

## Delay and misdiagnosis in adult myasthenia gravis: A case report

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### Introduction

Myasthenia gravis (MG) is a rare autoimmune disorder characterised by fluctuating and variable combination of muscle weakness and fatigue. Most cases are due to T-cell mediated autoantibodies against post-synaptic acetylcholine receptors (AChR-Ab), thus preventing acetylcholine from binding and signalling skeletal muscle to contract.<sup>1</sup>

The annual incidence is 7-23 new cases per million.<sup>1</sup> It can occur at any age but with two peaks; an early-onset (20-40 years) female-predominant and a late-onset (60-80 years) male-predominant peak. MG is classified into ocular and generalised (80%). More than half the patients initially present with ptosis and diplopia but half will progress to generalised disease with involvement of bulbar, limb and respiratory weakness. Those presenting as generalised MG can also develop eye signs later.<sup>1</sup>

It is important to recognise MG early because it is highly treatable. Untreated disease leads to permanent weakness.<sup>2</sup> Treatment reduces mortality from life-threatening myasthenic crisis.<sup>1,3</sup> Misdiagnosis leads to potentially harmful interventions and inappropriate management.<sup>4,5</sup> Diagnosis in late-onset MG is easily missed<sup>2,3,4,5</sup> because of overlapping symptoms with other diseases common in the elderly. We report a case of delay and misdiagnosis in an elderly patient with co-morbidities.

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### Case Report

A 68-year-old Chinese housewife first presented a year ago to primary care with intermittent "shifting" ptosis but no diplopia or diurnal variation. Her history is significant for asthma and mixed anxiety-depression (25 years) and Type 2 diabetes mellitus, hypertension

and dyslipidaemia (10 years). MG was strongly suspected and she was referred to a specialist. But during the 3-month appointment time, ptosis had completely disappeared. She instead developed neck and shoulder pain and weakness. She was diagnosed with cervical spondylosis based on radiographic changes.

Meanwhile she developed intermittent left-sided facial numbness, pain and drooling of saliva, which were attributed to diabetic cranial neuropathy. She described an episode of acute dyspnoea associated with head drooping while gardening. She thought it was due to the heat, excessive exertion and asthma exacerbation. The dyspnoea was not relieved by inhaled salbutamol and only subsided on resting. She had to support her head with both hands when watching movies and noticed breathlessness on walking short distances.

A month before diagnosis, she experienced intermittent difficulty in swallowing solids and sometimes choked when drinking fluids. By then, ptosis had become permanent. Diagnosis was finally confirmed after a year with positive acetylcholine receptor antibody (AChR-Ab).

On hindsight there were two previous MG-like events. Five years ago, she complained of breathlessness and persistently recorded low peak flow readings but without features of asthmatic exacerbation or poor control. Readings did not improve with inhaled salbutamol. This incongruence led to urgent respiratory referral. At a specialist clinic, her peak flow normalised and anxiety was thought to be the cause.

Three years ago, she developed postural vertigo mimicking benign paroxysmal positional vertigo but Dix-Hallpike manoeuvre was negative and there was no history of infection suggesting vestibular neuritis. In view of her age and chronic diseases, vertebrobasilar ischaemia was considered. Vertigo did not improve with betahistine but disappeared spontaneously within a month.

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## Discussion

Diagnosis is difficult, often delayed and easily missed by general practitioners and specialists,<sup>2,3,4,5</sup> more so if associated with pre-existing psychiatric disorders.<sup>6</sup> Mean time to diagnosis is more than a year with 54-69% diagnosed within a year.<sup>2</sup> Presentation and progression of disease is heterogeneous, with months of symptom-free remission interpolated with muscle weakness elsewhere, thus misleading less experienced doctors.

Late-onset MG has been underdiagnosed<sup>2,3</sup> and sometimes misdiagnosed<sup>3,4,5</sup> in the elderly because of the broad differential diagnoses from comorbidities in this age group. MG has been mistaken for hysteria, stroke, motor neurone and Parkinson's disease in the elderly.<sup>3,4,5</sup> The differential diagnoses of oculobulbar syndrome with limb girdle weakness ranges from neuromuscular junctional disorder to myopathy, radiculopathy, central nervous system and psychiatric disorders.<sup>4</sup> Overlapping symptoms from comorbidities have led to no treatment,<sup>2,3,4,5</sup> inappropriate investigations (26%)<sup>3</sup> and sometimes harmful interventions.<sup>4,5</sup> Neurologists are better at diagnosis of MG,<sup>2</sup> but they have also been deceived by negative clinical, electrophysiological findings and incidental false positive imaging findings.<sup>5</sup>

Our patient had somewhat atypical disease presentation and overlapping symptoms of aging and comorbidities which caused delay and misdiagnosis. Her ptosis was not worse in the evenings and disappeared for months. Ptosis due to stretching of the levator aponeurosis<sup>3</sup> is seen in the elderly. She had dysphagia but denied dysphonia.<sup>1</sup> If previous MG-like events are considered, onset of MG beginning with respiratory muscles is rare.<sup>1</sup>

MG should be painless but have been reported otherwise.<sup>1,3</sup> Patient's neck and shoulder pain and weakness could be due to co-existing cervical spondylosis. Spondylitic radiographic changes can be present in the elderly without symptoms of radiculopathy. Her neck pain is probably due to the overexertion of posterior

neck muscles to keep the head erect.<sup>1</sup> Facial pain can be due to over-mastication with weakened muscles, and saliva drooling to weakened lower jaw muscles rather than 5<sup>th</sup> and 7<sup>th</sup> diabetic cranial neuropathy. Facial and upper limb weakness and effort dyspnoea could be due to cerebrovascular and cardiovascular complications of longstanding diabetes, hypertension and dyslipidaemia. Dyspnoea can be attributed to pre-existing asthma and mixed anxiety-depressive illness<sup>6</sup> which like MG, are intermittent and precipitated by emotions.

There is a high prevalence of mental disorders, mainly anxiety and depression with MG; either primary (pre-existing) or secondary to the disabling, life-threatening, unpredictable progression of MG.<sup>6</sup> Fatigue and breathlessness are common symptoms in both diseases. MG has been misdiagnosed as psychiatric disorders.<sup>4</sup> Conversely diagnosis of depression in MG patients has been missed as Asians present with somatic symptoms rather than mood changes for affective disorders.<sup>6</sup> Undiagnosed psychopathologies exacerbate and interfere with optimal MG management.<sup>6</sup>

Could our patient be diagnosed a year earlier? It is possible if the doctor in the specialist clinic is aware of the fluctuating nature of MG and ordered AChR-Ab test. But this gold-standard test is expensive and relatively inaccessible. It is positive in 80-96% of generalised MG but only up to 50% in pure ocular disease.<sup>2</sup>

## Conclusion

Diagnosis in late-onset MG can be delayed or misdiagnosed due to MG's fluctuating nature, non-classical presentation, concomitant comorbidities and overlapping symptoms in the elderly. Better physician awareness of disease heterogeneity and cheaper specific tests might hasten diagnosis.

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