

## Myasthenia Gravis Mimicking Third Cranial Nerve Palsy: A Case Report

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### Introduction

Myasthenia gravis is an autoimmune condition of neuromuscular junctions. Two specific antibodies directed against post-synaptic nicotinic acetylcholine receptor and anti-muscle-specific tyrosine kinase antibody at the neuromuscular junction causes signal transmission impairment.

### Abstract

**Background:** The most common pituitary adenoma presentation is a visual field defect and inappropriate pituitary hormone secretion. The compression of the optic chiasm causes visual impairment. Large pituitary adenomas can rarely cause diplopia and ptosis secondary to adenoma's lateral extension into the cavernous sinus. Myasthenia gravis is an autoimmune disorder involving neuromuscular junctions. It is characterised by skeletal muscle fatigability, commonly involving extraocular muscles, face and limbs. It is estimated that 75% of myasthenia gravis patients present with ptosis and diplopia. The association of myasthenia gravis with pituitary adenoma is very rare. **Case Description:** A 30-year-old lady presented with headache, diplopia and ptosis of the left eye for 2 months. She was diagnosed with acromegaly secondary to pituitary adenoma. Ptosis is a rare presenting feature in pituitary adenoma. Her case was discussed in a multidisciplinary meeting, and the consensus was that her ptosis is likely secondary to pituitary adenoma, which was involving the left cavernous sinus. She underwent transsphenoidal resection of pituitary macroadenoma. Three weeks post-surgery, she developed bilateral ptosis, dysarthria and dysphonia, which was diagnosed as myasthenia gravis. **Clinical Implications:** Ptosis is a rare manifestation of pituitary adenoma. Nonetheless, pituitary tumour patients presenting with ptosis should be evaluated for the neuromuscular disorder. A high index of suspicion is required for early diagnosis and prompt treatment of myasthenia gravis.

**Key words:** Myasthenia gravis, pituitary adenoma, third cranial nerve palsy.

The hallmark of myasthenia gravis is off and on fatigability of skeletal muscles, including extraocular, face, limbs and thoracic muscles, which worsen with muscle activity. Double vision and ptosis are the presenting complaints in almost 75% of patients,<sup>[1,2]</sup> and these are mostly unilateral and asymmetrical.<sup>[3]</sup>

Pituitary adenoma comprises 15–20% of all primary intracranial tumours.<sup>[4,5]</sup> Somatotroph adenomas are growth hormone-producing pituitary adenomas, resulting in gigantism in younger patients and acromegaly in adults. Neuro-ophthalmological manifestations present in 10% of pituitary adenoma cases due to close anatomical proximity of the pituitary gland, optic chiasm and the cranial nerves in the cavernous sinus.<sup>[6]</sup> The classic ophthalmologic presentation is visual field defects, with bitemporal hemianopia being most commonly reported.<sup>[7]</sup> Oculomotor (3<sup>rd</sup>) nerve palsy is a rare but possible presentation of pituitary adenoma due to its lateral extension into the cavernous sinus.<sup>[8,9]</sup>

The presence of both pituitary adenoma and myasthenia gravis in a patient at the same time is rare. There are only a handful of case reports describing growth hormone-secreting pituitary adenoma and myasthenia gravis presenting simultaneously in a patient.<sup>[10,11]</sup> This study was exempted from taking informed consent by the local Institutional Review Board.

### Case Description

A 30-year-old lady presented with 2 months history of headache, diplopia and ptosis of the left eye. Her periods were regular, with no history of spontaneous galactorrhoea. She had no significant medical history. She had four children, and the youngest child was 2 years old. All pregnancies were uneventful.

The clinical findings demonstrated prominent supraorbital ridges, macroglossia, prognathism and partial ptosis on the left side. Both of the pupils were equal in size and reactive to light. Her visual fields could not be clinically assessed due to the presence of ptosis.

She underwent radiological and laboratory investigations, including magnetic resonance imaging (MRI) pituitary, insulin-like growth factor-1 (IGF-1), prolactin, FSH, LH, morning cortisol (9 am cortisol), TSH, free T4 and fasting glucose.

The MRI pituitary showed a pituitary mass measuring around 23 mm × 14 mm × 24 mm, causing the displacement of the pituitary stalk and partially extending into the parasellar region encircling the left internal carotid artery and compressing the left cavernous sinus [Figure 1]. There was no optic chiasm compression or hydrocephalus.

Her laboratory tests revealed markedly raised IGF-1 of 1073 ng/mL (normal range: 71–234 ng/mL) and marginally elevated prolactin of 35.1 ng/ml (normal range: 1.90–25 ng/mL). Other pituitary hormones were within normal ranges.

Her case was discussed in a multidisciplinary tumour board (MDT) meeting comprising endocrinologists, neuroradiologists, pathologists, clinical radiation-oncologists and neurosurgeons. The consensus was that the patient had acromegaly, and her unilateral ptosis was secondary to compression of the left oculomotor nerve by the pituitary adenoma.

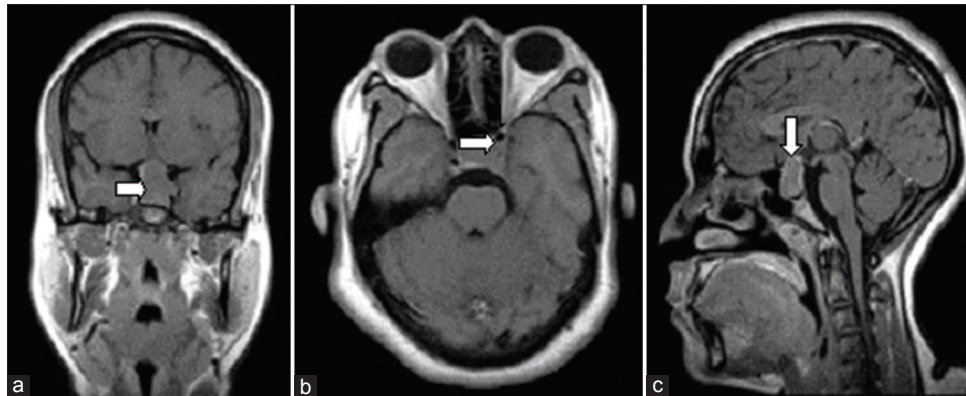
She underwent transsphenoidal resection of pituitary adenoma. The perioperative period was uneventful. The histopathology of the excised tissue was consistent with growth hormone-secreting pituitary adenoma.

Three weeks after surgery, she developed complete bilateral ptosis. In addition, she had difficulty in eating, dysarthria and dysphonia. Her neurological examination revealed muscle fatigability. Her anti-acetylcholine receptor antibodies were positive.

### Diagnosis and management

Based on the dramatic development of bilateral ptosis post-surgically, along with symptoms of difficulty in eating, dysarthria and dysphonia, clinical signs of muscle fatigability and positive anti-acetylcholine receptor antibodies test, a diagnosis of myasthenia gravis was made.

The patient was started on prednisolone 20 mg daily and pyridostigmine 90 mg daily (in divided doses) and had an excellent clinical response. The patient remained well on the treatment, except



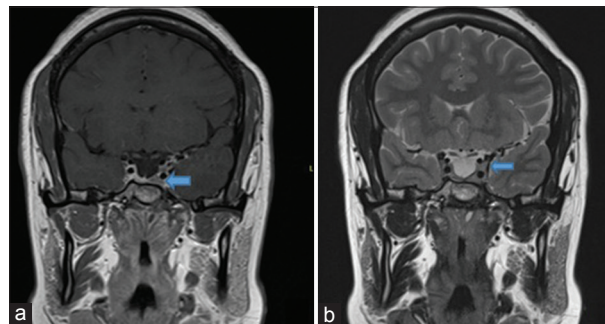
**Figure 1:** Post-contrast coronal (a), axial (b) and sagittal (c) images of magnetic resonance imaging (MRI) pituitary show heterogeneously enhancing pituitary macroadenoma encasing the left internal carotid artery and causing mass effect on the cavernous sinus (white arrows)

for weight gain, which was likely secondary to the corticosteroids. At her 6 months follow-up in the endocrine clinic post-surgery, her IGF-1 levels were 552 ng/mL (normal range: 71-234 ng/mL). The post-operative MRI pituitary showed a residual pituitary mass of 13 mm × 9 mm × 11 mm involving the left cavernous sinus [Figure 2].

Eight months after the diagnosis of myasthenia gravis, the patient presented to the emergency department with a 2-day history of decreased consciousness, shortness of breath and the inability to eat and communicate. Her arterial blood test showed type II respiratory failure. The family reported that the patient had stopped her medications due to weight gain, which lead to the diagnosis of myasthenia crisis. The patient was admitted to intensive care, where over 2 weeks, she had multiple plasmapheresis sessions.

During her stay, she had computed tomography (CT) thorax, which revealed thymic enlargement. She underwent video-assisted thoracoscopy and subsequently a radical thymectomy. The histopathology of the excised tissue was consistent with thymic hyperplasia.

At 21 months post-surgery follow-up, her IGF-1 level remained raised (321 ng/mL [normal range: 71-234 ng/ml]), oral glucose tolerance test failed to suppress growth hormone and the MRI pituitary



**Figure 2:** Post-contrast T1 (a) and pre-contrast T2 (b) coronal images of magnetic resonance imaging pituitary showing residual soft tissue involving the left cavernous sinus (blue arrows)

revealed a stable residual pituitary mass involving the left cavernous sinus. Her myasthenia gravis symptoms were well controlled on azathioprine 50 mg 3 times daily and pyridostigmine 60 mg 3 times daily, and the patient was no longer on corticosteroids.

Her case was rediscussed in the MDT meeting, and the board suggested that the patient undergoes radiation therapy or somatostatin analogue. The patient opted for radiation therapy due to financial constraints. She is due to receive radiation therapy.

## Discussion

Pituitary macroadenoma with extension into the lateral wall of the cavernous sinus can disrupt the

third, fourth and sixth cranial nerve. In this patient, the MRI study suggested that the adenoma was extending into the lateral wall of the cavernous sinus. However, due to the inherent limitation of the MRI study, the exact involvement of which specific cranial nerve was impacted could not be established. However, clinically patient had ipsilateral ptosis, which was suggestive of the third cranial nerve involvement.<sup>[12]</sup> The patient underwent transsphenoidal resection of pituitary adenoma.

Her myasthenia gravis must have been present at a very early stage at the time of her presentation. She had delivered her youngest child 2 years ago, without any neurological complications. Similarly, she had partial unilateral ptosis without any other neurological features. This assumption was further supported by the absence of any post-operative neurological complications after pituitary surgery. Many factors can precipitate a myasthenia crisis, including a concurrent infection, surgical intervention, pregnancy, childbirth or tapering of immunosuppressive medications.<sup>[13-15]</sup> Perioperative management of patients with myasthenia gravis requires careful thought and planning.<sup>[16]</sup> All these features make it very difficult to diagnose myasthenia gravis early during the course of the disease. The close proximity of pituitary macroadenoma with the third cranial nerve further complicated the perplexity of this clinical situation. Nonetheless, bilateral ptosis development a few weeks post-surgery prompted consideration for other possible explanations for her symptoms. The subsequent clinical assessments and laboratory investigations confirmed the diagnosis of myasthenia gravis.

The four accepted modalities for the treatment of myasthenia gravis include symptomatic treatment with an acetylcholinesterase inhibitor, such as pyridostigmine and neostigmine, intravenous immunoglobulin or plasma exchange, which provides a rapid but transient clinical improvement, immunosuppressive therapy consisting of corticosteroids, azathioprine, mycophenolate

mofetil, cyclosporine and methotrexate and thymectomy, which may provide therapeutic relief in selected patients.<sup>[17,18]</sup>

There is evidence in the literature to support a correlation between the immune system and the neuroendocrine system.<sup>[19-22]</sup> The growth hormone has been shown to promote the proliferation of different cells, including chondrocytes, fibroblasts, adipocytes, myoblasts and T lymphocytes. Similarly, studies exhibit deficiencies in lymphocyte development and function in hypophysectomised animals, which responded partially to exogenous growth hormone administration. Moreover, the replacement of growth hormone was found to enhance the development of the thymus in aged mice and promote the engraftment of human T cells in mice.<sup>[20,21]</sup> Furthermore, thymic atrophy has been observed with ablation of the pituitary gland.<sup>[22]</sup>

This case highlights the importance of a thorough history and clinical assessment. The association of ptosis without any other clinical neurological symptoms with pituitary adenomas is uncommon. Patients with ptosis without any other neurological signs and suspicious pituitary adenomas should undergo assessment for myasthenia gravis to avoid potentially severe consequences with post-surgical complications.

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#### Authorship Contributions

Conceived and designed the analysis; SAK, WS and AIS. Collected the data; SAK, WS and WA. Contributed data or analysis tools; AIS, UA and WA. Performed the analysis; WS and UA. Wrote the paper; SAK, WS, AIS, UA and WA.