CASE REPORT

JIACM 2023; 24 (3-4): 234-38

Thymoma associated Myasthenia Gravis with Polycythaemia

Mukesh Kumar Sarna, Nipun Goel**, Ravi Godra**, Nasreen Bano**, Abhishek Sanadhya**, Rahul**, Manish Raj Pahadia***, Pallaavi Goel*****

Abstract

A persistent post-synaptic autoimmune condition of the neuromuscular junction is known as myasthenia gravis. The skeletal muscles become feeble as a result of the autoantibodies destroying nerve-muscle connection. The goal of this case report is to emphasize the value of meticulous history taking, examination, investigations, anticipating difficulties, and taking prompt corrective action.

We discuss the case of a 38-year-old man who complained of drooping eyelids and generalised fatigue. Myasthenia gravis was initially identified in this patient; afterwards, thymoma and polycythaemia were identified. He had a very long, uncertain course in the hospital, but a multidisciplinary strategy was used to successfully manage him.

Key words: Secondary polycythaemia, myasthenic crisis, myasthenia gravis, thymoma.

Introduction

A persistent post-synaptic autoimmune condition of the neuromuscular junction is known as myasthenia gravis. Skeletal muscles become feeble as a result of the autoantibodies' destruction of nerve-to-muscle transmission[1]. It affects the body's voluntary muscles, particularly those in-charge of the limbs, mouth, throat, and eyes. It can happen to anyone at any age, but young women (between 20 and 30) and older males are more likely to experience it. Although the disease is usually curable and has an unknown aetiology, it can cause considerable morbidity and even death. With prompt disease diagnosis and effective treatment, this may typically be avoided. Thymoma, a rare tumour of the thymus gland, is seen in 10 - 15% of instances with myasthenia, and 50% of these tumours are cortical in nature[2]. Red blood cell synthesis is very high in polycythaemia. Rarely are thymoma and myasthenia gravis linked to it.

Case report

A 38-year-old man, presented with complaints of generalised fatigue for 15 days, difficulty in holding his neck, nasal twang of voice, drooping of both eyelids, double vision, difficulty in swallowing and chewing since 4 - 5 days, and difficulty in breathing since 2 days. This fatigue used to gradually worsen as the day progressed, maximum during evening and night hours, relieved after rest and sleep, it mainly involved neck muscles, hands, and legs; he was unable to lift his head up on his own and would use his hands to hold his neck and had difficulty in walking and lifting his arms above his head. There was drooping of both his eyelids which was gradually progressive, it was also more in the evening hours and involved the right eye more than the left. He had double vision on and off, more apparent on gazing towards the left side, and used to resolve automatically on forward gaze or on gazing towards the right. It was so prominent that he needed to turn his neck to look to the left side. There was difficulty in swallowing and chewing for both solids and liquids, which worsened along the day, hence he was unable to consume dinner, but was relatively better in the morning at breakfast. Difficulty in breathing progressively increased and was evident in supine position, relieved on leaning forward.

There was no history of fever, trauma to the head, seizure-like activity, snake bite, or any similar complaints. On examination, he had raised blood pressure, plethora, and bilateral ptosis. He was conscious, and oriented to time, place, and person, with a mini-mental score of 30/30. There was no difficulty in speech; only a nasal twang was present. There was involvement of bilateral 3rd cranial nerves, bilateral 5th cranial nerves, left 6th cranial nerve, bilateral 9th cranial nerves, and bilateral 11th cranial nerves. Fundus was normal and the bilateral pupils were reactive to light. The patient had hypotonia and power was 4/5 at all joints in all movements in both limbs; power used to vary after repeated examination. No cerebellar signs or involuntary movements were noted. All deep tendon reflexes were slightly diminished on both sides, and superficial reflexes were normal. The sensory system was intact. Gait was unstable.

**Professor and Unit Head, **Resident, ***Professor, ****Senior Resident, Department of Medicine, Mahatma Gandhi Medical College and Hospital, (MGUMST), Jaipur - 302 022, Rajasthan.*

Corresponding Author: Dr Abhishek Sanadhya, Resident, Department of Medicine, Mahatma Gandhi Medical College and Hospital, (MGUMST), Jaipur - 302 022, Rajasthan. Phone: 9461189080, E-mail: abhishek.sanadhya27@gmail.com.

Differential diagnosis

The first differential was myasthenia gravis since this patient had a classical history of easy fatiguability and weakness which was relieved on rest and used to worsen as the day progressed. Guillain Barrë Syndrome (GBS) was the second differential but the patient had no ascending paralysis and no history of fever. Miller- Fischer Syndrome (MFS) is a variant of GBS, that has a classical triad of areflexia, ataxia, and ophthalmoplegia which was absent in this patient. Lambert-Eaton Myasthenic Syndrome (LEMS) is a presynaptic neuromuscular junction disorder in which the symptoms classically worsen on rest and are improved after repeated work – not present in this patient. Multiple Sclerosis can be another differential, but it usually has a relapsing and remitting pattern, not in this patient. Amyotrophic lateral sclerosis (ALS) usually does not have an acute presentation like this case. There was no sensory deficit and no involvement of the spine; this ruled-out acute myelopathy. No history of consumption of canned and preserved foods ruled-out botulism, and no history of any obvious snake bite ruled-out snake envenomation, and no history of any obvious insect bite ruled-out tick paralysis.

Management

Since our patient had myasthenia-like symptoms, to make a primary diagnosis we did a basic nerve conduction velocity (NCV) and repeated nerve stimulation (RNS) study. NCV was normal; this ruled-out MFS and GBS. Whereas RNS was suggestive of decremental response that pointed to myasthenia gravis and also ruled-out LEMS. To confirm this diagnosis, we got the acetylcholine receptor antibody (AchR) and muscle-specific tyrosine kinase antibody (MUSK) titres. Till the results were awaited, a neostigmine test was done. Atropine 0.6 mg was administered introvenously, followed by Neostigmine 1 gm given slow IV, and the patient's ptosis, muscle weakness, and single breath count were assessed before and after. An improvement in ptosis, muscle weakness, and single breath count would be considered a positive test, but in our patient, the test was negative. The edrophonium test is the classical test used, but due to its unavailability, this could not be done. Since the diagnosis was still not confirmed and reports were awaited, a pyridostigmine challenge was given, the patient improved after the first dose of pyridostigmine and it was continued in a dose of 60 mg thrice a day. AchR Antibody levels later reported were 6.83 nmol/L, (>0.5 nmol/L is considered a positive titre value). MUSK antibody levels were 0.13 U/mL, (>0.4 is considered a positive titre value). A routine chest X-ray (Fig. 1) was done which suggested a mass-like lesion with mediastinal widening.

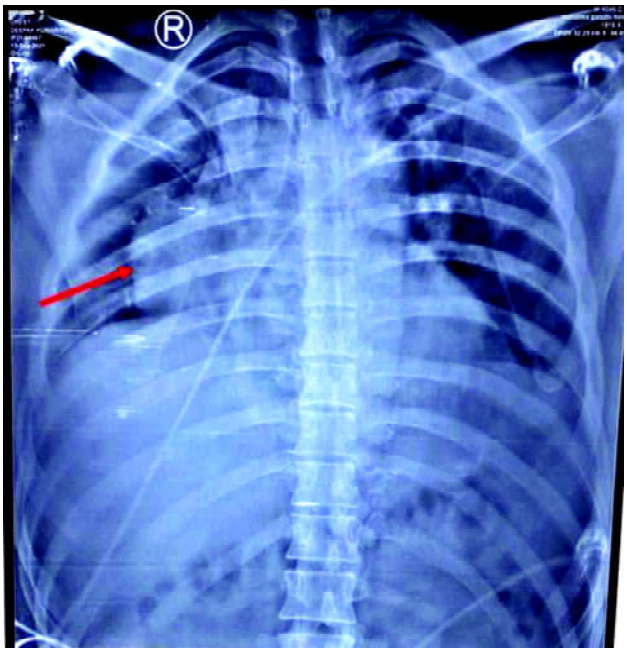

Fig. 1: *Mass lesion with mediastinal widening on chest X-ray.*

Contrast-enhanced chest computed tomography scan (CECT Chest) was done for further workup; it revealed a predominantly cystic mass lesion measuring approximately 7.5 cm x 10.6 cm x 13.7 cm in the anterior mediastinum on the right side at the level of the aortic arch, extending

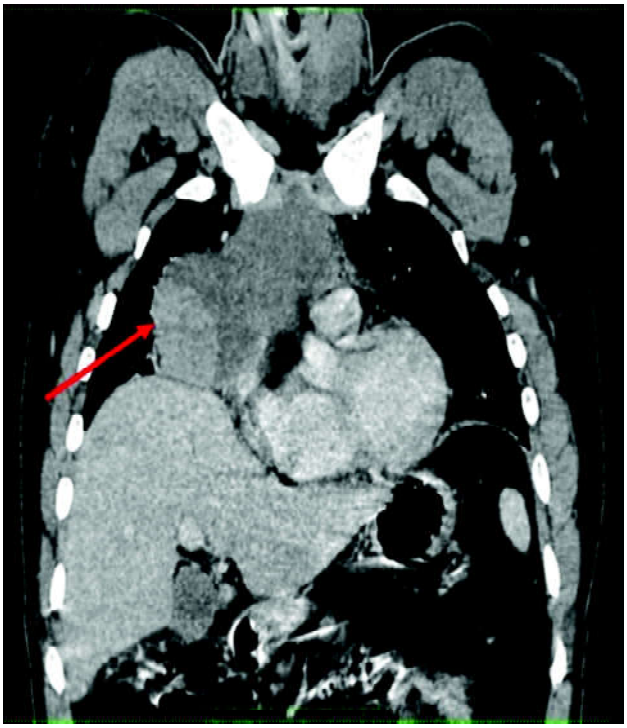

Fig. 2: *Thymoma on CECT chest coronal view.*

inferiorly to the level of the right ventricle, possibly of thymic origin (Fig. *2*, Fig. *3*). It was seen closely abutting the surrounding structures; however, no obvious infiltration or invasion was seen. According to MASAOKA staging, the diagnosis of stage 1 thymoma was made.

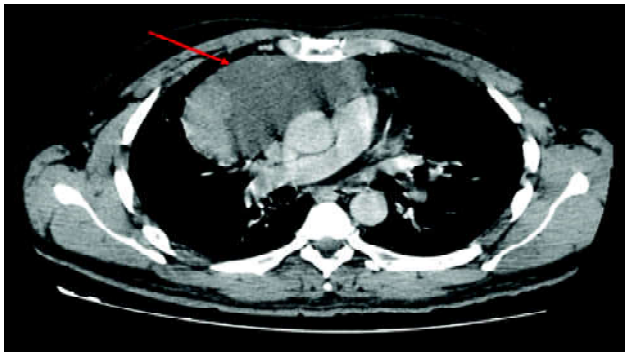

Fig. 3: *Thymoma on CECT chest axial view.*

CECT chest was also suggestive of a mass measuring 2 cm x 3 cm in the left adrenal gland; a possibility of Incidentaloma was kept. Triple phase CECT abdomen was done for further workup which suggested a well-defined hypodense cystic lesion with peripheral calcific foci in the left adrenal gland showing no significant enhancement – possibility of benign adrenal lesion – most likely adenoma (Fig. 4).

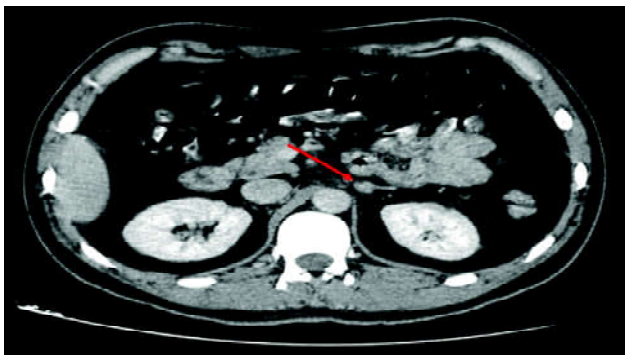

Fig. 4: *Adrenal incidentaloma on CECT abdomen axial view.*

Alfa-fetoprotein (AFP) and Beta-human chorionic gonadotrophin (beta-HCG) levels were done to rule-out a germ cell tumour; both were in the normal range. An ultrasound-guided biopsy was taken to know the nature of this mass. It was suggestive of a small round cell tumour, which was possibly lymphoproliferative or thymic in origin. Immunohistochemistry extended panel was done for further confirmation that was suggestive of a thymic neoplasm of WHO type B1, (which is a cortical thymoma) (Fig. 5), and ruled-out a lymphoproliferative disorder. Tumour, node, metastasis staging of this tumour was T1a N0 M0. A whole-body positron emission tomography scan was done to rule-out any other primary tumour in the body.

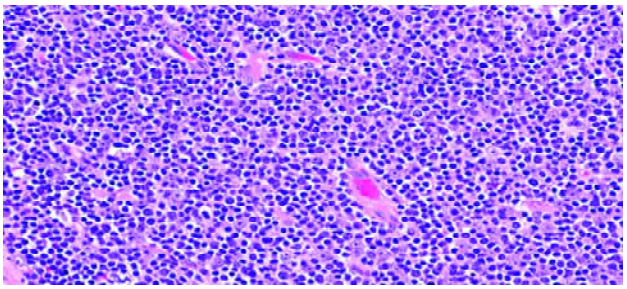

Fig. 5: *Type B1 thymoma on histopathology slide.*

Constant high levels of haemoglobin and haematocrit with a plethora was suggestive of polycythaemia. This is rarely seen to be associated with thymoma. 1-unit phlebotomy was done. Erythropoietin levels were very low, 1.03 mIU/mL. Janus Kinase 2 (JAK 2) mutation was negative. During this workup, the patient had complaints of difficulty breathing lying down flat. The patient was on antihypertensives, pyridostigmine, oxygen support and other supportive treatment. His difficulty in breathing gradually deteriorated and he had to be put on mechanical ventilatory support. This was diagnosed as a myasthenic crisis. Intravenous immunoglobulin (IVIG) therapy was started. A 2g/kg dose was given, and a total of 140 grams of IVIG was administered over 5 days. IVIG therapy did not show much improvement in the patient's condition. The patient was on continuous ventilator support and could not be weaned off the ventilator, hence tracheostomy was done. Thymectomy was planned and performed. After thymectomy too there was no significant improvement in the patient's breathing and he required ventilator support. Therefore, the decision for plasmapheresis was taken and 5 cycles of plasmapheresis were done every alternate day. Throughout this course, pyridostigmine was continued on a dose of 60 mg thrice daily, given up to a maximum dose of 300 mg/day.

Discussion

The most prevalent autoimmune condition that affects the neuromuscular junction is myasthenia gravis[1]. The symptoms might be simply ocular or quite severe, affecting the muscles of the limbs, bulbar region, and respiratory system. The age of onset ranges from childhood to maturity, with younger women and older men experiencing the highest incidence. Our patient a 38-year-old had an earlier onset. It is a common illustration of an antibody-mediated autoimmune illness. IgG autoantibodies react with intracellular or extracellular antigens in a class II hypersensitivity reaction that damages end-organs. As was the case with our patient, autoantibodies against acetylcholine receptors (AChRs) are present in the majority of myasthenia gravis patients[3]. Muscle-specific kinase

(MuSK)-directed antibodies are present in a small number of cases, although they were negative in this patient[4]. Thymus hyperplasia and thymoma are specifically associated with myasthenia gravis. An apparent thymoma-like growth on a chest X-ray in this patient raised the possibility of myasthenia gravis. Although our patient was a reasonably young man, myasthenic patients with thymomas often are usually much older. It is important to remember that having a thymoma does not always indicate a poor prognosis for remission from myasthenia gravis[5]. In patients with myasthenia gravis and thymomas, like in the case of our patient, there have been cases with satisfactory outcomes following thymectomy[6,7]. The abrupt onset of myasthenic weakness affecting the respiratory muscles is known as a myasthenic crisis, which necessitates ventilatory support to prevent death. Respiratory failure may result from upper airway obstruction brought on by respiratory muscle weakness or oropharyngeal muscular weakness[8]. In the intensive care unit (ICU), prompt respiratory assistance and management of the myasthenic crises results in favourable outcomes. The prognosis for myasthenic crisis may not be as good overall in underdeveloped countries, since many patients still receive treatment outside of the and immunomodulatory medication is prohibitively expensive[9]. Even though our patient was young and had early-onset myasthenia gravis, he nonetheless experienced a myasthenic crisis and was in a critical situation; for the same, plasmapheresis was performed and IVIG was given. He had a more serious illness than would be anticipated in a patient his age. According to studies, hospital IVIG use has grown dramatically in comparison to plasma exchange and thymectomy[10]. Pure red cell aplasia is typically linked to thymoma[11,12]. Althrough the JAK2 mutation was negative, this patient experienced polycythaemia that was possibly related to myasthenia gravis. Myasthenia gravis and thymoma instances connected to polycythaemia are extremely rare[13,14]. Myasthenia gravis and thymoma are known to be associated; however, it is uncommon for polycythaemia to also co-exist in this situation. Thymoma is just one of the underlying disorders that can cause polycythaemia. The condition is managed by treating the underlying cause and lowering the red cell mass. In addition, the patient had an adrenal tumour that was most likely an incidentaloma but was initially misdiagnosed as a phaeochromocytoma due to the patient's ongoing hypertension. A case report of subclinical hypercortisolism caused by an accidental adrenal tumour that later developed into myasthenia gravis exists[15]. Following thymectomy, plasmapheresis, and IVIG, the patient experienced complete remission[16,17]. Our patient too returned for follow-up visits while walking unassisted from home.

This patient's management needed a multidisciplinary strategy involving several teams. Thymectomy and immunosuppressive medication are used to treat myasthenia gravis. Thymoma is treated with surgical excision and ongoing monitoring for recurrence. Phlebotomy is used in the treatment of polycythaemia, along with addressing the underlying cause.

Conclusions

Myasthenia gravis is a chronic autoimmune disorder that can lead to significant morbidity and mortality if not diagnosed and treated in a timely manner. A thorough history and physical examination, along with appropriate investigations and a multidisciplinary approach, are essential for the successful management of this disease. The case report highlights the importance of considering myasthenia gravis as a differential diagnosis in patients presenting with weakness, easy fatiguability, and involvement of cranial nerves. The case also underscores the need for vigilant monitoring for potential complications associated with myasthenia gravis, such as thymoma and polycythaemia. Despite a prolonged hospital course, the patient, in this case, was managed successfully, emphasizing the importance of coordinated care in the treatment of myasthenia gravis. It outlines the complexity of managing patients with multiple comorbidities. Myasthenia gravis, thymoma, and polycythaemia are rare conditions that require a thorough evaluation and a unique approach to management. Early recognition and prompt treatment can lead to better outcomes for these patients.

References

1. Dresser L, Wlodarski R, Rezania K et al. Myasthenia Gravis: Epidemiology, Pathophysiology and Clinical Manifestations. *J Clin Med* 2021; 21: 2235.
2. Romi F. Thymoma in myasthenia gravis: from diagnosis to treatment. *Autoimmune Dis* 2011; 2011: 474512.
3. Patrick J, Lindstrom J. Autoimmune response to acetylcholine receptor. *Science* 1973; 25: 871-2.
4. Hoch W, McConville J, Helms S *et al*. Auto-Antibodies to the Receptor Tyrosine Kinase MuSK in Patients with Myasthenia Gravis without Acetylcholine Receptor Antibodies. *Nat Med* 2001; 7: 365-8.
5. de Perrot M, Liu J, Bril V *et al*. Prognostic significance of thymomas in patients with myasthenia gravis. *The Annals of Thoracic Surgery* 2002; 74: 1658-62.
6. Dahal S, Bhandari N, Dhakal P *et al*. A case of thymoma in myasthenia gravis: Successful outcome after thymectomy. *Int J Surg Case Rep* 2019; 65: 229-32.
7. Aydin Y, Ulas AB, Mutlu V *et al*. Thymectomy in Myasthenia Gravis. *Eurasian J Med* 2017; 49: 48-52.
8. Chaudhuri A. PO: Behan, Myasthenic crisis. *QJM: An Int J Med* Vol 102: 97-107.

9. Sharma S, Lal V, Prabhakar S *et al*. Clinical profile and outcome of myasthenic crisis in a tertiary carehospital: A prospective study. *Ann India Acad Neurol* 2013; 16: 203-7.
10. Alshekhlee A, Miles JD, Katirji B *et al*. Incidence and mortality rates of myasthenia gravis and myasthenic crisis in US hospitals. *Neurology* 2009; 72: 1548-54.
11. Rosu C, Cohen S, Meunier C *et al*. Pure red cell aplasia and associated thymoma. *Clin Pract* 2011; 1: 3981205.
12. Thompson CA, Steensma DP. Pure red cell aplasia associated with thymoma: clinical insights from a 50-year single-institution experience. *Br J Haematol* 2006; 135: 405-7.
13. Sasi S, Yassin MA, Kamran S. Association of polycythaemia vera with positive JAK2V617F mutation and myasthenia gravis: A report of two cases. *Clin Case Rep* 2020; 22: 531-4.
14. Voigt S. Polycythaemia vera associated with thymoma. Case report. *Acta Pathol Microbiol Immunol Scand A* 1986; 94: 351-2.
15. Petramala L, Marinelli C, Giallonardo AT *et al*. A case report of subclinical hypercortisolism due to adrenal incidentaloma complicated by myasthenia gravis after adrenalectomy. *Tumori* 2016; 11: 27103206.
16. AL-Bulushi A, Al Salmi I, Al Rahbi F *et al*. The role of thymectomy in myasthenia gravis: A programmatic approach to thymectomy and perioperative management of myasthenia gravis. *Asian J Surg* 2020; 44: 819-28.
17. Barth D, Nabavi Nouri M, Ng E *et al*. Comparison of IVIg and PLEX in patients with myasthenia gravis. *Neurology* 2011; 7: 2017-23.