Limb girdle myasthenia

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Pure limb-girdle type involvement without any oculobulbar impairment is an unusual presentation of acquired myasthenia gravis (MG). In view of the predominant proximal muscle weakness, many patients are diagnosed as myopathy or polymyositis despite a normal serum level of creatine kinase (CK).[1] The diagnosis of MG is established by the occurrence of a characteristic decremental muscular response to repetitive nerve stimulation (RNS), and by positive edrophonium test and acetylcholine receptor antibody (AChRab) assay.[2] We report here a 22-year-old woman with proximal limb weakness, that had existed since the age of 19.

She presented with proximal limb weakness. Symptoms had initiated 3 years ago. The weakness was predominantly in the upper limbs. Neurologic examination revealed bilateral deltoid and suprascapular muscle weakness. One year ago, she also started to notice weakness in lower limbs, thus, there was difficulty climbing stairs. She explained drop attacks due to fatigability. During the following period, facial muscles were involved, and she had difficulty in smiling, chewing, and closing her eyes. The clinical symptoms progressed without any fluctuation, and due to these findings myopathy was considered. On neurological examination, facial and proximal limb muscle weakness were found. She could hardly whistle, smile, and raise her eyebrows, therefore, she had a blurred face. There was no evidence of oculobulbar weakness like ptosis, diplopia, and nasal regurgitation. Deep tendon reflexes were normal; both plantar responses were flexor. Examination of sensory systems revealed no abnormalities. There was no aggravation in symptoms by provocative tests. Routine blood examinations and serum CK were normal. We could not find any signs of neuropathy/myopathy on electrophysiological investigation. The recording showed decremental response on the orbicularis oculi and extensor digitorum communis (EDC) muscles (**Figure 1**). The level of AChRab was 110 nmol/L (normal range: 0-0.4). These features were consistent with the diagnosis of MG. Treatment with acetylcholinesterase inhibitor (AChEI) was initiated with an improvement of weakness, especially in the facial muscles. Chest CT was normal. Thymectomy was applied after observation of symptom improvement with AChEI. Biopsy revealed thymic hyperplasia. In this case, weakness of facial and proximal limb muscles without any oculobulbar involvement and also a lack of myasthenic diurnal fatigability led us to diagnose limb girdle myasthenia.

The term 'myasthenic myopathy' was used, for the first time by Walton and Nattrass in 1954,[3] to define patients with proximal muscle weakness and fatigability, who responded to AChEI. Then this definition was replaced by the term 'limb-girdle myasthenia' (LGM), including familial and non-familial autoimmune cases.[4] Familial LGM usually begins in the first decade of life with involvement of the proximal muscles.[4,5] Extraocular muscles are not involved. Serum CK level is often increased. In this condition, the AChRab is negative and thymic alterations do not exist. A decremental response in proximal muscles is found on RNS. Muscle biopsy is characterized by the presence of tubular aggregates. Patients generally respond to AChEI.[4] Oh and Kuruoglu[1] described some cases of the non-familial autoimmune form. In this form, no patient had positive familial history, and the onset of the disease was in adulthood. The frequent association with thymoma, positivity of AChRab, and absence of tubular aggregates in skeletal muscle are the characteristics. The patients had a poor response to AChEI, but benefitted from immunotherapy.[1] In another report, the symptoms were confined to the extremities during the first months of disease in 10% of MG patients.[1] The chronic limb girdle form of MG was considered to be a MG variant. Oh and Kuruoglu[1] reported the percentage of chronic LGM patients as 3.8%. They all had evidence of limb girdle muscle weakness without oculobulbar involvement. In LGM, sparing of the oculobulbar muscles is the most important distinction from typical MG. There can be slight facial weakness and ptosis in some cases. Facial weakness imparts a distinctive physiognomy because of its insidious progress. The patients cannot laugh comfortably, they speak slowly, and can hardly whistle.[1,6]

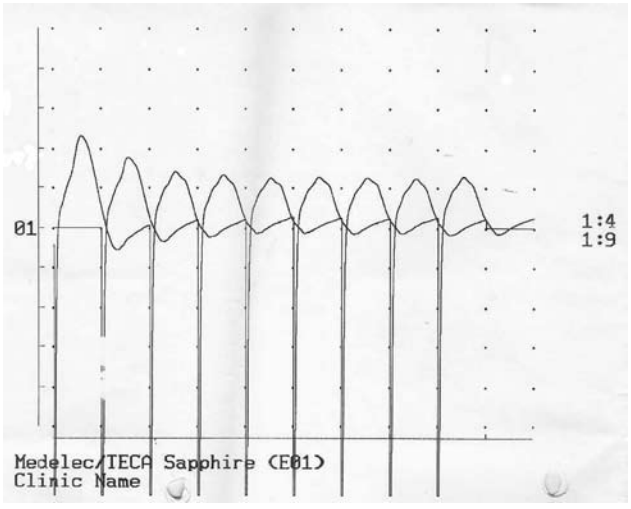

Figure 1 - Decremental response at low rate of stimulation on orbicularis oculi muscle.

Disease onset occurs between the ages of 14-42 in autoimmune LGM.[4] Symptomatology does not show fluctuations during the day, and there is no progression of weakness by exercise. Therefore, the initial diagnosis in these patients is distinct from MG. Myopathy is considered primarily.[2] Diagnosis is established by a positive decremental response on RNS. The AChRab is positive in most cases, and all patients respond to AChEI. Some cases improve with immunotherapy.[1,2,6] The nerve-muscle contact area at the LGM junction was only half of that found in controls, but the mean diameter of the LGM muscle fibers was 12% larger than that in the controls, thus, the LGM junction is inappropriately small for the size of the muscle fibers. Acetylcholine receptor number per junction was reduced in proportions to the size of the junction. Therefore, the density of receptors per unit area of synaptic contact could be assumed to be normal. Ultrastructural analysis of the postsynaptic region showed that the junctional folds are shorter and smoother than normal at some junctions.[6]

The illness had begun at the age of 20 years in our case. She had no family history. She had muscular fatigability with proximal muscle weakness without any oculobulbar involvement. We did not see progression of weakness by provocative tests. There were no diurnal fluctuations. Facial mobility and expression were altered, her usual smiling became strange. The RNS test was performed on EDC and orbicularis oculi. We tested the variation of compound muscle action potential amplitude at low and high rates of stimulation. The test could be considered positive for myasthenia if there were a reproducible decrement more than 10% between the first and fourth response. We suspected MG by a positive decremental response on RNS. She had anti AChRab and these findings supported the existence of autoimmunity. The diagnosis of non-familial autoimmune LGM was made on the basis of clinical manifestations and electrophysiological findings. Treatment with AChEI was started, and she responded to this therapy.

In conclusion, our observations confirm that, in the patients who present with persistent limb girdle involvement, without oculobulbar impairment, and with absence of typical clinical fluctuations, LGM must be considered in the differential diagnosis.

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