



An Unusual Presentation of Myasthenia Gravis

Une présentation inhabituelle de la Myasthénie

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ABSTRACT

BACKGROUND: Myasthenia gravis (MG) is generally a rare disorder and may thus be easily misdiagnosed. Misdiagnosis is even more likely when the presentation is atypical.

OBJECTIVE: To present and discuss an unusual presentation of myasthenia gravis

METHOD: A 67-year-old man presented with progressive weakness of three months duration. Full clinical and limited laboratory evaluations were carried out and therapeutic treatment embarked upon.

RESULTS: Illness started with generalized weakness and inability to maintain a conversation. Illness become so severe that he could not get up from sitting position This was accompanied by development of double vision. On examination he looked generally healthy except for bilateral ptosis and presence of diplopia. There was a prompt response to an injection of neostigmine methylsulphate. Haematological, biochemical and hormonal studies yielded essentially normal results. A clinical diagnosis of myasthenia gravis was made. Patient was placed on pyridostigmine and prednisolone to which he responded very satisfactorily.

CONCLUSION: Typically myasthenia gravis presents with ptosis but clinicians should be aware that that is not invariable and that it may start with limb weakness. *WAJM* 2009; 28(6): 391–393.

Keywords: Myasthenia gravis, case report, autoimmunity, Nigeria.

RÉSUMÉ

CONTEXTE: La myasthénie grave (MG) est généralement une maladie rare et peut ainsi être facilement mal diagnostiquée. Erreur de diagnostic est encore plus probable lorsque la présentation est atypique.

OBJECTIF: Présenter et discuter d'une présentation inhabituelle de la myasthénie grave

MÉTHODE: A 67-year-old man présenté avec une faiblesse progressive d'une durée de trois mois. Full évaluations cliniques et de laboratoire limitées ont été effectuées et un traitement thérapeutique entrepris.

RÉSULTATS: La maladie a commencé par une faiblesse généralisée et l'incapacité à maintenir une conversation. Maladie sont si graves qu'il ne pouvait pas se lever de la position assise Ceci a été accompagné par le développement de la vision double. À l'examen il avait l'air généralement en bonne santé, sauf pour ptose bilatérale et la présence d'une diplopie. L'a été une réponse rapide à une injection de néostigmine méthylsulfate. Hématologiques, biochimiques et études hormonales cédé l'essentiel des résultats normaux. Un diagnostic clinique de la myasthénie grave a été faite. Patient a été placé sur la pyridostigmine et la prednisolone à laquelle il a répondu de manière très satisfaisante.

CONCLUSION: En général la myasthénie se présente avec un ptosis mais les cliniciens doivent être conscients que ce n'est pas immuable et qu'il peut commencer par une faiblesse des membres. *WAJM* 2009; 28 (6): 391–393.

Mots-clés: myasthénie, rapport de cas, l'auto-immunité, au Nigeria.

INTRODUCTION

Myasthenia gravis (MG) is an immunological neuromuscular disease due to circulating antibodies that block acetylcholine receptors at the post-synaptic neuromuscular junction which inhibits the stimulating effect of acetylcholine leading to fluctuating muscle weakness fatigability.¹ It is a rare disease among Africans but the prevalence rates in Caucasian adults vary from 1 in 10,000 to 50,000.² The disease is not age or gender specific, although it is common in women under 40 years with male predilection after 50 years of age.^{2,3} The hallmark of MG is muscle weakness that increases during periods of activity and improves after periods of rest. Muscles at increased susceptibility include those that control eye and eyelid movement, facial expression, chewing, talking, swallowing, breathing and limb movement in decreasing order.⁴ The degree of muscle weakness varies greatly among patients ranging from localized to generalized forms in which virtually the whole body is involved. MG can be difficult to diagnose if the symptoms are subtle as it can hardly be distinguished from normal variants and other neurological diseases.⁴ However, in suspected cases, serology of the blood can identify antibodies to the acetylcholine receptors which has a sensitivity of 90% in generalized disease but may be negative in up to 50% of ocular myasthenia gravis.

Case Report

The patient a 67-year-old businessman was admitted into the medical ward of the University of Ilorin Teaching Hospital in central Nigeria because of three months history of progressive generalized body weakness. He was in his usual state of health when he observed difficulty in sustaining physical activity like taking his bath and inability to maintain conversation as his voice would become progressively weak. Six weeks prior to presentation he had observed drooping of his eyelids. The ptosis was absent on rising in the morning but as the day progressed it would become worse. Two weeks prior to his admission he developed double vision and two days before entry he could

not get up from lying position without support. He had no history of fever, cough, weight loss, loose bowel motions or urinary symptoms. There was no history to suggest thyroid disease or diabetes mellitus. He was not known to be hypertensive and neither took alcoholic beverages nor smoked tobacco. He was married to three wives and had 10 children.

Examination revealed an alert, well oriented, elderly man with bilateral ptosis which was worse on the right side (Fig. 1). There was diplopia which was more marked on left lateral gaze. There was no lid lag, lid retraction or proptosis. The pupils were of normal size and reacted equally to light. There were no cranial nerve deficits. Tone and deep tendon reflexes were normal in all limbs. The power in the upper and lower limbs was four and three respectively. He had a pulse of 80 beats/min, BP of 130/80mmHg, and normal heart sounds. There was no demonstrable thyroid enlargement. The other systems were essentially normal.

A tentative diagnosis of MG was made. The inability to sustain conversation and easy fatigability of limb and eyelid muscles were demonstrated by the bed side. Weakness improved after rest and worsened again on repeat of the exerting test. Improvement in the strength of the muscles was observed within 10 minutes of intramuscular injection of neostigmine methylsulphate which lasted for about two hours. Atropine 0.5mg was given prior to neostigmine to prevent the muscarinic effects like hypotension, bradycardia, heart block, cardiac arrest or gastrointestinal symptoms. Blood film was normal with a PCV of 38%, total white cell count of $7.5 \times 10^9/L$, and ESR of 12mmHr. The serum electrolytes, urea, creatinine, calcium, phosphate and urate were within normal limits. The thyroid function tests (T3, T4, and TSH) and fasting blood sugar were normal. The chest and thoracic inlet x-rays were essentially normal.

He was commenced on pyridostigmine 60 mg eight hourly with improvement in the weakness which was not sustained before the next dose of the drug. Prednisolone at the dose of 10mg tds was added to the medication 48 hours



Fig. 1: Bilateral complete ptosis as the patient attempts to open his eyes



Fig. 2 Definite relief of bilateral patient's ptosis following administration of neostigmine.

later which improved the weakness of his limbs and relieved the ptosis (Fig. 2). He made steady progress and was fit for discharge from hospital after six weeks. The patient had remained stable more than 12 months after on pyridostigmine and prednisolone at the dose of 60mg tds and 5mg tds respectively.

DISCUSSION

The actual prevalence of myasthenia gravis in the West African sub-region is largely unknown. However, hospital-based reviews have shown that the disease is uncommon and majority of patients are in the third to fifth decade and below.^{5,6} MG is not a rare disease in Europe and North America. Its prevalence in the United States of America is estimated to be 20 cases per 100,000 population.^{7,8} The risk factors are female gender, age between 20–40 years, family history and auto-immune diseases.^{7,8} Earlier reports of the disease in West Africa have noted the rarity of the disease and relatively young age of the patients with the oldest being 36 years and the youngest 1½ years.^{9,10} A recent review by Ojini et al in Lagos, Nigeria also noted that the disease was rare with a peak incidence in the third decade of life. In a

related retrospective study by Bakari et al¹¹, it was observed that the disease was rare in the northern part of Nigeria. They could only identify four cases over a 10-year period.

Although the disease can present at any age, this patient's presentation in the 7th decade was unusual. Also of interest is the sequence of symptoms which is the reverse of the usual presentation. In most cases, the first noticeable symptom is the weakness of the eye muscles followed by difficulty in swallowing and slurred speech before limb weakness. In the report by Ojini *et al.*⁶ the commonest feature was ptosis followed by diplopia and limb weakness with dysphonia being rare. Dysphonia was a prominent feature in our patient.

The diagnosis of MG is not difficult as in this case as when the patient presents with classical physical signs. However in subtle cases, serologic and neurophysiologic studies may need to be performed in order to make the diagnosis. Blood tests to identify antibodies against acetylcholine receptors have a sensitivity of 36–96%, although in ocular myasthenia gravis the test may be negative in up to 50% of cases. In specific situations, testing is performed for Lambert-Eaton syndrome in which other antibodies against voltage-gated calcium ion channel can be found. In single fibre electromyography, which is considered to be the most sensitive test for myasthenia gravis, a thin needle electrode is inserted into a muscle to record the electrical potential of individual muscle fibres.

The patient responded well to a combination of cholinesterase inhibitor and steroids. Although we did not carry out serologic tests to detect antibodies against acetylcholine receptors, his response to steroids support of autoimmune basis of the disease. Steroids interfere with the production of antibodies responsible for the degradation of cholinergic receptors, protect acetylcholine receptors from the antibodies and facilitate neuromuscular transmission.⁸

In the area of novel therapies, researchers have found that high doses of cyclophosphamide reboots the immune system in patients who do not respond to conventional agents or who experience serious adverse effects. The drug eliminates mature white blood cells but spares the bone marrow stem cells. There is a strong suspicion that rebooting may cause tolerance to existing auto-antigens or reset the immune system so that patient becomes less prone to auto-immunity. A synthetic antisense RNA molecule called EN101 (Monarsen) has been developed which acts against the human acetylcholinesterase gene thereby allowing acetylcholine more time to interact with available receptors. As research continues to reveal new insight into the genetics and immunology of MG, it is hoped that scientists will identify other targets that might have therapeutic utility.¹³

REFERENCES

1. Conti-fine BM, Milani M, Kaminski HJ. Myasthenia gravis past, present and future. *J Clin Invest* 2006; **116**: 2843–54.
2. Schwab RS, Leland CC. Sex and age in myasthenia gravis as critical factors in incidence and remission. *J Am Med Ass* 1953; **153**: 127–130.
3. Beekman R, Kuks JBM, Oosterrhus HJGH. Myasthenia gravis: Diagnosis and follow-up of 100 consecutive patients. *J Neurol* 1997; **244**: 112–118.
4. Scherer K, Bedlack RS, Simal DL. Does this patient have myasthenia gravis? *J Am Med Ass* 2005; **293**: 1906–1914.
5. Ogun SA, Oyegunle AO. Myasthenia gravis and Anaesthesia- A review of Literature. *Afr J Neuro Sci* 2003; **22**: 1–15.
6. Ojini FI, Danesi MA, Ogun SA. Clinical manifestation of myasthenia gravis- A review of cases seen at the Lagos University Teaching Hospital. *Nig Postgrad Med J* 2004; **11**: 193–197.
7. Kurtzke JF, Kurland CT. Epidemiology of Neurologic disease In Joynt RJ ed. *Clinical Neurology Rev. ed. Vol 4. Philadelphia J.B.* 1992: 80–88.
8. Drachman DM. Myasthenia gravis. *New Eng J Med* 1994; **330**: 1797–1809
9. Abson CP, Celfard M. Myasthenia gravis in the African. *Central Afr J Med* 1978; **24**: 189–194.
10. Jaretzki A, Barohn RJ, Emstoff RM. Myasthenia gravis. Recommendation for clinical research standards. *Neurology* 2000; **55**: 16–23.
11. Bakari AG, Onyemelukwe GC. Rarity of myasthenia gravis in Northern Nigerians. *Ann Afr Med.* 2002; **1**: 25–27.
12. Calhoun RF, Ritter JH, Guthrie TJ, Pestronk A, Meyers BF, Patterson GA, *et al.* Results of transcervical thymectomy for myasthenia gravis in 100 conservative cases. *Ann Surg* 1999; **230**: 555–561.
13. Hampton Tracy. Novel therapies target myasthenia gravis. *JAMA* 2007; **298**: 163–164.