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Case Report

A rare case of dysphonia in mitochondrial myopathy

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ABSTRACT

The mitochondrial myopathy consists of diverse group of disorders which is characterized by primary dysfunction of mitochondrial respiratory chain leading to muscle disease. The involvement of larynx is very rare and only few cases have been reported in the literature. This study presents the fourth published case of dysphonia in the setting of mitochondrial myopathy. A patient with dysphonia with laryngeal involvement in mitochondrial myopathy is presented with literature review. A 43 year old man presented with progressive dysphonia and muscle weakness. Laryngeal examination showed bilateral adductor weakness of vocal cords and biopsy revealed findings typical of mitochondrial myopathy (MM). He underwent conservative trial for dysphonia with no relief and subsequently medalization thyroplasty showed some improvement in dysphonia. Mitochondrial myopathy should be considered in the differential diagnosis of dysphonia for early diagnosis and management.

Keywords: Dysphonia, Mitochondrial myopathy, Diagnosis, Treatment

INTRODUCTION

Mitochondrial myopathy includes spectrum of disorders which is characterized by primary dysfunction of mitochondrial respiratory chain leading to muscle disease. The incidence of this disease is 1:4000 and is the most common form of inherited metabolic disorders.[1,2] In 1966, Engel et al first reported this disease, following which several cases were reported having similar findings on histochemical and electron microscopic studies.[3] As mitochondria are the main centre of energy production in mammalian cells, clinical features mainly involve tissues requiring highest energy. The disease can involve multiple organ system and the most commonly affected organ systems are the nervous system, cardiac, endocrine, and muscles. It has varied clinical presentation with regard to age at onset, signs, symptom progression of disease and prognosis. Patient may present with wide spectrum of symptoms due to varied genetic penetrance and may range from fibromyalgia, skeletal muscle weakness, extraoccular muscle weakness, pain, fatigue, multiorgan failure which progressively worsens with time.[1,4] So clinician should consider the diagnosis of MM when myopathy is accompanied by clinical feature of multi organ dysfunction. The normal and intact neuromuscular function of larynx enables us to provide a good voice, assist in respiration and protection of airway from aspiration. Dysphonia results from impairment of neuromuscular function of larynx and can be a presenting feature of various diseases involving multiorgan system. The involvement of larynx in Mitochondrial myopathy is rare and only three case reports have been mentioned in literature so far, to the best of my knowledge.[5,6]

We hereby present a rare case of dysphonia due to mitochondrial myopathy.

CASE REPORT

A 43 year old man presented to tertiary ENT centre in south India with complaints of progressive dysphonia from last 8 years. It was breathy in nature and affecting his daily life activities. He didn't have stridor or breathing difficulty. He also had occasional dysphagia to both solid and liquid along with nasal regurgitation of food. He was managing from last eight years with the condition but now because of increased occupational demand and unclear speech he was concerned for his voice. Family history was negative. He also complained of generalized fatigue. Clinically he had mild ptosis, Rt side body weakness, Slow rate of movement of tongue, lip, slight deviation of angle of mouth, respiration for speech and phonation was inadequate. On videolaryngoscopy and stroboscopy bilateral adductor palsy was seen with phonatory gap. Voice evaluation showed hoarse and breathy voice with hypernasal component. The loudness was reduced and it was fatigable, with voice breaks.

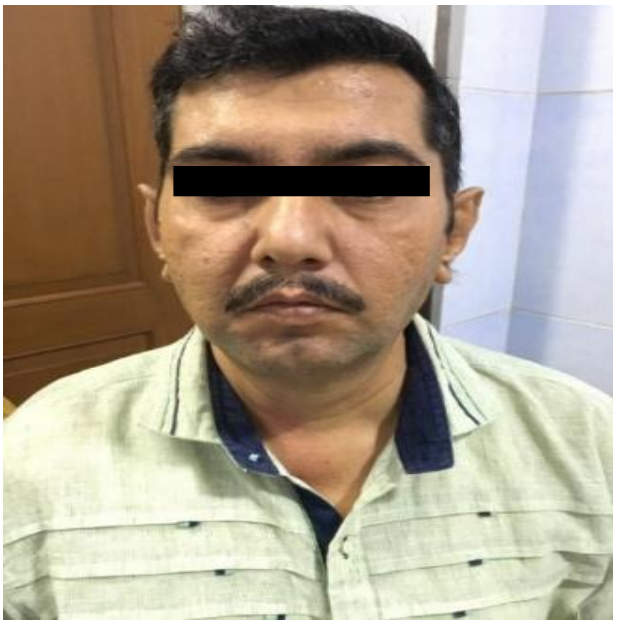

Figure 1: Ptosis present left side more than right.

Vocal Pitch was inadequate and vocal range was less. GRBAS score was 12. He had seen neurologist in the past and was diagnosed to have reduced muscular responses of orbicularis occuli and peripheral limb muscle on EMG. His cardiac state was normal including echocardiogram. Heamatological, biochemical levels and imaging brain were normal. Biopsy was done from left biceps muscle and light microscopic examination showed myopathic features, variation in fibre size, necrosis, phagocytosis, and regenerating fibres. Modified Gomori stain showed ragged red fibres more than 30% which suggest subsarcolemmal accumulation of mitochondria; NADH/SDH stain showed ragged blue fibres more than 30%, Cox/ SDH stain- showed several COX deficient fibres (40-50%). The above findings were typical of mitochondrial myopathy (MM). The patient had already undergone speech therapy with not much improvement in his voice. He was taken up for augmentation laryngoplasty and medialization thyroplasty was done. He was counselled regarding results as not very good responses have been seen due to reduced breath support. In postop his glottal closure improved and breathy voice also showed some improvement. His GRBAS score improved from 12 to 9. He was continued on speech therapy and supplemental medicines. Presently he is stable and managing his occupation better.

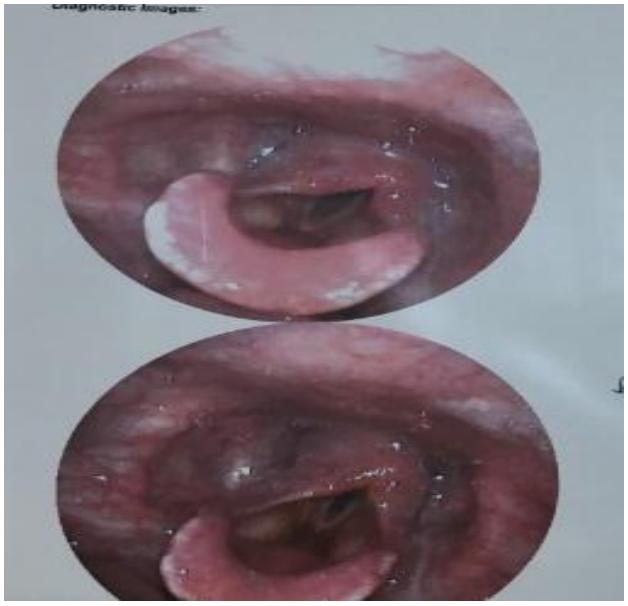

Figure 2: Bilateral adductor weakness of vocal cords.

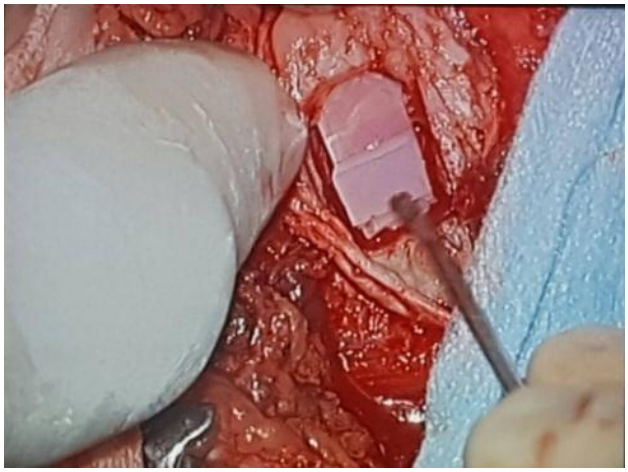

Figure 3: Medialisation thyroplasty.

DISCUSSION

The worldwide prevalence of mitochondrial myopathies (MM) was estimated to be 0.025%, however because of difficulty in diagnosis of disease due to varied clinical and genetic heterogeneity the accurate frequency is difficult to estimate.[7] Mitochondria (mt) are the

intracellular organelles having their own DNA and make their own RNA and protein. Mitochondrial myopathy (MM) can result from mutation, deletion of DNA affecting protein synthesis. The transmission of mt DNA mutation is complex and not very well understood; mutation is passed forward at a level of heteroplasmy which is quite variable.[8] The disease has highly variable clinical presentation, onset, severity and prognosis. Generally the severe form present early in life (Pearson syndrome) and Keams sayre syndrome (milder variety) presenting in early childhood or adolescence. Progressive external ophthalmoplegia is a milder variety of syndrome presenting in childhood upto late adulthood.[9] Though clinical features is quite variable including slowly progressive muscle weakness to multisystem organ failure to severe respiratory insufficiency requiring ventilator support.[10] Dysphagia is common but laryngeal involvement is quite rare, with mention of only three cases in literature.

The diagnosis is mainly by muscle biopsy and genetic testing with features of active or inactive myopathy on electromyography.[1]

On light microscopy characteristic features are seen including deletion of ragged red fibres on modified trichrome Gomori stain and ragged blue fibres on SDH stain. The demonstration of COX deficient and SDH positive muscle fibres is quite sensitive and specific for diagnosis of mitochondrial myopathy as seen in our case.[11,12]

The photoghaphs of the histopathology slides were not available as the biopsy was done at a different ENT centre in another city. Since it was an invasive procedure patient didn't give consent for a repeat biopsy. Genentic testing was not done because patient was not willing to undergo testing.

Once the diagnosis is confirmed the treatment aims to reduce morbidity and improve quality of life. There is no disease modifying medical therapy available for mitochondrial myopathy and several agents (nutritional supplements) have been tried without much efficacy in the end point of the disease.

Laryngeal involvement is quite rare and no standard treatment regime has been established for these patients. Speech therapy, vocal fold augmentation by injection or medialization thyroplasty has been mentioned. They only alter the glottis closure in a static manner leading to some improvement in voice strength but not necessarily improve the glottis closing force or dynamic alterations.[13]

The vocal fold augmentation done in our patient improved the glottis closure and not the tone or respiratory support for voice leading to limited improvement in voice. Our results are similar to Kelly et al who augmented vocal cords with injection laryngoplasty.[6] The first case of laryngeal involvement in MM was described by Hartley et al, where patient had dysphonia, cough n poor glottis closure, he was given speech therapy.[5] Kelly et al described the second case who had similar presentation to our case with progressive dysphonia, dysphagia and positive family history.[6] Ramakrishnan et al described the third case and probably the first case from india where patient had vocal cord involvement along with chronic progressive external opthalmoplegia.[14]

Our patient was also given the option of electrolarynx but he was not happy with the idea and preferred surgical intervention. Speech therapy improves the breath support and may prove beneficial in the long run and it supplements vocal fold augmentation procedure in mitochondrial myopathy patients.

CONCLUSION

Mitochondrial myopathy with laryngeal involvement is a rare entity and should be kept in mind in differential diagnosis of patients with early onset atrophy of vocal cords and breathy dysphonia. Awareness of atypical presentation, characteristic light microscopy features, limited improvement in voice by surgical corrections help in avoidance of unnecessary surgery, grounded expectations and to promote us for further research. We report the fourth known case of mitochondrial myopathy with vocal cord involvement and second case in India.

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