

Unilateral vocal cord adductor weakness: an atypical manifestation of motor neurone disease

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ABSTRACT

Background Bulbar involvement is a recognised feature of motor neuron disease/amyotrophic lateral sclerosis (MND/ALS), both as a presenting complaint and as a consequence of advancing disease. Hoarseness and dysphonia have been associated with vocal cord adductor weakness. This is usually bilateral and has also been reported as the presenting clinical feature in a handful of patients with superoxide dismutase 1 (SOD1) gene mutations. Presentation with an isolated, unilateral vocal cord adductor weakness, however, is atypical and rare. **Case** In this report, we detail the case of a 38-year-old woman with dysphonia and a family history of an SOD1 mutation. Neurological features remained confined to the territory of the left vagus nerve for the next 12 months, before a more rapid rate of disease dissemination and progression.

Conclusions This case highlights the importance of recognition of vocal cord palsy as an early manifestation of MND/ALS and the critical need for monitoring to recognise potential disease progression.

INTRODUCTION

Bulbar-onset motor neuron disease/amyotrophic lateral sclerosis (MND/ALS) usually presents with dysarthria and accounts for around 25% of all cases. Superoxide dismutase 1 (SOD1) gene mutations underlie up to 20% of familial cases of MND/ALS, usually beginning with limb symptoms.¹ However, an initial presentation with hoarseness or dysphonia caused by vocal cord dysfunction has been described in a handful of patients with MND/ALS related to various mutations of the SOD1 gene.²⁻⁵ When characterised, these patients have shown asymmetric or bilateral vocal cord abduction weakness. In this report, we describe an atypical, initial manifestation of MND/ALS in a young woman with an isolated, unilateral vocal cord adductor paresis associated with an SOD1 gene mutation.

CASE PRESENTATION

This 38-year-old woman had dysphonia for 1 year when she first attended our service. At onset, there had been a change in the quality

of her singing voice over the course of a week. Her voice was dysphonic but had preserved articulation. No infective symptoms were recalled. She had also been aware of intermittent facial twitching, mainly around her eyes during times of stress, or after drinking coffee. Soon after the onset of her dysphonia, she was examined by an ENT surgeon and a neurologist. Fiberoptic naso-endoscopy revealed an abducted left vocal cord with only flickers of movement. The rest of the neurological examination was normal. MRI of her brain and CT of the chest and neck looking for a structural cause were unremarkable.

There was a strong family history of MND/ALS with her father, paternal aunt and uncle all affected. Genetic testing in her father had demonstrated an SOD1 mutation (Val149Gly). Our patient had elected not to proceed with predictive gene testing.

Over the first 12 months, her dysphonia gradually worsened. She had difficulty with coughing and developed dysphagia to some solids, such as bread, with a feeling of food stuck in the pharynx. There were a few occasions of nasal regurgitation when trying to swallow. Although she described intermittent exertional breathlessness, spirometry showed a forced vital capacity (FVC) of 125% predicted. At this point, she sought genetic counselling and proceeded to genetic testing. Before the test results were known, the geneticist referred her to the MND service for assessment, due to concern over her symptoms.

Neurological examination at that time revealed severe dysphonia, with a nasal, breathy voice but no dysarthria. The cough was bovine and there was left palatal weakness. Occasional fasciculations were present in the periocular muscles. The rest of the neurological examination was normal. Repeat naso-endoscopy confirmed a failure of the soft palate to close completely on the left-hand side. The left vocal cord was now paralysed. A repeated MRI of the brain and cervical region



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showed no abnormalities. Over the subsequent month, the patient appeared to have an accelerated deterioration in her condition with increased dysphonia, more widespread facial fasciculations and the onset of fasciculations in her shoulder girdle. Examination confirmed this along with new weakness in the intrinsic muscles of her left hand and left-finger extensors. Evidence of upper motor neuron involvement was also present with brisk reflexes in the left arm. Electromyography demonstrated sparse fibrillation potentials and minor neurogenic changes in the arms and simple fasciculation potentials in the tongue. Nerve conduction was normal. Repeated respiratory function showed that her FVC was now 84% predicted, and maximal respiratory pressures were reduced. Genetic testing results confirmed the presence of an SOD1 mutation (Val149Gly). Serial neurological examination a month later showed further deterioration with mild wasting of the tongue along with fasciculations, increased wasting in the left hand and pathologically brisk reflexes of the left upper and lower limbs. Following discussion, the patient elected to explore non-invasive ventilation, percutaneous endoscopic gastrostomy and injection thyroplasty to assist with symptom management.

DISCUSSION

This patient's presentation is unique in our experience and is not fully replicated in previous case studies. The onset of symptoms of severe dysphonia but preserved articulation, in a patient with normal spirometry, is highly unusual for bulbar onset MND/ALS. Furthermore, the patient was shown to have unilateral vocal cord adductor weakness, different from published cases of laryngeal dysfunction in MND/ALS, even those with known SOD1 mutations. For a whole year, clinical findings were

confined to the territory of the left vagus nerve. Thereafter, the disease spread rapidly to multiple myotomes bilaterally, with the appearance also of upper motor neuron features.

Patterns of vocal cord dysfunction

Anatomically, the superior laryngeal nerve, a branch of the vagus nerve, innervates the cricothyroid muscle of the larynx. This muscle stretches, tenses and adducts the vocal cord. Innervation of all intrinsic muscles of the larynx aside from the cricothyroid is via the recurrent laryngeal nerve, including the posterior cricoarytenoid muscles, which are the sole vocal cord abductors.⁶ In our case, the subsequent development of palatal and pharyngeal weakness pointed to a more proximal lesion of the vagus nerve or nucleus ambiguus.

Vocal cord dysfunction in MND/ALS can manifest as hoarseness, dysphonia, a non-explosive cough, laryngospasm or stridor. Hoarseness was noted as the initial manifestation in 3.9% of 441 patients with MND/ALS seen by an otolaryngologist.⁷ While episodic laryngospasm is common in MND; reported in 19% on direct questioning, more sustained stridor is rare.^{8,9} In one study, bilateral vocal cord abductor paresis (VCAbdP) was found in 30% of patients with bulbar-onset MND.¹⁰ Van der Graaff reported four cases with bilateral VCAbdP presenting with episodes of laryngospasm in the setting of MND with established dysarthria and dysphagia or limb signs.¹¹ Laryngeal electromyography in one case showed tonic activity at rest in the laryngeal adductors and evidence of denervation in cricoarytenoid abductor muscles. Glottic narrowing through either paralysis of the abductors or overactivation of the adductors is, therefore, postulated to be the mechanism behind the laryngospasm/stridor observed. This is also the pattern of abnormality usually

Table 1 Patients presenting with hoarseness/dysphonia and their SOD1 gene status

Reference	Mutation/FH	Laryngoscopic findings	Disease presentation	Survival
Fukae <i>et al</i> ²	SOD1 (I 149 T)	Bilat VCAbdP Asymmetric	Hoarseness followed 10 months later by dysphagia/fasciculations	Not stated
Origone <i>et al</i> ⁴	SOD1 (Gly 147 Ser)	Bilat VCAbdP R then L cord after 3 weeks	Episodic dyspnoea and hoarseness, stridor	8 months
Tan <i>et al</i> ⁵	SOD1 (Asp 101 Tyr)	Bilat VCP unspecified	Hoarseness for 3 months, followed by dysphagia	11 months
Bigliardi <i>et al</i> ⁸	No FH	Bilat VCAbdP	6 month history of hoarseness. Admitted with dyspnoea and stridor, no dysarthria/dysphagia	Not stated
Levian and Gupta ¹⁴	No FH	Bilat VCAbdP	4 month history of hoarseness/dysphonia	Not stated
Hermann <i>et al</i> ³	SOD1 (I 113 F)	Bilat VCP unspecified laryngospasm	Hoarseness for 5 weeks and rapid involvement of other areas	15 months
Our case	SOD1 (Val 149 Gly)	Unilateral VCAdd P	Hoarseness/dysphonia	20 months

ALS, amyotrophic lateral sclerosis; FH, family history of MND/ALS; MND, motor neuron disease; SOD1, superoxide dismutase 1; VCAbdP, vocal cord abductor paresis or paralysis; VCAddP, vocal cord adductor paresis or paralysis; VCP, unspecified vocal cord paresis or paralysis.

observed in multiple system atrophy (MSA), a neurodegenerative condition much more strongly associated with stridor.¹² Pathologically, only the posterior cricoarytenoid muscles showed denervation atrophy in a postmortem study in MSA, while both abductor and adductor muscles of the larynx were affected in MND.¹³

SOD1 manifestations

We found six cases presenting with symptoms of dysphonia or hoarseness, preceding the development of other typical MND symptoms (table 1).^{2-5 8 14} Four of these cases were associated with SOD1 mutations.²⁻⁵ No gene testing or family history was noted in the other two cases. Typically, these patients developed dysphagia, 3–10 months after onset of symptoms, followed by or concurrent with other features of MND/ALS. Rapid disease progression was common. Of these six cases, four were shown to have bilateral VCAbdP/paralysis on otolaryngologic examination.^{2 4 8 14} The other two cases had unspecified bilateral vocal cord weakness.^{3 5} One, however, experienced episodes of laryngospasm suggesting overactivity rather than weakness of the adductor muscles.³ No cases in the literature had explicit weakness of vocal cord adduction, as in our patient.

Focal and asymmetric onset of weakness is characteristic of MND/ALS, yet the underlying disease process is usually already more disseminated at the time of first presentation. This case study illustrates how symptoms and signs become apparent as compensatory mechanisms within molecular or neuronal systems decompensate—sometimes appearing as abrupt changes in the tempo of the disease.¹⁵

CONCLUSION

Our case adds to phenotypic knowledge about SOD1 mutations, highlighting that early stability and unilateral laryngeal involvement do not exclude an underlying diagnosis of MND/ALS, particularly in patients at risk of familial disease. Recognition of potential symptoms of MND/ALS reduces the burden of diagnostic uncertainty and allows the patient and their family more time to consider their choices for management. Emerging novel disease-modifying therapies such as antisense oligonucleotides will also drive the need for early diagnosis and intervention.

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