Silent microaspirations: The forerunner to the diagnosis of bulbar onset myasthenia gravis in a young woman

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SUMMARY

Recurrent pneumonia warrants a diligent work-up to identify the underlying cause that perpetuates the disease process. Insidious bulbar dysfunction is arguably the most devastating as it would be diagnosed late after significant pulmonary complications due to chronic micro-aspiration. Bulbar disorder should be considered as the potential aetiology of recurrent pulmonary infections in the young population after excluding immunodeficiency disorder and respiratory anatomical anomaly. This report illustrates a rare case of bulbar onset myasthenia gravis which manifested as focal bronchiolectasis due to recurrent undiagnosed aspiration pneumonia three years earlier. Absence of hallmark features of Myasthenia Gravis (MG) such as ptosis, opthalmoplegia and proximal muscle weakness contributed to the diagnostic delay and challenges in this case. The diagnosis was established with the collaboration of multidisciplinary teams. Subsequent correct therapeutic interventions resulted in remarkable recovery in functional status and prevented her from further aspiration in the long run.

INTRODUCTION

Myasthenia gravis (MG) is the commonest neuromuscular junction disorder, caused by an autoimmune antibodies against the acetylcholine receptor (AChR), which causes a compromise in the end-plate potential with resultant ineffective synaptic transmission. Among early onset AChR positive MG, selective involvement of bulbar muscle weakness with chronic aspiration as the initial presenting symptoms in the absence of ocular or facial involvement represent a rare manifestation of MG.[1,2]

CASE REPORT

A 25-year-old woman presented with recurrent lungs infection requiring intubation and mechanical ventilation since three years ago. There was no difficulty in weaning from mechanical ventilation in each admission. With anti-microbial therapy, she managed to recover and discharged home well. Investigations aimed at excluding connective tissue disease, primary as well as secondary immunodeficiency all showed normal study. Serum creatinine kinase level was normal. Due to the frequent hospitalisations, she lost 18 kilograms with body weight of 35 kg (BMI 14.1 kg/m^2). Otherwise, family history did not suggest any heritable immunological or neurological disorders.

After three years, she was referred to the respiratory physician for recurrent unexplained lungs infection. During consultation, we detected the presence of hyponasal speech. Of most concern, her High Resolution Computed Tomography (HRCT) thorax identified centrilobular ground glass opacity nodules and tree-in-bud pattern with multifocal areas of lungs fibrosis suggestive of chronic micro-aspirations (Figure 1 & 2). In addition, soft tissue density measuring 1.1cm x 5.2cm x 6.3cm, which was likely to be thymic hyperplasia was noted at anterior mediastinum.

Subsequently, Fiberoptic Endoscopic Evaluation of Swallowing (FEES) confirmed the presence of aspiration. Nasogastric tube feeding was commenced and she was referred to neurology team for opinion. Further history revealed that she had episodes of transient voice deepening with intermittent coughing during meals prior to each hospitalisation. There was no obvious precipitating events prior to each admission. During neurology consult, we detected presence of bifacial lower motor neuron weakness, hyponasal speech and bilateral temporalis muscle wasting. Tongue muscle bulk was preserved, but the gag reflexes were sluggish. There was no fasciculation seen. Neck flexion and extension power was graded MRC scale 5/5. No signs of opthalmoplegia, ptosis, proximal myopathy and fatigability was present. However, her limbs reflexes were reduced.

Nerve conduction study (NCS) and electromyogram (EMG) conducted subsequently were normal. Repetitive nerve stimulating test was inconclusive as the patient was unable to tolerate pain during needle stimulation. Overall, there was no evidence of neuropathy and myopathy. The diagnosis of MG was established based on clinical ground and autoantibody profiles in which the serum acetylcholine receptor antibody was 8.4nmol/L (positive is more than 0.5nmol/L).

Treatment paralleled to conventional management of MG was started in which she received pyridostigmine 60mg bd, prednisolone 20 mg OD and azathioprine 50 mg OD. Remarkable improvement in bulbar and facial muscles strength was observed after one week of MG therapy. She was

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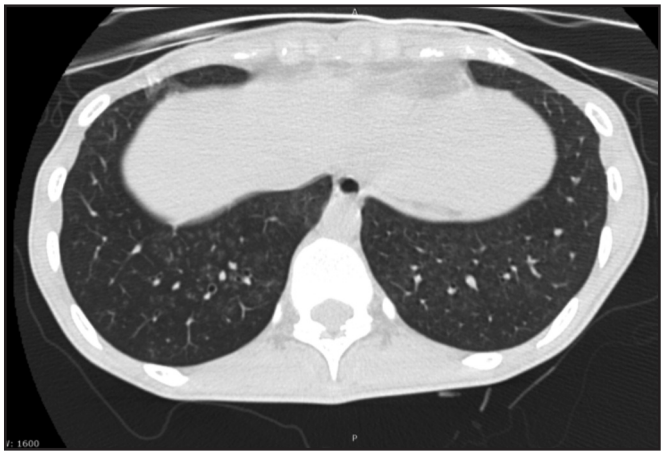

Fig. 1: Axial HRCT thorax demonstrating areas of ground-glass opacity nodules in right lower lobe.

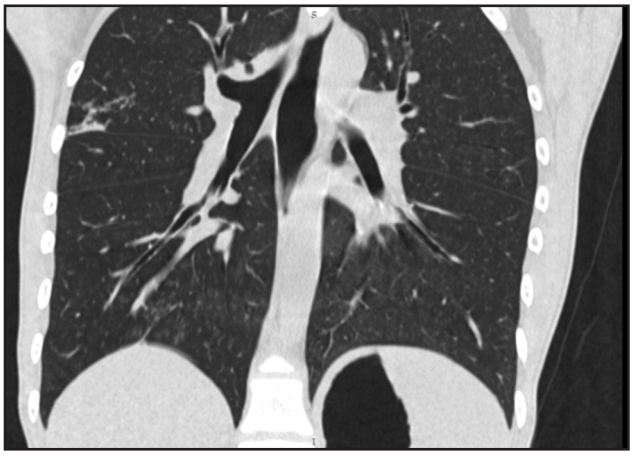

Fig. 2: Coronal HRCT thorax illustrating lung fibrosis and bronchiolectasis in right upper and right lower lobes.

successfully transitioned from nasogastric feeding back to normal oral feeding at the fifth month of MG therapy. Follow up FEES and barium swallow test showed normal study. Prednisolone was tapered off after seven months of MG treatment. Most importantly, she did not develop further lungs infection and had gained 13 kg with BMI 19.7 kg/m^2. At the time of reporting, she remained in remission while being on tab azathioprine 75mg OD (1.56 mg/kg) and tab pyridostigmine 90 mg tds for more than one year.

DISCUSSION

In young immunocompetent adults with unexplained recurrent pneumonia, considerations should be given to possible occult microaspiration secondary to swallowing aberrations.[3] Microaspiration is defined as inhalation of oropharyngeal or gastric contents into the larynx and lower respiratory tract, especially when the volume of aspirate is small and therefore subjects normally are not aware of it. Subtle bulbar dysfunction frequently masquerades as silent micro-aspirations, punctuated with aspiration pneumonia as illustrated in our case in which the underlying aetiology was discovered only 3 years later.[4]

Vicious cycle of aspiration has deleterious effects on the lungs which may be complicated with bronchiectasis due to chronic aspiration pneumonitis and pneumonia. HRCT thorax evidence of chronic pulmonary microaspirations such as centrilobular nodules, ground-glass opacities and bronchiolectasis with a predilection for the lower lobes, which were present in our patient are important as it compels the clinician to search for the aspiration aetiology to prevent further damage to the lungs.[5] When bronchiectasis develops, it has the potential to develop into life-long pulmonary disease with considerable disability.[6] Therefore, it is imperative to intervene as early as possible to halt the aspiration.

Bulbar onset MG, which was more commonly described in late onset MG (onset of disease after the age of 50 years) with detectable anti-muscle specific kinase antibody is rare in the young populations.[1,2,7] Additionally, hallmark features of MG such as ptosis, opthalmoplegia, limbs fatigability and proximal muscle weaknesses which commonly preceded the occurrence bulbar weakness were absent in our case. Llabres et al has reported a case series of three young MG patients with similar dysphagia manifestation and the interval of symptom onset to diagnosis ranged from four to 24 months.[8] A detailed history, neurological examination and multi-disciplinary collaborations remained as the cornerstone to the diagnosis in this challenging case. Despite the atypical manifestation of MG, she demonstrated favourable response to first line MG treatment and neither dysphagia nor symptoms attributable to MG recur in the last one year.

Keeping in mind that pneumonia could be associated with neurological disorder, clinicians should be familiar with bulbar onset neurological disorder and able to posit them during clinical evaluation.[9] Pharyngeal-cervical-brachial variant of Guillain-Barre syndrome (GBS) could present in similar manner with predominant bulbar muscle weakness and reduced limb reflexes.[10] Yet, in contradistinction to MG, the former disease is a monophasic disease which normally reaches the peak in the fourth week and recurrence is rare. Also, this was excluded by EMG and NCS test as there was no evidence of demyelinating process. Recovery of limb reflexes and improvement of temporalis muscle bulk after gaining weight further distinguish MG from GBS.

Lastly, young stroke or brainstem infarct should also be considered. However, this was negated by the absence of other brainstem stroke symptomatology such as crossed signs, ocular signs and corticospinal tract involvement. Other less likely aetiology such as motor neuron disease and muscular dystrophy were excluded by the clinical history, physical examination and neurophysiological studies.

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DECLARATION

Declaration of interest: None

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