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RESEARCH ARTICLE

FATIGABILITY – LONG-LASTING DISEASE DIFFICULT TO TREAT

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ABSTRACT

Fatigability is an abnormal decrease in muscle strength with a negative impact on the patient's quality of life and socio-professional activity. Since it is a feature of modern society, the doctor must determine whether the patient's condition is the result of physical or intellectual exertion. The approach is complex and requires a multidisciplinary collaboration between the internist, psychologist, psychiatrist, neurologist, rheumatologist, endocrinologist and the infectious disease doctor. We present the case of a 22-year-old female patient who underwent multiple medical examinations for 6 months and whose main symptom was fatigability. The female patient went to the neurology practice where speech and swallowing disorders were found, palpebral ptosis with intermittent diplopia, accentuated by exertion. The female patient performed brain magnetic resonance imaging (MRI) - within normal limits. Electromyography (EMG) - 10% decrease. Histopathological examination of the thymus revealed thymic tissue showing histopathological lesions of thymic lymphocytic hyperplasia. One month after the confirmation of the diagnosis of myasthenia gravis and after the histopathological test result, laparoscopic thymectomy was performed by a left transpleural approach with a favourable postoperative evolution. The patient was subsequently treated with Medrol and Mestinon. In the past, myasthenia gravis was associated with high mortality, and now the long-term prognosis has changed and life expectancy is approaching normal limits.

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INTRODUCTION

Fatigability refers to the universally familiar state of weakness and exhaustion, resulting from physical or intellectual exertion. The frequent clinical history and the elements that accompany fatigability, its significance and its physiological and psychological basis will be better understood if we initially consider the effects of fatigability on the normal individual. (1) Fatigability is an abnormal decrease in muscle strength with a negative impact on the patient's quality of life and socio-professional activity. The approach is complex and requires a multidisciplinary collaboration between the internist, psychologist, psychiatrist, neurologist, rheumatologist, endocrinologist and the infectious disease doctor. Patients consider fatigability to be one of the most annoying symptoms, much more annoying than nausea and vomiting, for example, which can be treated with medication. Compared to fatigability in healthy people, it is more severe and does not go away after rest (2). Most patients with constant reports of low energy levels, without a previous febrile condition and without one of the medical conditions associated with fatigability, have elements of depression (1).

In this case, fatigability is the key clinical factor in recognizing the condition.

CLINICAL CASE: We present the case of a 22-year-old female patient who underwent multiple medical examinations for 6 months and whose main symptom was fatigability. The female patient went to the neurology practice where speech and swallowing disorders were found, palpebral ptosis with intermittent diplopia, accentuated by exertion. The female patient performed brain magnetic resonance imaging (MRI) – within normal limits and an EMG – 10% decrease. At the clinical examination: BP (blood pressure) 110/70 mmHg, VR (ventricular rate) 98 beats per minute, QMG score (Quantitative Myasthenia Gravis) 10.5 p with positive myostin test. Predominantly bulbar myasthenic deficit. No other changes during the clinical examination. Biological test - acetylcholine anti-receptor antibodies - 0,4 nmol/l. Uroculture - sterile. Pharyngeal exudate - absence of pathogenic flora. Heart-lung radiography - no active pleuro-pulmonary changes. EKG (electrocardiogram) - sinus rhythm, ventricular rate, QRS axis without terminal phase changes.

Thyroid ultrasound - RL (right lobe) 40/14/14 mm, LL (left lobe) 36/13/13 mm, bosselated thyroid contour inhomogeneous echotexture in ranges, possibly hypoechoic micronodules in both lobes, diffuse and unevenly increased vascularization in bilateral parenchyma. Isolated bilateral laterocervicalmicroadenopathies. CT (computed tomography) scan of the mediastinum - residual thymus. Endocrinology consultation - chronic autoimmune thyroiditis. Histopathological examination of the thymus reveals thymic tissue showing histopathological lesions of thymic lymphoid hyperplasia. One month after the confirmation of the diagnosis of myasthenia gravis and after the histopathological test result, laparoscopic thymectomy was performed by a left transpleural approach. The postoperative evolution was favourable. Genetic consultation - the patient was informed that myasthenia gravis is an autoimmune condition for which it is currently not possible to perform genetic diagnosis or specific prenatal testing. The risk of transmitting the disease is also higher than in the general population. The risk of transient myasthenia gravis in the newborn or arthrogryposis (secondary to transplacental transmission of anti-acetylcholine antibodies) is worth mentioning. Following the hygiene-diet plan and the medicines recommendations (Medrol, Mestinon), after about 11 years, the patient is in a favourable clinical condition, complaining only of paraesthesia in the antero-median areas of the forearm and left arm. EMG conclusions - pathological decrease in ulnar nerve stimulation, without pathological increase. There are no electrophysiological abnormalities in the upper limbs observed during the driving study or the EMG examination with needle (paraesthesia on the antero-median face of the left hand and inconsistently on the antero-median face of the left forearm, most likely due to a radicular condition in C8.)

DISCUSSION

Initially, the doctor's task is to determine if the patient is suffering from the usual effects of physical or mental exhaustion (1). A diagnosis error would be to attribute fatigability to overwork, when in fact it is a manifestation of an infectious medical, endocrinological, neurological, psychiatric condition. Myasthenia gravis is an autoimmune disease that consists of fatigability that sets in easily caused by cell-mediated destruction and by antibodies to acetylcholine receptors. The disease is more common in young women and older men but may occur at any age (3). Fatigability is a key clinical factor in recognizing the condition. The symptoms worsen in the second part of the day or after physical exertion. During the neurological examination it can be noticed by asking the patient to perform certain exercises, such as looking up repeatedly or performing arm raises or knee bends. During an objective examination, the deep tendon reflexes are always normal and there is no sensitivity disorder (4). Which clinical features of neuromuscular junction disease can be elicited by history?. Fatigability is the hallmark of diseases affecting the neuromuscular junction, such as myasthenia gravis. Because strength improves with rest, fatigability does not usually manifest as steadily progressive decline in function; rather, it presents as waxing and waning weakness. When the muscles fatigue, the patient must rest, leading to recovery of strength, which permits further use of the muscles, causing fatigue, which necessitates rest and recovery again. This cycle of worsening with use and recovery with rest produces a variability or fluctuation in strength that is highly characteristic of neuromuscular junction diseases. (5)

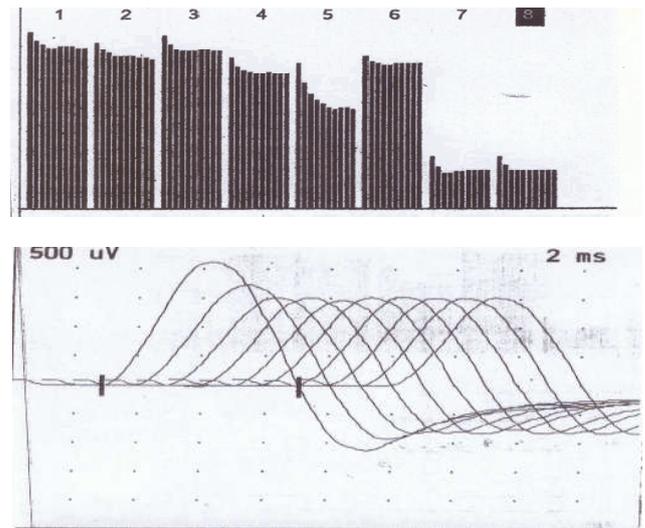


Figure 1. EMG

Core features

- Muscle fatigability. Muscle weakness is worse following exertion and overheating and better after rest and cooling.
- Extraocular muscle (EOM) weakness. Asymmetric and variable ptosis and diplopia are the most common symptoms. The EOMs are involved in 90% of patients with myasthenia gravis, and are the only muscles involved in 15% of patients (“ocular myasthenia gravis”).
- Acetylcholine receptor antibodies (AChR Abs) in serum. Present in 80% to 90% of patients with generalized myasthenia gravis and 60% of patients with ocular myasthenia gravis. AChR-seronegative cases should be tested for muscle-specific kinase (MuSK) autoantibodies and anti-low-density lipoprotein receptor-related protein (LRP4) autoantibodies. Some cases remain “triple seronegative.”
- On electrodiagnostic studies, the width of the compound muscle action potentials (CMAPs) waveform decreases by 10% to 15% with repetitive nerve stimulation.
- Single-fiberelectromicrography (EMG) shows increased “jitter.” Single-fiber EMG is a technically difficult test but can be diagnostically helpful in mild or purely ocular cases. (6)

Patients with myasthenia gravis can be classified according to the Osserman criteria:

- Group 1: ocular, 15% to 20%
- Group 2A: mild generalized, 20%
- Group 2B: moderately severe generalized, 20%
- Group 3: acute fulminating, 11%
- Group 4: late severe, 9% (7)

Most patients with myasthenia gravis present to the emergency department with an exacerbation of the disease or medication complications. On rare occasions, the patient presents with the disease as yet undiagnosed (8). Unrecognized, unexpected deaths and prolonged hospitalizations occur. Since The serological investigation of these antibodies takes days and may not be conclusive and therefore the assessment at the emergency department relies on the recognition of signs and symptoms of myasthenia gravis (8)

CONCLUSION

Fatigability is a characteristic of modern society, its approach requiring a multidisciplinary collaboration so to avoid a diagnosis error. A careful assessment of the patient's personal medical history, disease history, serious clinical and paraclinical examination will help doctors establish the appropriate diagnosis and treatment. The diagnosis of myasthenia gravis in the emergency department relies on the recognition of signs and symptoms. In the past, myasthenia gravis was associated with high mortality, and now the long-term prognosis has changed and life expectancy is approaching normal limits.

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