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Neurology & Neurotherapy Open Access Journal
ISSN: 2639-2178

# Late-Onset Myasthenia Gravis in a Patient with Recurrent Breast Cancer: A Case Report

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**Case Report**

**Volume 9 Issue 2**

**Received Date:** August 16, 2024

**Published Date:** October 04, 2024

DOI: 10.23880/nnoaj-16000193

## Abstract

**Introduction:** Myasthenia gravis (MG) is an autoimmune disorder characterized by fatigable weakness, typically affecting voluntary muscles. Myasthenia gravis as a paraneoplastic syndrome (PNS) of a thymoma is well known, but it is rare to have MG PNS due to extrathymic neoplasms.

**Case:** We present a case on an 80-year-old female who was diagnosed with myasthenia gravis in the presence of recurrent metastatic breast cancer.

**Discussion:** The question remains whether MG is truly a neoplastic syndrome of breast cancer, or if older individuals are more likely to suffer from both breast cancer and late-onset myasthenia gravis (LOMG) at the same time. It was found that those diagnosed with LOMG are more likely to have extrathymic neoplasms. Regardless, the underlying malignancy should be treated, MG treatment should be initiated, and if PNS is suspected immunosuppressants are indicated.

**Conclusion:** This case highlights the complexity of classifying MG in elderly patients with a concomitant neoplasm, but nonetheless, MG as a PNS of breast cancer remains a possibility.

**Keywords:** Late Onset Myasthenia Gravis; Breast Cancer; Paraneoplastic Syndrome

## Abbreviations

MG: Myasthenia Gravis; PNS: Paraneoplastic Syndrome; LOMG: Late-Onset Myasthenia Gravis.

## Introduction

Myasthenia gravis (MG) is an autoimmune disorder where autoantibodies against the acetylcholine receptor at the post-synaptic membrane of the neuromuscular junction are produced. It is characterized by fatigable weakness, typically affecting voluntary muscles which include but are not limited to ocular, bulbar, respiratory, and limb muscles [1]. It is the most common disease of the neuromuscular junction, and it usually affects younger females or older men [2,3]. However, more recently there has been an increase in the diagnosis of late-onset myasthenia gravis (LOMG), and some studies have found an increase in the severity of symptoms within this MG subgroup [4,5]. A well-known paraneoplastic cause of MG is a thymoma which makes up around 10-15% of all MG cases [2]. However, MG as a paraneoplastic syndrome resulting from other primary tumors remains quite rare. Currently, there is very little literature regarding MG as a paraneoplastic cause of breast cancer [6,7]. We present a rare case on an 80-year-old female who was diagnosed with MG in the presence of recurrent metastatic breast cancer.

## Patient Presentation

The patient is an 80-year-old female with a past medical history of breast cancer diagnosed in 2022 that was currently in remission. She presented to the emergency room with a 5-day history of bilateral upper extremity weakness, ptosis, dysarthria, dysphasia to both solid and liquids, dyspnea, and generalized fatigue. The patient stated that she woke up most mornings asymptomatic but as the day progressed her symptoms worsened. She felt her symptoms had become more severe over the last 48 hours which prompted her to seek treatment. The patient denied any history of autoimmune disease. Of note, the patient was taking Letrozole and Palbociclib for her breast cancer but stopped taking them in February of 2023 due to loss of insurance.

Upon initial evaluation, the patient was alert and oriented to person, place, and time. She was dysarthric, and motor strength and range of motion were diminished in the bilateral upper extremities. Ptosis was present bilaterally and improved with the ice pack test. Reflexes were 2+ bilaterally in the upper and lower extremities and her sensation was intact to light touch throughout. At that time the patient was started on IV pyridostigmine 2mg 3x a day and plasmapheresis was scheduled for a suspected myasthenia crisis. Due to impending respiratory failure, the decision was made to admit this patient to the intensive care unit and she was electively intubated to protect her airway.

A comprehensive workup was completed. Initial laboratory results were unremarkable with blood counts, thyroid studies, electrolyte, and vitamin levels all falling within normal limits. Moreover, infectious causes were also ruled out. The patient had negative blood cultures and tested negative for influenza A/B, HIV, and the SARS-Cov-2 viruses. Muscle-specific kinase antibodies, voltage-gated calcium antibodies, and double-stranded DNA antibodies came back negative. Acetylcholine receptor-blocking antibodies, acetylcholine receptor antibodies, and anti-nuclear antibodies were all elevated. After reviewing the antibody results the diagnosis of myasthenia gravis was made.

Screening CT of the chest without contrast showed no thymoma, but a left breast mass with metastasis to the left axillary and mediastinal lymph nodes was found. There were also moderate osteolytic lesions of the ribs that could represent metastasis. These findings were suspicious for breast cancer recurrence. Screening CT of the head without contrast showed no intracranial metastasis but did show right parieto-occipital and right fronto-parietal calvarial lytic changes and CT of the abdomen and pelvis showed diffuse osseous metastasis.

The patient was treated with 5 rounds of plasmapheresis and is now on pyridostigmine 90mg oral which improved her myasthenia symptoms and allowed for extubation. The patient did not tolerate mycophenolate mofetil so IVIG was given throughout her hospital stay. She was discharged to sub-acute rehabilitation and was to follow up with hematology/oncology outpatient along with her neurologist.

## Discussion

Breast cancer as a cause of paraneoplastic syndromes (PNS) has been established, but it remains uncommon. It is estimated that only 1% of those diagnosed with breast cancer will develop neurological PNS [8]. The most common neurological PNS syndrome associated with breast cancer is cerebellar degeneration, other syndromes include opsoclonus-myoclonus syndrome, stiff person syndrome, neuropathy, and encephalitis [9,10]. At this time, myasthenia gravis and Lambert Eaton syndrome are exceedingly rare neurological paraneoplastic syndromes associated with breast cancer [10].

Morrison DG, et al. [11] described a case of a 53-year-old female with isolated vocal cord paralysis on adjuvant treatment for invasive ductal carcinoma who was positive for anti-acetylcholine receptor antibodies. Moreover, Dunn C, et al. [7] reported on a 60-year-old patient who developed alopecia areata and MG in the presence of invasive ductal carcinoma. As far as we know, this would make our patient the third reported case of breast cancer-associated myasthenia gravis PNS in the last two years.

The mechanism behind MG as a PNS is thought to be immune-mediated and several proposed mechanisms have been put forward [12]. Breast cancer has been associated with the loss of the p53 gene, this leads to unchecked cell division allowing for the creation of mutant proteins which in turn can cause the immune system to view these proteins as allogenic. BCRA ½ can cause a similar effect due to a lack of DNA repair [9]. Lastly, hormone receptor-positive breast cancer has an increased association with autoimmune disease [12]. More research will need to be done to explore if there is a link between lymph node spread, as in this patient's case, or if disease severity leads to an increased chance of MG PNS.

The question remains whether MG is truly a neoplastic syndrome of breast cancer, or if older individuals are more likely to suffer from both breast cancer and LOMG at the same time. There has been conflicting research on this topic, but it was found that those diagnosed with LOMG are more likely to have extrathymic neoplasms [13]. Moreover, the temporal onset of MG in relation to this patient's breast cancer makes a paraneoplastic cause more likely. Regardless, treatment does not vary significantly. The underlying

malignancy should be treated, and MG treatment should be initiated. Removal of the underlying malignancy often does not resolve the PNS, and therefore patients should be treated with immunosuppressants [14].

## Conclusion

Overall, LOMG is becoming more common, and clinical recognition of MG in elderly patients is crucial for symptomatic management and prevention of myasthenia crisis. Specifically, this case highlights the complexity of classifying MG in elderly patients with a concomitant neoplasm, but nonetheless, MG as a PNS of breast cancer remains a possibility. More research on extra-thymic neoplasms as a cause of MG PNS is warranted, as it could lead to an increased need for cancer screening in patients who are diagnosed with LOMG.

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