Adductor laryngeal breathing dystonia in NBIA treated with botulinum toxin-A

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Abstract

We report a rare case of neurodegeneration with brain iron accumulation (NBIA) presented with episodic inspiratory stridor. A 10-year-old boy presented with 3-year history of gradually progressive spastic gait and generalized dystonia (involving all four limbs, neck, jaw, and speech). MRI brain showed "Eye of Tiger" sign. He recently developed severe inspiratory stridor associated with almost gasping respiration. Direct video laryngoscopy showed paradoxical vocal cord closure during inspiration. He was treated with EMG-guided botulinum toxin-A injection given into bilateral thyroarytenoid muscles, resulting in dramatic response with complete disappearance of the stridor within a week. The effect lasted 18 months.

Key Words

Adductor laryngeal breathing dystonia, botulinum toxin, stridor

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Introduction

NBIA is a rare neurodegenerative disorder, characterized by iron accumulation in the basal ganglia. It is an autosomal recessive disorder, associated with pantothenate-kinase 2 (PANK-2) gene mutation.[1] Classical presentation is in first decade with rapidly progressive extrapyramidal syndrome with dementia, retinal pigmentary degeneration, and optic atrophy. MRI brain typically shows the 'Eye of Tiger' sign on T2-weighted images. Clinical correlation of 'Eye of Tiger' sign on imaging and PKAN-2 mutation is very high.[2]

Adductor laryngeal breathing dystonia (ALBD) is a rare dystonia, which manifest as adduction of vocal cords during inspiration (normally vocal cords abduct during inspiration). ALBD has to be differentiated from spasmodic adductor dysphonia, in which adductor dystonia is task-specific, i.e. only during speaking and not during breathing (as in ALBD).[3] In literature, only a few case reports of ALBD has been described. ALBD has been reported in multiple system atrophy,[4] progressive supranuclear palsy,[5] cerebral palsy,[6] and Lubag syndrome.[7] It has not been described in NBIA.

Botulinum toxin is commonly used to treat various dystonias, including ALBD.[3] However, this is the first case report to demonstrate the role of botulinum toxin-A in successful treatment of ALBD in NBIA, hence avoiding tracheostomy.

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Case Report

This 10-year-old boy, product of non-consanguineous marriage, with normal birth history and milestones, presented at 7 years of age with stiff legs with scissoring of lower limbs and frequent falls while walking. Over next 2 years, he had abnormal episodic posturing in form of flexion at elbows, hyperextension of neck, lower limbs, and sometimes trunk. He had severe jaw-opening dystonia and anarthia for last 6 months. For last 3 months, he had episodes of severe inspiratory stridor lasting 1-3 minutes, which was absent during sleep. He was almost gasping during these episodes, with corresponding fall in SPO_2 of as low as 65% (noted at the time of admission to this hospital), that would relieve temporarily after a deep breath at the end of long inspiratory stridor. There was no past history of preceding febrile illness, jaundice, drug or toxic exposure, or positive family history.

On examination, vitals were stable, except tachycardia. During inspiratory stridor, his SPO_2 was very low. He had severe generalized dystonia involving flexion at elbows, wrist, and

all interphalangeal joints, hyperextension of knee, dorsiflexon of ankle, hyperextension of neck, severe jaw-opening dystonia, and inspiratory stridor (ALBD) every 2-5 minutes. Frequency and severity was more during activity. His Barke-Fahn Marsden (BFM) dystonia severity score was 96 / 120. He was conscious and was fully oriented and following verbal commands. His all limbs were spastic with exaggerated reflexes with extensor planters. Ophthalmological examination excluded retinitis pigmentosa and Kayser-Fleischer ring. His other routine biochemical tests including liver function test, serum ceruloplasmin, serum copper, and 24-hour urinary copper were normal. No acanthocytes were seen in peripheral blood smear examination. T^2W images of brain showed hypointense bilateral globus pallidi with central hyperintensity, suggestive of typical 'Eye of Tiger' sign [Figure 1]. Videolaryngo-scopy showed paradoxical closure of vocal cords during inspiratory phase, suggestive of ALBD.

Patient was planned for botulinum toxin-A therapy treatment for ALBD. Pre-procedural preparation included pre-anesthetic evaluation for general anesthesia (in case required to intubate this patient, if would develop severe vocal cord spasm during procedure), availability of anesthetist with preparation for intubation, and ventilatory support. In awake state, bilateral thyroarytenoid muscles were injected with 3 IU of botulinum toxin (Botox, Allergan) on each side, under electromyography guidance using Myoject needle (Teva, USA). Effect of botulinum toxin started within hours, with complete disappearance of stridor in next 7 days. The effect of this injection lasted for next 18 months, and he needed another injection recently. There was no adverse effect during or following botulinum toxin injection. Two months after botulinum toxin injection, he underwent bilateral GPi deep brain stimulation surgery, and at 6 months follow-up, his BFM score had improved to 54/120 (improvement of 56%), but gradually his improvement has reduced at 18 months follow-up.

Discussion

The presented case of NBIA had life-threatening severe inspiratory stridor, suggestive of ALBD. He was successfully managed by injection botulinum toxin therapy. ALBD has not been reported in NBIA in literature. In our series of 16 patients with NBIA,[8] none of the patient had respiratory stridor, though 14 patients had speech dystonia. In another case series of 13 patients from India,[9] dysarthria was reported in all, but none had ALBD.

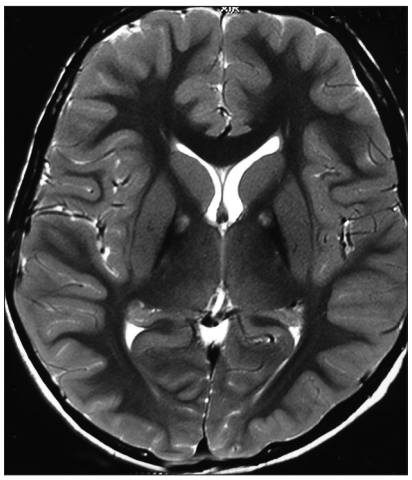

Figure 1: T2W MRI brain showing classical "Eye of Tiger sign"

ALBD was first described by Blitzer and Brin.[3] Most patients have no oxygen desaturation despite significant stridor, whereas our case had severe desaturation. Worley G *et al*.[6] described laryngeal dystonia causing inspiratory stridor in 3 cases of cerebral palsy. They presented with generalized dystonia with episodic inspiratory stridor. One of the 3 patient was given botulinum toxin injection in vocalis muscle to avoid tracheostomy. Grillone GA *et al*.[3] reported successful use of botulinum toxin in 7 patients with ALBD. All patients were injected in bilateral thyroarytenoid injections, and effect started in 72 hours (reaching maximal effect within 2 weeks) with sustained improvement for an average of 13.8 weeks. Adverse effects included breathy voice and mild choking on liquids, which resolved within 2 weeks. In another series of 9 patients of ALBD, 7 were idiopathic and 2 were secondary to phenothiazine use.[3] Patients have undergone tracheostomy for ALBD when not treated with botulinum toxin.

In conclusion, ALBD as a presentation of NBIA is rare, which could be life-threatening. Since ALBD during inspiration leads to severe respiratory distress and can be fatal, early recognition of the condition and treatment may be life-saving for the patient. Prompt intervention in the form of botulinum toxin injection can avoid tracheostomy and save patient from longstanding morbidity and mortality.

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