

Case Report

Juvenile myasthenia gravis

Prastiya I. Gunawan, Darto Saharso

Myasthenia gravis is a potentially serious but treatable autoimmune disorder characterized by weakness and fatigability of the voluntary muscles caused by auto-antibodies against nicotinic acetylcholine receptor (AChR) on the postsynaptic membrane at the neuromuscular junction.^{1,2} Its prevalence has been reported as 2–7/10,000 population in the UK and around 1.5/10,000 in central and western Virginia. Approximately 1% of patients are children.¹ Although many deviations may occur, most immune-mediated childhood myasthenia gravis can be divided into three categories: neonatal transient, neonatal persistent, and juvenile myasthenia gravis.¹

Myasthenia gravis used to be a very disabling and often fatal disease (hence, the name *gravis*) in the past. However, significant advances in its diagnosis and treatment have dramatically improve the prognosis and nearly all patients are now able to lead full, productive lives.^{2,3}

Case report

An 11 year-old girl was referred to the Neurology outpatient clinic in the Pediatric Department with suspected myasthenia gravis. Her main complaint was weakness since she was 10 years old. The weakness was sudden, usually after exertion. After resting a few seconds, her power improved. Sometimes, it started with difficulty to lift her upper eyelid and might end with falling. Her psychological development was normal. On physical

examination, she was an alert girl with body weight 46 kg. The pulse was 100/minute, respiratory rate 16/minute, blood pressure 110/80 mmHg and body temperature 36.7°C. The patient showed mild ptosis of the left upper lid with normal ocular movement (**Figure 1**).

Neurological examination revealed an alert girl with GCS 4-5-6. The pupils were symmetrical, 3 mm/3 mm with strong light reflexes. Meningeal signs were negative.



Figure 1. Mild ptosis of the left upper eyelid

From the Department of Child Health, Medical School, Airlangga University, Surabaya, Indonesia.

Reprint requests to: Prastiya Indra Gunawan, MD, Department of Child Health, Medical School, Airlangga University, Dr. Soetomo Hospital, Prof. Dr. Soetomo 6-8, Surabaya, Indonesia. Tel. 62-31-70584054. Fax. 62-31-5501748. E-mail: prastiya_ig@yahoo.co.id

Babynski and Chaddock reflexes were negative. Motoric evaluation showed no lateralization and no paresis, but a mild decrease of motoric function. The physiological reflexes were normal. The laboratory studies showed Hb 12.4 g/dL, leukocytes $5.7 \times 10^9/L$, platelet $199 \times 10^9/L$, Ht 31%, SGOT 12.8 U/L, SGPT 17.2 U/L, BUN 8.2 mg/dL, creatinin 0.64 mg/dL, potassium 4.3 mEq/L, calcium 10.1 mEq/L, sodium 142 mEq/L, glucose 75 mg/dL, TSH was 3.646 $\mu IU/mL$, FT₄ was 0.84 ng/mL.

Lumbosacral AP/lateral projections were normal. Chest roentgenogram revealed normal heart and lungs. No enlargement of thymus gland was found. We performed an ice pack test and prostigmine test; the results were positive. Repetitive nerve stimulation (RNS) on resting showed decrement 20%, contraction in 1 minute showed decrement 8.6% and 1 minute after contraction showed decrement 23%.

Based on the history, supported by the specific ice pack test, prostigmine test and EMG-RNS, the diagnosis of myasthenia gravis was established. The patient was treated with pyridostigmine-bromide 30 mg three times a day. On follow-up, her power increased. She could move well, walk, run and jump. She never falls again.

Discussion

The progression of weakness in myasthenia gravis usually occurs in a *craniocaudal direction*: ocular to facial to lower bulbar to truncal and limb muscles. The weakness of intercostal muscles and diaphragm leads to dyspnea on exertion or at rest. Breathlessness can develop suddenly over hours and these patients should be closely monitored with regular measurements of their forced vital capacity.^{2,4-6}

In our patient the progression of weakness also occurred craniocaudal, starting from the eyelids to trunk and limb muscles. There was mild weakness of intercostal muscles and diaphragm and she felt mild difficulty with breathing.

The tests for the diagnosis of myasthenia gravis are edrophonium (tensilon) test, ice pack test, and electrophysiological test. Edrophonium is an AChR inhibitor that works within a few seconds (30 seconds) and the effect lasts for about five minutes. It is administered intravenously. There should be a demonstrable

weakness to monitor the response. A fractionated dose is usually employed, beginning initially with 1–2 mg and the remaining 8–9 mg is given only if there is no response until 60 seconds after the first dose.^{3,7} Since edrophonium was not available in Indonesia, we changed to the prostigmine test. Prostigmine was given subcutaneously (usually in deltoid region) to the patient with generalized weakness. The test is considered positive if there is a definitive improvement in the weakness.⁷ The result in our patient was positive.

An ice pack test can be employed when ptosis is present. A number of small studies reported improvement of myasthenia ptosis following application of ice cube, wrapped in a towel or surgical glove, applied to the elevator muscle of eyelid for at least two minutes. The test is claimed to be both sensitive and specific for myasthenia.^{1,8}

The repetitive nerve stimulation test (RNS) shows progressive reduction in the amplitude of the compound muscle action potential from the fourth stimulation when a nerve is subjected to repetitive supramaximal electrical stimulations at a frequency of 3 Hz. If the reduction in amplitude of the compound muscle action potential is $> 10\%$, the test is called positive (a decremented response). Overall, sensitivity is about 75%.^{1,2}

In our case the result of RNS showed decrement more than 10%. The test is more likely to be positive on testing several muscles or when a weak muscle is tested. This test is virtually always positive in generalized myasthenia gravis.

Myasthenia gravis can be classified according to the age of onset, presence or absence of anti-AChR antibodies and severity. Based on the age of onset, myasthenia gravis can be classed as congenital, transient neonatal, juvenile or adult autoimmune. Transient neonatal myasthenia gravis is due to the transfer of maternal anti-AChR antibodies through the placenta which form a reaction with the AChR of the neonate. 10%–15% infants with these antibodies will manifest symptoms of myasthenia (hypotonic, weak cry, respiratory difficulty, etc) within the first few hours of life. Symptoms usually resolve spontaneously within 1–3 weeks, though temporary supportive treatment and pyridostigmine may be required.^{2,9-11}

Our case was classified as juvenile myasthenia gravis. The clinical symptoms began at 10 years. Juvenile myasthenia gravis has many parallels with adult

myasthenia gravis. Manifestations usually appear after 10 years of age, although in one study the mean age of onset was 7.7 years. The disease is more common in girls.^{1,10}

The treatment of myasthenia gravis involve three steps: (1) An initial treatment using acetyl cholinesterase inhibitors. We chose this step for our patient. However, sometimes this is not adequate. (2) An immunologically directed treatment is then added, either thymectomy or high dose corticosteroids. (3) In the long term, steroid-sparing medications are usually also added to facilitate the tapering phase. Short term therapies, that is, intravenous immunoglobulin or plasmapheresis—may be effective in the early stages of treatment, before thymectomy, or later during an exacerbation.^{2,3,12-14}

In our case, the patient was treated with pyridostigmine bromide 30 mg three times a day. Pyridostigmine is an AChR inhibitor, and thus increase the availability of acetylcholine to act on the AChRs. They are usually the initial drug used for treating myasthenia gravis and may be successful for mild disease. However, they do not modify the course of the disease and confer only symptomatic benefits.

Untreated myasthenia gravis has 1 to 10 year mortality of 20%-30%. However, with modern treatment, the prognosis is excellent with practically zero mortality.^{2,3} Considering her good clinical response with medication, our patient had a good prognosis.

In summary, A diagnosis of juvenile myasthenia gravis was established on the basis of history, clinical findings, and supported by the specific ice pack test, prostigmine test and EMG-RNS. The patient was treated with pyridostigmine bromide and resulted in a good response.

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