

## CASE REPORT

# A Rare Association between Myasthenia Gravis and a Growth Hormone Secreting Pituitary Macroadenoma: A Single Case Report

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## Abstract

Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disease. Although it is well known that patients with myasthenia gravis have a higher incidence of other autoimmune disorders, however, its association with pituitary adenomas is extremely rare. We believe that our case represents the 8<sup>th</sup> of this association and the 2<sup>nd</sup> case involving a GH-secreting adenoma. Here we report a case of a 45-year old Syrian woman who presented with typical complaints of myasthenia gravis as she was suffering from variable painless and effort-related dysphagia and dysarthria. Her complaints became more evident at the end of the day, while acromegaly only manifested as a 4-month history of headache and a special facies that was noted by the physician. Brain MRI scan demonstrated a 3.21 x 2.42 x 2.35 cm pituitary mass for which the patient underwent a trans-sphenoidal pituitary tumor resection. In addition, postoperative histopathological investigations confirmed the diagnosis of a GH-secreting macroadenoma. On following up, it was observed that her myasthenic symptoms improved significantly on Pyridostigmin and Prednisolone. In conclusion, the presence of headache in a myasthenic patient should raise the attention for other underlying causes including pituitary tumors.

## INTRODUCTION

Myasthenia gravis (MG) is an autoimmune antibody-mediated disease that affects post-synaptic acetylcholine receptors of the neuromuscular junction. The classical presentation is characterized by fluctuating weakness of the skeletal muscles that exacerbate with exertion, particularly affecting muscles innervated by the motor nuclei of the brainstem [1–3].

The most common intracranial neoplasms are pituitary tumors. GH-secreting pituitary adenomas resemble approximately 20% of all pituitary tumors. They present usually with

the clinical syndrome of gigantism in children and acromegaly in adults [4]. On the other hand, acromegaly is caused by GH-secreting pituitary adenoma in more than 98% of patients [4–5].

The association between MG and pituitary adenomas is extremely rare. Our search through medical literature revealed only 8 cases of this association. Five of these cases involved prolactin-secreting adenoma [1, 6–8]; two cases involved a non-functional pituitary adenoma [9–10] and only one case involved a GH-secreting adenoma [11]. Thus, we believe that this is the 2<sup>nd</sup> report of a GH-secreting adenoma in a myasthenic patient.

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## CASE REPORT

A 45-year old Syrian woman presented to our neurology clinic complaining of painless fluctuating dysphagia, dysarthria and headache. Speech and swallowing disorders started 2 months prior to her visit to our clinic and were related to effort as they worsened at the end of the day. Painless transfer dysphagia was for both solids and liquids and was associated with nasal regurgitation plus frequent choking incidents. Her dysarthria was clearly noted and her voice demonstrated a nasal tone on prolonged speech. She also complained of a 4-month history of mild generalized headache that responded to over the counter analgesics and did not impede daily activities. It was not associated with intracranial hypertension features. Her medical, surgical and family history were all unremarkable except for mild hypertension. On observation, the patient had thick lips, wide nose ridge, as well as protruding lower jaw and brow arches, which suggested an acromegalic facies. She also had an obvious asymmetrical bilateral ptosis which is fatigable and worsened at the end of the day. However, she denied having any diplopia. Ice pack test was clearly positive and her ptosis improved by 4 mm after 5 minutes.

Full neurological exam revealed weakness of neck flexors and extensors with grades of 3/5 and 4/5 on the MRC scale for muscular strength respectively. On the other hand, muscle power examination was normal. There were also no UMN signs, fasciculation, myotonia, muscular hypertrophy or tenderness. In addition, examination of the patient's mental status, sensory functions, balance, coordination and deep and superficial reflexes was normal. Examination of her chest, abdomen, and lymph nodes was all normal. Fundoscopy was also performed and revealed no abnormalities.

Furthermore, baseline laboratory tests and creatine kinase (CPK) were all within normal ranges. However, serum AChR antibodies using radioimmunoassay was 39,7 nmol/L (n.v. <0.25 nmol/L). CXR and CT scan were negative for any mediastinal mass. According to this characteristic clinical presentation, we suspected the diagnosis of MG, which was confirmed by the remarkable positivity of the ice pack test and the highly positive test of AChR antibodies.

Due to the unexplained headache and patient's special facies, brain MRI imaging was ordered which revealed a 3.21 x 2.42 x 2.35 cm T2w-hyperintense pituitary mass that was suggestive of macroadenoma (Fig. 1).

Endocrinal laboratory tests revealed excessive random GH serum level (46.7 ng/mL; n.v. <2.4 ng/mL), GH suppression test (GH serum level after 2 hours of 75 mg oral glucose administration) (40.2 ng/mL; n.v. <1 ng/mL) and IGF-1 (1468 ng/mL; n.v. 95–343 ng/mL). Other endocrinal tests were all within normal ranges [PRL (4.0 nmol/L; n.v. 0.3–4.1 nmol/L), TSH (2.4 mIU/L; n.v. 0.5–4.5 mIU/L); FT4 (16.8 pmol/L; n.v. 10–23); ACTH (4.6 pmol/L; n.v. 2.2–13.3 pmol/L); cortisol (440 nmol/L; n.v. 138–690 nmol/L); FSH (19.2 IU/L; n.v. 4.5–21.5 IU/L) and LH (7.4 IU/L; n.v. 5–25 IU/L)].

According to the laboratory tests and MRI features, the diagnosis of a GH-secreting pituitary macroadenoma was confirmed. The patient underwent trans-sphenoidal pituitary tumor removal surgery, and the post-operative histopathological techniques came to an agreement with our diagnosis. On following up, it was noted that all her serum endocrinal tests were normal. On the other hand, we prescribed Pyridostigmin (60 mg q.i.d) and Prednisone (1 mg/kg/day) for her myasthenic symptoms. She responded very well to her medications and her symptoms were almost eliminated.

## DISCUSSION

We present a rare association between MG and a GH-secreting macroadenoma.

Pituitary adenomas cause symptoms by two etiologies. The first one is the mass effect of macroadenomas, which was probably responsible for the headache complaint of our patient. The second etiology is the hormonal effect, which in the case of a GH-secreting adenoma manifests as gigantism in children and acromegaly in adults [4].

In our case, we suspected acromegaly due to the special facies and the unexplained headache. Thus, we ordered serum GH test, GH suppression test and IGF-1 that indicated excessive secretion of growth hormone. We also did a brain MRI scan that detected the presence of a 3.21 x 2.42 x 2.35 cm T2w-hyperintense pituitary macroadenoma. In addition, our diagnosis was confirmed by postoperative histopathological findings which were compatible with GH-secreting macroadenoma.

It is well documented that MG has a high incidence of other autoimmune disorders, most importantly thyroid disorders (5–10%), Rheumatoid arthritis, Systemic lupus erythematosus, polymyositis and dermatomyositis [2, 6]. Our patient had no evidence of thymus disorders on CXR or her chest CT scan. Thyroid dysfunction in such case can be either an autoimmune association with MG [2, 6], or a complication of acromegaly [5]. However, in our patient's case, thyroid function tests and thyroid ultrasound were normal. We also ordered creatine kinase (CPK) to check for muscular dystrophies, polymyositis or any other myopathies.

Although both MG and Acromegaly are common diseases in medical practice, yet their association in the medical literature is extremely rare. Our search in the medical literature revealed only 8 reported cases of an association between MG and pituitary adenomas. 5 cases involved a prolactin secreting adenoma [2,6–8]; 2 cases involved a non-functional adenoma, and this case represents the second of a GH-secreting adenoma, while the first one was reported by Hokkanen et al. in 1969 [11].

The 2 cases of non-functional pituitary adenomas were alveolar endothelioma (Negri et al, 1953) and Ganglioneuroma (Lapresle et al, 1976) [9–10]. The description of the stimulative effect of PRL on the autoimmune activation of MG was first reported by Cahill et al. in 1980 [1, 6]. This was followed by Tsinzerling et al. in 2006 who reported two case reports and a cohort study discussing the relationship between the severity of MG and serum PRL levels [1, 7, 8]. In 2013, Harris et al. discussed the role of PRL and its potential therapeutic use for MG in the future [1, 8]. In 2018, Zoli et al. suggested that MG should be considered in the differential diagnosis of neurological symptoms of patients with macroprolactinoma [1].

A growing body of evidence demonstrates a bi-directional relationship between immune functions and the neuroendocrine system. Many *in vitro* and animal studies described an important role of GH in the regulation of the immune system as it stimulates T and B cells proliferation and immunoglobulin synthesis [7, 8, 12]. It is important to note that the combination of these two diseases can be a mere coincidence. However, the fact that symptoms of both disorders have manifested within a short period of time can indicate an existing association. However, further studies are needed to explain any potential underlying mechanisms or etiologies beyond this association.

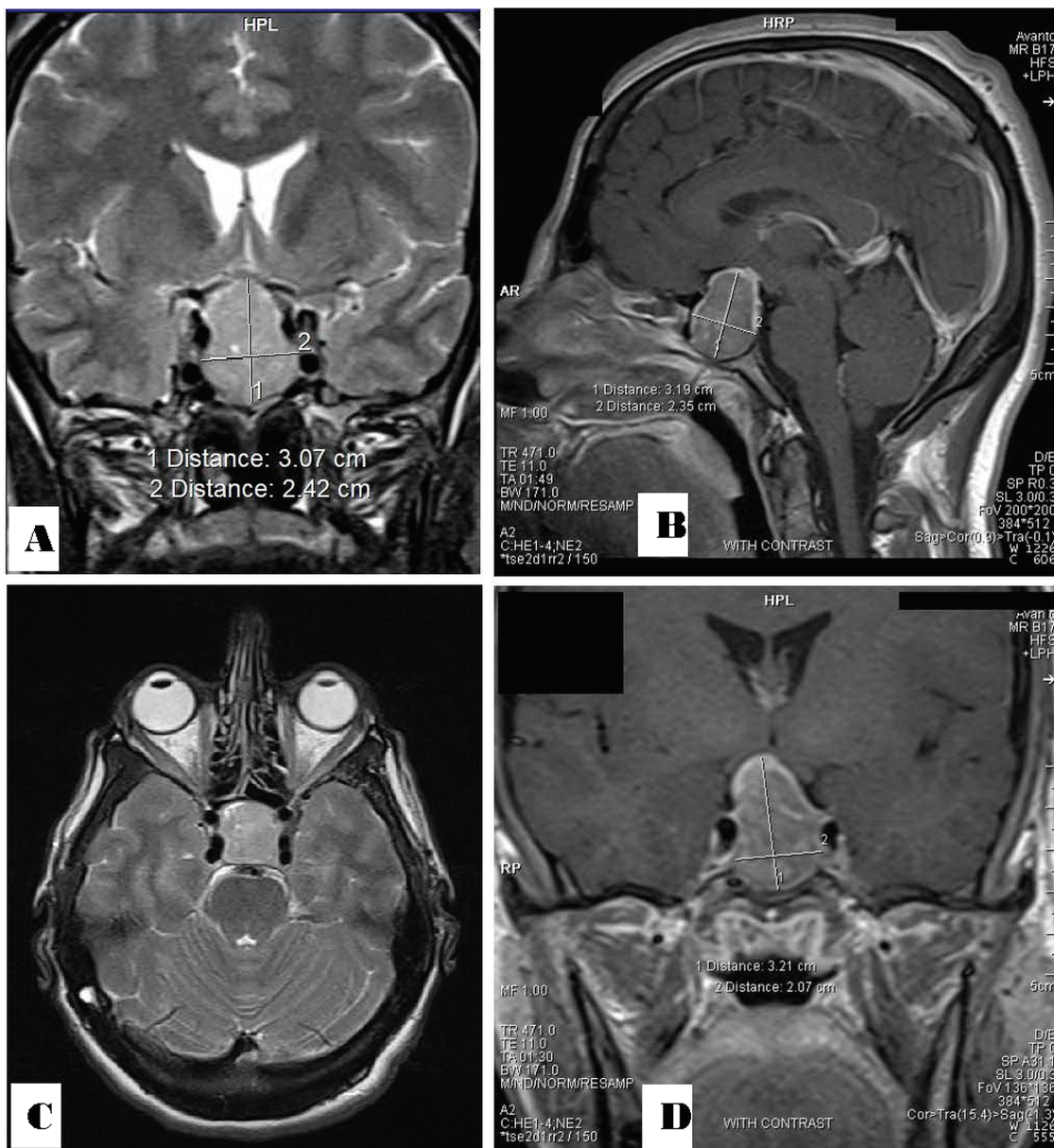


Figure 1: Brain MRI scan: Brain MRI sections that reveal the presence of an assymmetric pituitary mass filling the sella turcica. A: coronal view (T2w). B: sagittal view with contrast (T1w). C: axial view (T2w). D: coronal view with contrast (T1w).

**CONCLUSION**

Although it is rare, the association of MG and pituitary adenomas should have more attention in order to assess the real frequency of this association and to study the potential underlying interaction between these two conditions. On the other hand, the presence of headache in a myasthenic patient should raise the attention for other underlying causes including pituitary tumors.

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## CONSENT

Informed written consent was obtained from the patient for publication of this report and any accompanying images.

## GUARANTOR

The corresponding author is the guarantor of the submission.

## AUTHOR CONTRIBUTION

Farfouti MT is the patient's physician, he contributed in: Data Curation, Supervision. Ghabally M: Resources, Data Curation, Writhing Original Draft, Visualization. Roumieh G: Resources, Data Curation, Writhing Original Draft, Visualization. Farou S: Resources, Data Curation, Writhing Original Draft, Visualization. Shakkour M: Resources, Data Curation, Writhing Original Draft, Visualization. All authors issued final approval for the version to be submitted.

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