Parkisonism with Shy-Drager Syndrome- a case report

B Paudel, K Paudel, R Paudel and K Pandru

Department of Medicine, Manipal College of Medical Science and Teaching Hospital, Pokhara, Nepal

Corresponding author: Dr. Badri Paudel, Lecturer, Dept. of Medicine, Manipal College of Medical Science and Teaching Hospital, Pokhara, Nepal. email: badribmu@gmail.com

ABSTRACT

A previously healthy 60 years old female patient presented with bradykinesia, postural instability and increased rigidity of both upper and lower limbs for 2 years and was diagnosed as Parkinsonism for last years. Later on she developed features of autonomic dysfunction including postural hypotension, hyperhydrosis and urinary incontinence so was diagnosed as Shy-Drager Syndrome. She was treated with fludrocortisone and nefidipine for the management of postural hypotension. Patient developed aspiration pneumonia during oral feeding, despite of ICU management for the same cause patient died of respiratory arrest.

Keywords: Autonomic nervous system, Degenerative, Parkinsonism, Postural hypotension

INTRODUCTION

James Parkinson first described Parkinson disease (PD) in 1817. PD is one of a number of chronic progressive CNS neurodegenerative diseases that typically occur in adults aged more than 65 years. PD is characterized by rigidity, bradykinesia, rest tremor, impaired postural reflexes, asymmetric onset, good to excellent response to levodopa, and pathologically by degeneration of pigmented neurons insubstantia nigra along with the presence of Lewy bodies. Incidence of PD, based on several worldwide studies, is about 10-20 cases per 100,000 population per year.[1] A great emphasis is being placed on the identification of clinical clues in patients who have a IPD with additional or atypical clinical features. These are classified as having Parkinsonism plus syndromes which includes "Shy-Drager Syndrome" (currently referred to as "Multiple System Atrophy" or MSA).[2]

Shy-Drager syndrome (SDS) is a rare progressive disorder of the central autonomic nervous system. SDS was named for neurologists Milton Shy, M.D., from the National Institutes of Health, and Glenn Drager, M.D., from the Baylor College of Medicine, who first described the condition in 1960. The autonomic nervous system controls vital involuntary body functions such as heart rate, breathing, and intestinal, urinary, and sexual functions. The autonomic nervous system also controls skin and body temperature, and how thebody responds to stress. Autonomic dysfunction pateints will present with problems that include: joint rigidity, muscle weakness, tremor, ataxia, impotence, bowel and bladder dysfunction, impairment of speech and difficulties with breathing and swallowing. Micrographia and anhydrosis also characterize this disease.[3]

CASE REPORT

A previously healthy 60 years old female, ex-smoker, non-alcoholic patient presented with bradykinesia, postural instability and increased rigidity of both upper and lower limbs for 2 years. At the time of presentation there was no tremor of the body. Examination revealed the slowness in initiating the speech with expressionless face (masked face). Mild decline in the intellectual function was noticed. Repetitive tapping over the bridge of the nose produce a sustained blink response (Myerson's sign). Rigidity in the all limbs was found with slowness of voluntary movement. Gait was characterized by small shuffling steps and loss of normal automatic arm swing, there was unsteadiness on turning, difficult on turning, difficult in stopping, and tendency to fall. On the basis of the clinical manifestation was diagnosed as Parkinsonism. She was treated with Sinemet 10/100 (carbidopa/levodopa) TID, Selegiline 5 mg BID. Gradually the patients' symptoms were aggravated and doses were titrated. 6 months back she developed postural hypotension. On standing BP was not recordable, while on supine position BP was 160/90 mmHg; on sitting position BP was 80/? mmHg. She also had developed urinary incontinence and hyperhydrosis for the same period of time. Examination revealed extrapyramidal sign with positive cerebellar signs. She was diagnosed as Shy-Drager syndrome. In the view of orthostatic hypotension, was treated with Fludrocortisone 0.1 mg/day. To control the supine hypertension, head-up tilt of bed at night, elastic stockings or tights, increased salt intake, and was given Clonidine 0.1g/day. Since she developed rashes so the Clonidine was discontinued and Nefidipine was initiated 5 mg before bed. Her supine BP was well controlled to 130/80mmHg, sitting BP was 120/75 mmHg and while standing BP was also 120/75 mmHg. Patient developed aspiration pneumonia during oral feeding, despite of ICU management for the same cause patient died of respiratory arrest.

DISSCUSSION

The American Autonomic Society has defined SDS as a sporadic, progressive, adult onset disorder characterized by autonomic dysfunction, parkinsonism, and ataxia in any combination. The features of the disorder include: 1.) Parkinsonism, 2.) Cerebellar or Corticospinal Signs, and 3.) Orthostatic Hypotension, Impotence, Urinary Incontinence or Retention, usually preceding or within two years after the onset of the motor symptoms, and that are poorly responsive to levodopa or dopamine agonists (Table-1).[4] The cause is unknown. It affects 1 in 10,000 people and is most often diagnosed in men older than 60. It is two or three times more common among men than among women.

Depending upon which part of the brain is affected first, SDS may appear in different ways. There are 3 types of Shy-Drager syndrome: **1). Parkinsonian-type** which may include symptoms of Parkinson's disease such as slow movement, stiff muscles, and mild tremors; **2). Cerebellar-type** which may include problems such as loss of balance and the tendency to fall; and **3). Combination-type** which may include symptoms of both types 1 and 2. Parkinsonian symptoms and symptoms of autonomic dysfunction such as constipation and sexual impotence in males predominate early in the course of the disease. Constipation may be unrelenting and hard to manage in some patients.

SDS may be difficult to diagnose in the early stages; however, within a year of onset most patients develop orthostatic hypotension – an excessive drop in blood pressure when the patient stands up causing light-headedness or dizziness - is a universal feature of SDS. It is worse after meals and early in the day. When orthostatic hypotension becomes severe (i.e. blood pressure of less than 70/40) 'blackouts' may result. When the patient falls to a prone position, the blood pressure returns toward normal and the patient will regain consciousness. Many patients also complain of dry mouth and dry skin, and because of abnormal sweating have problems with relation of body temperature. The hands and feet will be cold. Symptoms sometimes can be mild as well and are misdiagnosed as having anxiety or hypertension. Other symptoms may also develop, such as generalized weakness, double vision and/or other vision disturbances, impairment of speech, sensory changes, difficulties with breathing and swallowing, arrythmias, and diarrhea. During the final stages of the disease, patients have trouble chewing, swallowing, speaking. As a result of autonomic dysfunction, some patients develop breathing problems including loud respiration and cessation of breathing during sleep.

On examination parkinsonian movements (tremor, rigidity, and slow movements) are common. Patients generally have postural hypotension. Eye examination

Table-1: Guidelines established by the American Autonomic Society and the American Academy of Neurology for the clinical diagnosis of SDS (MSA).[4]

Domain	**Criterion**	**Feature**
Autonomic and urinary dysfunction	Orthostatic fall in blood pressure by 30 mmHg systolic or 15 mmHg diastolic)	Orthostatic hypotension
Parkinsonism	Bradykinesia *plus* rigidity *or* postural instability or tremor	Bradykinesia (progressive reduction in speed and amplitude of voluntary movements during repetitive actions) Rigidity Postural instability (loss of primary postural reflexes) Tremor (postural, resting or both)
Cerebellar dysfunction	Gait ataxia plus Ataxic dysarthria Or Limb ataxia Or Sustained gaze evoked nystagmus	Gait ataxia (wide based stance with irregular steps) Ataxia dysarthria Limb ataxia Sustained gaze evoked nystagmus
Corticospinal tract dysfunction	No defining features	Extensor plantar responses with hyperreflexia

may reveal atrophy of the iris and paralysis of eye muscles. Neuromuscular examination may reveal abnormal reflexes and may show severe muscle wasting.

There are no specific tests to confirm this disease. A neurologist can make the diagnosis based on the history of symptoms, the findings during physical examination, and ruling out other causes of symptoms. A combination of parkinsonism and certain autonomic problems (especially impotence, incontinence, and postural hypotension) are clear indications of the syndrome.[4] Testing to help confirm the diagnosis may include the following: **1.) Plasma norepinephrine levels:** In normal patients, blood levels of norepinephrine rise when they stand up. This doesn't happen in people with SDS. Norepinephrine is a hormone that helps maintain blood pressure by triggering certain blood vessels to constrict when blood pressure falls below normal. Another test for the condition is the Valsalva maneuver. In this test, the patient holds his or her breath and strains down as if having a bowel movement while the doctor monitors blood pressure and heart rate for 10 seconds. Patients with SDS will not have the normal increase in blood pressure and heart rate, **2) urine catecholamines**, and **3.) MRI of head** to rule out other pathology. There are no specific abnormalities on imaging associated with SDS.

Table-2: Practical management of Shy-Drager Syndrome

A. Pharmacotherapy

For akinesia-rigidity

- Levodopa up to 800-1000 mg/day, if tolerated
- Dopamine agonists as second line antiparkinsonian drugs
- Amantadine as third line drug, 100 mg up to three times daily

For focal dystonia

- Botulinum toxin A

For orthostatic hypotension

- Head-up tilt of bed at night
- Elastic stockings or tights
- Increased salt intake
- Fludrocortisone 0.1-0.3 mg/day
- Ephedrine 15-45 mg TID
- L-threo-DOPS (300 mg BID)
- Midodrine 2.5 – 10 mg TID

For postprandial hypotension

- Octreotide 25-50 mg s.c. 30 min before a meal

For nocturnal polyuria

- Desmopressin (spray: 10-40mcg/night or tablet: 100-400mcg/night)

For bladder symptoms

- Oxybutynin for detrusor hyper-reflexia (2.5-5 mg BID- TID)
- Intermittent self-catheterisation for retention or residual volume >100 ml

B. Other therapies

- Physiotherapy
- Speech therapy
- Occupational therapy
- Provision of wheelchair
- CPAP (rarely tracheostomy)

Unfortunately there is currently no curative therapy for autonomic dysfunction and so the therapeutic strategy is symptomatic and determined by the extent of impairment of the quality of life in these patients. In all cases it is important to remember that the progressive course of SDS means that a regular review of the treatment is mandatory to adjust measures according to clinical needs. However, typical antiparkinsonism drugs such as carbidopa-levodopa (Sinemet) should be used with caution, since they often worsen the postural hypotension and may cause fainting, black-outs.

The rationale in treating the symptoms of orthostatic hypotension is based on increasing the intravascular volume with a reduction of volume shift to lower body parts when changing to an upright position. The selection and combination of therapies depends on the severity of symptoms in the individual patient, rather than the extent of blood pressure drop during a tilt test. The simplest non-pharmacological options include sufficient fluid intake, high salt diet, more frequent along with smaller meals per day to reduce postprandial hypotension (by spreading the total carbohydrate intake) and custom made elastic body garments. During the night, head-up tilt (at least 13 cm) increases the intravascular volume by up to 1L within a week, which is particularly helpful in improving early morning hypotension. This approach is especially successful in combination with fludrocortisone, which further supports sodium retention.[5] The next group of drugs to consider are the sympathomimetics. These include ephedrine (with both direct and indirect effects), although at higher doses side effects develop including

tremulousness, loss of appetite, and urinary retention in men. Among the large number of vasoactive agents that have been evaluated in SDS only one, the directly acting α- adrenergic agonist midodrine, meets the criteria of evidence based medicine.[6,7] Side effects are usually mild and only rarely lead to discontinuation of treatment because of urinary retention or pruritus, predominantly on the scalp.

Another promising drug appears to be the norepinephrine precursor L-threo-dihydroxyphenylserine (L-threo-DOPS), which has been used for this indication in Japan for years and the efficacy of which has now been shown by a recent open, dose finding trial.[8] If the above mentioned drugs do not produce the desired effects, selective targeting is needed. The somatostatin analogue octreotide is often beneficial in postprandial hypotension, presumably because it inhibits release of vasodilatory gastrointestinal peptides and importantly it does not enhance nocturnal hypertension.[9]

The vasopressin analogue, desmopressin, which acts on renal tubular vasopressin-2 receptors, reduces nocturnal polyuria and improves morning postural hypotension. Pharmacological options with cholinergic agonists or antagonists or α–adrenergic substances are usually not successful in reducing postvoid residual volume in SDS, but anticholinergic agents like oxybutynin can improve symptoms of detrusor hyperreflexia or sphincter-detrusor dyssynergy in the early course of the disease. Recently, α -adrenergic receptor antagonists (prazosin and moxisylyte) have been shown to improve voiding with reduction of residual volumes in SDS patients.[10] Urological surgery must be avoided in these patients because post-operative worsening of bladder control is common.

The necessity of a specific treatment for sexual dysfunction needs to be evaluated individually in each SDS patient. Male impotence can be partially circumvented by the use of intracavernosal papaverine, prostaglandin E_1 or penile implants. Preliminary evidence in PD patients[11] suggests that sildenafil may also be successful in treating erectile failure in SDS: a recent trial confirmed the efficacy of this compound in SDS, but also suggested caution because of the frequent cardiovascular side effects.[12] Erectile failure in SDS may also be improved by oral yohimbine.

Constipation can be relieved by increasing the intraluminal volume which may be achieved by using a macrogol-water-solution, increased dietary fibre or laxatives. Inspiratory stridor develops in about 30.0% of patients. Continuous positive airway pressure (CPAP) may be helpful in some of these patients. In only about 4.0% of cases is a tracheostomy needed (Table-2).

The probable outcome is poor. There is a progressive loss of mental and physical functions until general debilitation develops. Shy-Drager usually ends in death 7 to 10 years after the onset of symptoms. The rate of progression differs in every case and the speed of decline may vary widely in individual patients. It is unusual for someone to survive more than 15 years after diagnosis. Pneumonia is the most common cause of death, although arrhythmias may be responsible for death in some patients. The exact cause of SDS is still mysterious and there is no way to prevent the condition.

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