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Distal Myasthenia Gravis: A Missed Clinical Diagnosis

ABSTRACT

Myasthenia gravis (MG) is an immune mediated, post-synaptic neuromuscular transmission disorder, presenting with predominant ocular, bulbar, and/or proximal fluctuating weakness and fatiguability. Distal and asymmetric onset of symptoms in MG is rare and could lead to delay in diagnosis especially when fatiguability or fluctuation is not clearly reported as a prominent initial symptom – as seen with our patients. We report three cases of distal MG who presented with predominant distal, asymmetric hand weakness. Their clinically diagnoses for referral to the electrodiagnostic (EDx) laboratory were: Chronic inflammatory demyelinating peripheral neuropathy, C8T1 motor radiculopathy, and multifocal motor neuropathy. It was in the EDx laboratory that the diagnosis of MG was suspected in these patients. Since the routine EDx tests were normal in all three patients – A repetitive nerve stimulation test (RNST) was done – which was positive in the affected muscles and hence a diagnosis of distal MG made. (This is the protocol followed in our laboratory) These patients were then found to have high serum levels of antibodies to acetyl choline receptors – confirming the diagnosis of MG. RNST is not routinely done in all patients sent for EDx testing and none of these patients had a reference for the same – however, using a protocol based method of EDx testing, lead to the diagnosis of a treatable condition. Electrodiagnostician need to be aware of this presentation of MG and follow protocols or the diagnosis could be missed.

Key words: Distal limb weakness, Myasthenia gravis, Repetitive nerve stimulation test, Repetitive nerve stimulation test

Key message: The diagnosis of MG could be missed when patients present with symptoms of isolated distal hand weakness. Clinicians and electrodiagnosticians must be aware of this rare presentation of a treatable condition. In our EDx laboratory a protocol is followed – When all routine tests are normal in a patient with history of weakness, a RNST test performed is on the weak muscles. What is well known: Myasthenia gravis presents with ocular, bulbar, and proximal limb weakness
What is less known: Myasthenia gravis can rarely present with predominant distal weakness of hand muscles

INTRODUCTION

Distal limb weakness in myasthenia gravis (MG) is rare.[1-8] It may present along with ocular, bulbar, and proximal limb symptoms or may be the presenting symptom, which is rarer still.[5] In the latter event, the diagnosis could be missed as MG primarily presents with proximal limb weakness, ocular, and/or bulbar symptoms.[9] MG is diagnosed clinically and confirmed by electrodiagnostic (EDx) tests such as repetitive nerve stimulation test (RNST) and single fiber electromyography (sfEMG).[10] Anti-acetylcholine receptor (AChR) and anti-muscle-specific tyrosine kinase antibodies aid diagnosis.[11] We describe a series of three patients with MG presenting to the EDx laboratory with isolated distal hand weakness.

CASES

Three patients were seen in the EDx laboratory of a tertiary hospital between 2015 and 2018 with symptoms of weakness affecting primarily the distal hand muscles. Two were male (mean age, 53.5 years) and one was female (age, 37 years). These patients had presumed clinical diagnoses of multifocal motor neuropathy, chronic immune demyelinating polyradiculoneuropathy, and C8-T1 motor radiculopathy. None of patients had ocular or bulbar symptoms [Table 1]. Neurological examination was normal including distal muscle strength and reflexes. All patients underwent sensory and motor nerve conduction studies which were normal. No motor conduction blocks were detected on proximal stimulation and F wave latencies and persistence from upper limb nerves were also normal. Needle electromyographic examination (NEE) in patient one was normal. Patient two showed ill sustained fibrillation potentials in few muscles of the lower and upper

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limbs and face muscles - Not in any root distribution, with normal motor unit potentials, normal firing rate and a full interference pattern. In patient three, NEE showed small duration and short motor units – but with a very reduced interference pattern in the muscles of the forearm (extensors > flexors) along with ill-sustained fibrillation potentials. She had marked decrement on RNST in these muscles. NEE was normal in all other muscles. RNST testing was done as these findings could not explain the weakness reported by the patients and it showed decrement in all three patients, consistent with MG, with most marked decrement in the distal and semi-distal muscles. Ten seconds of exercise repaired the decrement and 1-min of exercise produced increased decrement-testing 2–3 min after the exercise. Patient three had decrement isolated to the semi-distal upper limb and lower limb muscles, with no evidence of decrement in the proximal limb muscles Figure 1. The patients underwent antibody testing for anti-AchR, which were positive. Table 1 summarizes the clinical and EDx findings. The patients were treated with steroids and acetyl choline inhibitors and all experienced improvement in symptoms. Two patients developed symptoms of weakness in face and lower limb muscles, 3 and 12 months after the onset of distal hand weakness.

DISCUSSION

Distal MG was first reported in 1998 by Janssen *et al*. as "Myasthenic hand."[1] Nations *et al*.[2] reported that 3% of 234 myasthenic patients had distal > proximal weakness by grade1 medical research council scale. Karacosta *et al*.[4] reported a case of MG with isolated hand weakness as the only initial presenting symptom. Carvalho and Geraldes[3] reported a case presenting with isolated hand weakness with MG and concluded that RNST should be included as part of routine EDx testing for weakness. Fearon *et al*.[7] reported a case similar in presentation to patient three in our series, with weakness of finger extensors and small short motor units on EMG previously diagnosed as a myopathy. Werner *et al*.[5] reviewed the frequency of distal MG among 84 patients over 20 years. They reported only 6–84 patients had distal weakness, of which this was the presenting symptom in just two patients. They also found that besides the pattern

Table 1: Clinical and laboratory observations

Patient	Sex	Age (years)	Presenting symptoms	Duration years	Weakness oriental	RNIST	AChR antibody nm/l Normal 0.0-0.04 nmol/L
1	Male	57	Asymmetric finger drop (L>R)	4	Nixie	Positive: EDC, El>APB Past exercise fatigue: TA Negative: Trapezius and nasals	54.3
2	Male	60	Difficulty buttoning shirt, counting money	1	None	Positive: APB>Trapezius and orbicularis oculi	50.8
3	Female	37	Difficulty plaiting daughters hair, drops objects held for a while	2.6	None	Positive: El, EDC>>. TA Negative in all other muscles	70.4

EDC: Extensor digitorum communis, EI: Extensor indicis, APB: Abductor pollicis brevis, TA: Tibialis anterior, RNST: Repetitive nerve stimulation test

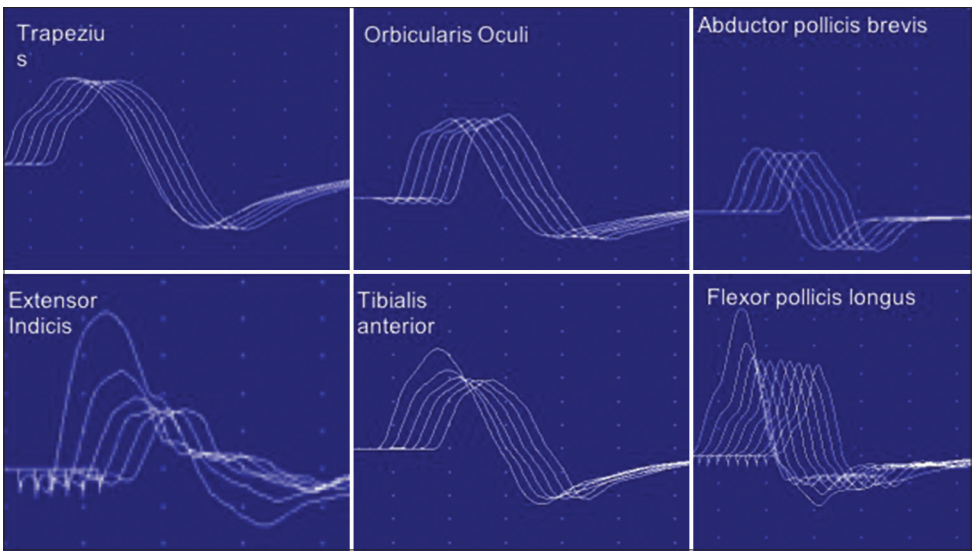

Figure 1: Repetitive nerve stimulation test: Patient 3. Note the decrement in the extensor indicis, flexor pollicis longus, and tibialis anterior muscles only

of involvement, the other EDx features of distal MG were identical to the classic disease. Rodolico *et al*.[8] reported three of 508 over 27 years had asymmetric distal hand weakness. All three patients in our series complained of predominant/isolated bilateral hand weakness and had normal neurological examination – What is important here is that, MG was not suspected as a clinical diagnosis and it required alert, protocol-based electrodiagnosis to document the condition using RNST. NEE showed ill-sustained fibrillation potentials in two patients This could be explained by "functional" denervation due to the reduction of the trophic effect of acetylcholine release on the muscle fiber membrane.[12] RNST was performed in these patients even though the history and examination was not classic for MG and there was no clinical referral as, our laboratory reflexes to RNST if other EDx tests are inconclusive, and this series exemplifies the importance of this protocol. MG is the greatest mimicker and one should employ a low degree of suspicion. To the best of our knowledge, there is no report of distal MG in the Indian literature.

CONCLUSION

Distal, asymmetric, hand weakness maybe a rare, first presenting symptom of MG. The electrodiagnostician must consider MG in the differential of such patients and perform an RNST when other tests are unrevealing.

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