of salt intake may also be helpful.

Finally, depending on the details of the disease progression, patients may benefit from physical, occupational, and speech therapy as supportive care for these patients. As with all chronic diseases, clinicians should work closely with patients to determine their treatment goals and design appropriate interventions accordingly.

Conclusion:

SDS is a condition that affects the functions of the autonomic nervous system in an unpredictable manner. Management of this condition becomes difficult because of this uncertainty in the pattern of symptoms and outcomes. Providers must be extremely careful when managing symptoms of this condition, as the combination of the disease process and medications can lead to the exacerbation of health problems. Close follow-ups in a timely manner of small increments are essential to allow the patient to lead close to normal lives as the disease only progresses further toward disability. Helping the patient determine their needs and setting up assistance is important for the safety of the patient.

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