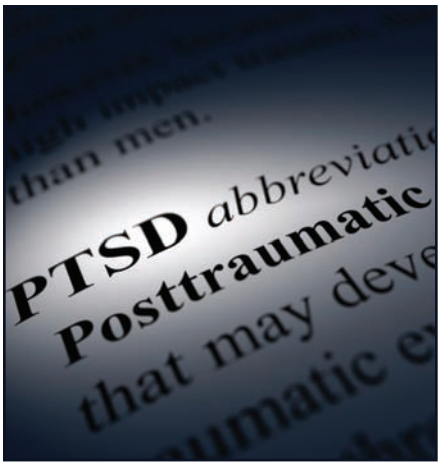

[CASE REPORT]

Differential Diagnosis of Hallucinations in a Patient with Myasthenia Gravis

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ABSTRACT

We present the case of a 63-year-old woman with comorbidity of myasthenia gravis and psychosis. Different diagnostic hypotheses based on a review of the literature are discussed. A protracted history of physical spousal abuse, patient symptoms, and results of different investigations allowed us to conclude that the patient had a form of posttraumatic stress disorder with secondary psychotic features. Psychosis due to myasthenia gravis is rarely seen, and it remains unclear what is the pathophysiology, if any, for such an association. The present case highlights the difficulties the physician faces in disentangling psychosis as a potential manifestation of myasthenia gravis itself versus being caused by a medical side effect of treatment, or psychosis due to a distinct co-occurring neurologic or psychiatric condition.

INTRODUCTION

Although there have been reports of associations between psychosis and myasthenia gravis (MG), these remain few and far between. It is unclear if psychotic symptoms in MG are an integral part of the various manifestations of this disease, or are due to another co-occurring distinct disorder.[1,2]

CASE REPORT

Mrs. S. was a 63-year-old woman with unremarkable family history. At the age of 35, she presented with strabismus, diplopia, swallowing difficulties, and fatigue. She was admitted to hospital and diagnosed with MG. Her condition deteriorated resulting in a myasthenic crisis for which she was transferred to the intensive care unit, ventilated, and started on pyridostigmine 480mg daily. A thymoma was discovered and a thymectomy performed. The patient was put on corticosteroids for seven weeks before being discharged home. She was kept on pyridostigmine 240mg daily. Her condition remained stable and she no longer reported any myasthenic symptoms.

When the patient was 63, she was referred to us for investigation of visual hallucinations that first occurred around the age of 30, prior to any symptoms suggestive of MG. Pyridostigmine and corticosteroids, which were prescribed for her MG a few years later, greatly improved strabismus, fatigue, and swallowing difficulties, but had no effect on these hallucinations, which had recently become more common and invalidating. During the initial psychiatric interview, the patient talked about regular marital violence since the age of 18. She was victim of

several head traumas and multiple scalp and facial wounds. She described her hallucinations as horrifying, bringing back slightly distorted real scenes, which occurred in the past, or completely different scenes made of bloody creatures, cut off heads, barking dogs, and wells full of blood. These hallucinations were seen as a threat to her life and were accompanied by intense fear and even escape reactions. She also complained about anterograde amnesia, which fluctuated with her emotions. All neurological symptoms, including amnesia and diplopia, appeared prior to any head trauma. Neurological examination did not show any focal signs. Her myasthenia score was 75/100. Her Mini-mental State Examination (MMSE) score was 20/30, with deficits mainly affecting calculation and verbal memory. The five-word test showed that the verbal memory impairment improved with cueing. Her Beck Depression Inventory (BDI) score was 29 (moderate depression). Blood chemistry and thyroid tests were normal. Anti-acetylcholine receptors (Anti-Ach R) antibodies were positive at 1.08nmol/L, a common finding in MG. No antinuclear antibodies or antiphospholipid antibodies were found. Electromyography (EMG) showed no abnormalities. Electroencephalography (EEG) was normal and magnetic resonance imaging (MRI) examination of the head revealed two one-centimeter vascular lesions affecting the corona radiata on the right and the internal capsule on the left. These lesions were attributed to silent lacunar infarctions.

DISCUSSION

Differential diagnosis. Several hypotheses were considered to explain the relationship between MG and psychosis in this patient.

According to the first hypothesis, hallucinations could be explained by an unusual involvement of the central nervous system in MG.[2,3] Although the exact mechanism is not clearly known, there is evidence that anti-Ach R antibodies are present in the cerebrospinal fluid (CSF) of myasthenic patients,[2] and it has been hypothesized that these antibodies might also interact with nicotinic receptors found in the central nervous system (CNS). EEG abnormalities have often been cited elsewhere to support this hypothesis.[1] However, in our case, EEG was normal and the location of the lesions on the MRI could not explain our patient's psychotic symptoms. The anti-Ach R antibodies level in the CSF was not performed in this case because the test is nonspecific; even patients with schizophrenia without any signs of MG have been found to have a high titer of CSF anti-Ach R antibodies.[4]

A second hypothesis would be the existence of a paraneoplastic autoimmune neuropsychiatric syndrome that sometimes can be seen in in patients with thymoma, a hypothesis put forth by Musha et al.[1]

Ananth et al[5] reported the occurrence of acute psychosis in a patient whose autopsy revealed a thymoma and whose death was attributed to a myasthenic crisis.

Musha et al[1] reported four cases of psychotic symptoms in patients with thymoma. Our patient shared some features described in these four cases: history of thymoma, history of myasthenic crisis, and the psychotic features inaugurating the disease. Nevertheless, our patient's psychotic symptoms were different from those reported by the aforementioned study (e.g., absence of olfactory and gustative hallucinations, absence of any signs of mental automatism in our case), had a course totally distinct from that of symptoms and signs involving the neuromuscular junction, and finally persisted and even exacerbated after thymectomy.

According to the third hypothesis, psychotic features in patients with MG could be explained from a purely psychopathological view: hallucinations and delusional thoughts would be compensatory for the different manifestations of MG and would thus be a way for the patient to deny the reality of his or her disease.[6] However, there did not seem to be any link between the content of the hallucinations and the symptoms of MG in our case.

The fourth hypothesis stipulates psychosis and MG might be two unconnected conditions fortuitously occurring in the same patient.[2] This was likely in the present case. Psychotic symptoms, however, can be due to a number of conditions, described as follows.

Medication side effect. While it is known that both pyridostigmine bromide[7] and corticosteroids[8] can cause psychosis, our patient's psychotic symptoms occurred years before the administration of these drugs.

Neurological condition. Hallucinations occurring in Mrs. S. could not be explained by epilepsy or brain tumor. Head trauma can lead to psychotic symptoms, but her psychosis appeared prior to any trauma. MRI examination revealed two small silent lacunar infarctions, the location of which could not explain the psychotic manifestations.

An MMSE score of 20/30 and hallucinations might be suggestive of dementia, but depression (BDI score=29) could also explain the MMSE score (especially with the memory impairment being improved with cueing), and her psychotic symptoms had been present for more than 30 years.

Schizophrenia/depression with psychosis. The possibility of paranoid schizophrenia and that of major depressive disorder (MDD) with psychotic features were investigated but the patient did not meet the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) *Fourth Edition-Text Revision*[9] or *Fifth Edition*[10] criteria for any of these disorders.

Posttraumatic stress disorder (PTSD). This patient met criteria for chronic PTSD. This raises the question of the link between PTSD and psychotic symptoms. According to Auxemery,[11] the presence of

psychotic symptoms in PTSD can have multiple explanations: they may indicate severity of PTSD; they may be due to co-occurring substance abuse, which is common in patients with PTSD; or they may express the decompensation of a latent psychotic disorder.[11]

Longden et al[12] insisted on the role of trauma in developing psychotic symptoms, mainly auditory hallucinations. Some so-called "psychotic" symptoms can be thought of as dissociative manifestations, which can occur following a massive trauma.[12]

Coentre et al[13] reported the case of a woman who developed PTSD with psychotic symptoms after she witnessed the murder of her nuclear family in a civil war. Norredam et al[14] reported six cases of Middle-Eastern refugees who had severe PTSD with psychostic manifestations.

Sareen[15] studied co-occurrence of PTSD with positive psychotic symptoms and concluded that such symptoms were not rare in patients with PTSD (with persecutory delusion occurring in 27.5% and visual hallucinations in 19.8% of the cases). These psychotic symptoms are not due to a co-occurring schizophrenia,[16,17] but to a severe form of PTSD dubbed "PTSD with secondary psychotic features" (PTSD –SP).[17-19]

Based on our patient's history, we believe she developed a form of chronic PTSD-SP. She was started on sertraline 50mg, with no antipsychotic medication, and within two months of treatment, she became euthymic and her hallucinations and PTSD symptoms completely disappeared. No antipsychotic treatment was needed.

CONCLUSION

Psychosis in myasthenic patients is rare and is not without bringing about diagnostic issues. Many hypotheses might explain the association between both conditions.

In our case, the absence of any sort of parallelism between psychosis and symptoms due to the neuromuscular junction involvement, as well as a particular psychological background, made us think of psychosis as caused by a separate and distinct condition: PTSD-SP. The excellent response to sertraline reinforced our diagnosis.

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