

## Multisystem Atrophy Presenting with Hypercapnic Respiratory Failure

### ABSTRACT

Respiratory failure as the presenting feature is uncommon in neurodegenerative diseases. We report a case of 58-year-old male presenting as hypercapnic respiratory failure and stridor due to vocal cord paralysis accompanied with severe autonomic dysfunction, gait, and sleep changes. Examination showed cerebellar ataxia and autonomic dysfunction. Tracheostomy was necessary. Magnetic resonance imaging showed bilateral signal abnormality in middle cerebellar peduncles and favoring multisystem atrophy (MSA). The objective of this case report is to remind readers that MSA should be considered in differential diagnosis of unexplained respiratory failure, stridor, and vocal cord paralysis in appropriate clinical circumstances. Relevant literature is reviewed.

**Key words:** Multisystem atrophy, Middle cerebellar peduncle, Hypercapnic respiratory failure

### INTRODUCTION

Multisystem atrophy (MSA) is a chronic neurodegenerative disease characterized by progressive deterioration of various parts of the central nervous system such as cerebellar and extrapyramidal and autonomic nervous system. Uncommonly, patients present with stridor and respiratory failure even before the diagnosis is made.<sup>[1,2]</sup> Such a presentation leads to diagnostic and therapeutic difficulties.

We present here one such case for its rarity and review the relevant literature.

### CASE REPORT

A 58-year-old male presented with 1 month history of intermittent breathing difficulty, orthostatic intolerance, and hyper somnolence. On further enquiry, he gave the history of slowness and imbalance of gait, sleep disturbances such as frequent nocturnal awakenings. These were present for the past few months along with chronic constipation. There was neither history of sleep behavioral disorders nor any urogenital complaints. He was taking levetiracetam for longstanding convulsions. There was no relevant family history.

On neurological examination, he had cerebellar ataxia, significant postural drop of blood pressure (supine BP –112/70 mm of Hg and on standing – 60 systolic mm of Hg) without accompanying tachycardia. Another important observation was of intermittent stridor leading to episodic breathing difficulty. During the hospital admission, he developed hypercapnic respiratory failure (Arterial blood gas: pH 7.31 PCO<sub>2</sub> 74, PO<sub>2</sub> 90, and HCO<sub>3</sub> 26) requiring non-invasive ventilation and later had to be intubated in view of persistent hypercapnia and respiratory acidosis. Following causes of Type 2 respiratory failure were evaluated but

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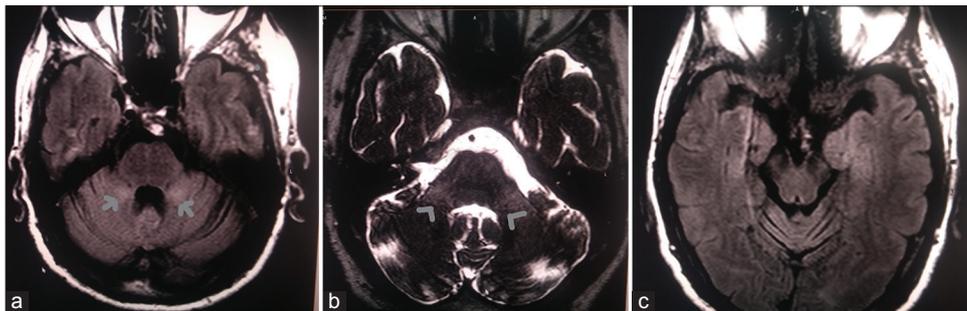
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none was detected. There was no evidence of obstructive pulmonary disease, drug overdose, no chest wall deformities and metabolic and endocrine parameters were within normal limits. In view of his seizure disorder, electroencephalogram was done which did not show any epileptiform activity. Cerebrospinal fluid (CSF) studies were performed to rule out the rare possibilities of autoimmune encephalitis or Guillain-Barre syndrome presenting as severe dysautonomia, which were normal. (CSF protein 31 mg%, glucose 84 mg%, White blood cells 01, and Red blood cells 01/cmm).

Magnetic resonance imaging (MRI) brain gave the clue to the diagnosis; by showing bilateral middle cerebellar peduncles (MCP) signal abnormalities [Figure 1a-c]. Following stabilization of overall clinical status, extubation trial was given but patient continued to have intermittent stridorous breathing and needed re-intubation. On direct laryngoscopy, vocal cords were found to be in the midline position; hence, tracheostomy was done. Clinical features of cerebellar ataxia, orthostatic



**Figure 1:** (a-c) Anomalous FLAIR and T2 hyperintense signal in bilateral brachium pontis with mild prominence cerebellar foliae

hypotension, and inspiratory stridor in association with imaging findings were compatible with MSA cerebellar (C) MSA-C.

## DISCUSSION

This case makes the point that respiratory failure can be one of the important and early manifestations of MSA. Only a few cases with this presentation have been reported in the literature.<sup>[1,2]</sup> The awareness of this uncommon occurrence is important in the effective management.

MSA is a rare, sporadic, adult onset progressive, neurodegenerative disease involving MSA-C, or extrapyramidal MSA Parkinson (P) MSA-P along with autonomic nervous systems in various combinations. Symptoms tend to appear in the fifth decade of life and rapidly progress over few years (mean survival from symptom onset being 5.7 years). Autonomic dysfunction commonly manifests as orthostatic hypotension, urogenital, or gastrointestinal dysfunction, sleep behavioral disorders, sleep apnea, and at times nocturnal stridor. Early instability, rapid progression, abnormal postures, bulbar dysfunction, respiratory dysfunction, and emotionality help to distinguish it from the more common Parkinson's disease. A European MSA Study Group concluded that two out of the above-mentioned six red flags are highly specific with a good sensitivity for differential diagnosis when considering MSA-P.<sup>[3]</sup>

In the current case, the clues toward diagnosis of MSA were severe symptomatic autonomic dysfunction, stridor, and rapid progression to hypercapnic respiratory failure (also likely vocal cord paralysis) with clinical background of mild motor disturbances such as gait dysfunction, sleep disturbances, and chronic constipation evolving over 1 year.

MSA presenting primarily as respiratory failure is very uncommon and only a few cases have been reported. In 2004, Cormican *et al.* reported<sup>[4]</sup> that multiple system atrophy should be considered in the differential diagnosis of late onset central sleep apnea and progressive hypoventilation. In 2006, Glass *et al.*<sup>[1]</sup> reported six cases of irregularities in respiration, found in early course of MSA. The mechanisms underlying such respiratory insufficiency remain unclear. It may be explained by upper-airway obstruction as a result of vocal cord abductor paralysis, over-activity of the vocal-cord adductors, and under activity of the abductors leading to narrowing of the glottic

space. An impairment of the respiratory center or an impaired hypoxic ventilatory response or denervation of laryngeal muscles have also been postulated.<sup>[5]</sup>

Neuroimaging can be helpful in diagnosis of MSA.<sup>[6]</sup> The findings differ between its two types: In MSA-C, atrophy of pons, cerebellum, or MCP is characteristic. On T2-weighted MRI, hyperintensity can be seen in the pons ("hot cross bun sign"),<sup>[6,7]</sup> MCP and cerebellum. Putaminal abnormalities are more commonly seen in MSA-P<sup>[6,7]</sup> with T2-hyperintensity of the lateral putaminal rim or hypointensity of the posterior putamen. Neurodegenerative processes affecting MCP have distinct mechanisms;<sup>[8]</sup> in general, there is preferential loss of Purkinje cells, or grey matter nuclei in the brain stem in diseases such as MSA-C, fragile X associated tremor-ataxia syndrome or some spinocerebellar ataxias leading to axon loss, and degeneration of the associated MCP fibers. Abnormal T2 signal of MCP has been reported in 43% of cases of MSA-C, concomitant volume loss is the rule.<sup>[6]</sup> Even though closely associated with MSA, the MRI findings are not specific for MSA, for example, "Hot cross bun sign" has been reported in spinocerebellar ataxia-6 previously.<sup>[9]</sup> Other pathological processes affecting MCP are demyelination, toxic or metabolic diseases, adrenoleukodystrophy, Wilson disease, cirrhosis of the liver, cerebrovascular diseases, including posterior reversible encephalopathy syndrome, hypertensive encephalopathy, HIV encephalopathy, and neoplasms.<sup>[8]</sup>

## CONCLUSION

When MSA presents with stridor and respiratory compromise, high index of clinical suspicion is necessary to make the diagnosis. Autonomic failure coupled with cerebellar or parkinsonian features support the diagnosis in this clinical situation. MRI findings can be highly suggestive of the diagnosis of MSA and can be used in conjunction with the clinical features. Early recognition is important for effective and often lifesaving management.

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