Myasthenia gravis (MG) is a chronic neuromuscular disorder with a tendency for remissions characterized by abnormal fatigability of the voluntary muscles which is worsened by muscular activity or improves with rest. The disease may be confined to a single group of muscles of progress to general paralysis which may be fatal in the absence of treatment. The basic defect in MG is impaired synaptic conduction at the cholinergic neuromuscular junction. The physiologic and pharmacologic phenomena confirming the neuromuscular junction to be the site of defect are used for its diagnosis and treatment. The patients respond well to cholinesterase inhibitors, when the curare test is positive, and when the electromyogram is characterized by gradual diminution on repetitive nerve stimuli.

Histopathologic examination of MG patients show dystrophic and dysplastic changes in the neuromuscular junctions. Lately a decrease in the level of the acetylcholine receptor in the postsynaptic membrane was demonstrated and it has also been shown that the size of the "packets" of acetylcholine released from the presynaptic membrane in MG are abnormally small although their number is normal. Evidence is accumulating that the disease is autoimmune in origin. In most cases there are changes in the thymus; thymectomy and especially corticosteroid treatment are of benefit and it is sometimes associated with other autoimmune diseases. Antibodies against muscle cells, "myoid" cells in the thymus, antinuclear factor as well as decrease in complement level were demonstrated in the serum of some MG patients. The patients' lymphocytes have cytotoxic effect on muscle and thymus cells in tissue culture and immunologic sensitivity to muscle, thymus and brain in the macrophage inhibition test.

MG is of particular interest to ophthalmologists since they are often able to diagnose its first manifestations, which are frequently ocular. Variable ptosis is the first symptom in almost half the cases and it subsequently appears in almost all of them. The ptosis is either asymmetrically binocular or monocular—a useful diagnostic sign being the lid twitch—occasionally lid retraction rather than ptosis may be present. External ophthalmoplegia with diplopia is the second most common sign of MG being its first manifestation in 35 percent of the cases and subsequently appearing in about 80 percent of them. The ophthalmoplegia is variable, usually asymmetric and occurs in almost any combination, horizontal deviations being most common. The extraocular muscles manifestations of MG may mimic any other motility disorder. No nystagmus is present and pupillary functions are usually normal although there are some reports of sluggish light response. The amplitude of accommodation is often reduced. Any other group of muscles can be involved in MG—most commonly affected are the muscles innervated by cranial nerves, especially the oropharyngeal and facial muscles. However, the respiratory
and limb musculature is also commonly affected.

The severity of the affectation varies from permanently mild forms to severe and fatal ones. The prevalence of the disease is about 2.4 per 100,000.2.4 MG in childhood is even rarer. Various surveys estimate that only 1-2 percent appear under two years of age, 2.7-7.3 percent appear under 10 years and 23.3-26.3 percent appear under 20 years.

Since the basic defect in MG is in the cholinergic synaptic transmission, it is possible to augment this mechanism by giving anticholinesterase drugs such as neostigmin or pyridostigmin. The dosage should be adjusted to achieve the best functioning results without causing parasympathetic side effects, e.g., bradycardia, bronchospasm, diarrhea, excessive salivation, and colic. Another very useful treatment is long-term high single dose—alternate day corticosteroids therapy.

Characteristically MG in infants and children presents itself first with ptosis and ophthalmoplegia, with generalized muscular weakness appearing later. Thus, in spite of the relative rarity of this disease in children, pediatric ophthalmologists should be particularly aware of MG and consider it in the differential diagnosis of ptosis and strabismus. Since treatment is effective in many cases, especially in the pediatric age group where even complete remission can be expected, early diagnosis can prevent a lot of unnecessary suffering from the affected children and in the severe cases, even be life saving. The two cases presented in this report are typical of late diagnosis of the disease with the resulting complications.

CASE REPORTS

Patient No. 1

A five-year-old child was admitted to the intensive respiratory care unit of the Hadassan University Hospital, Jerusalem, with respiratory failure. His past history as given by the parents was unremarkable except for a hospitalization for respiratory insufficiency in another hospital four months previously. He was then diagnosed as suffering from Guillain-Barre Syndrome. Upon direct questioning the parents admitted that the child was always considered a "weakling." They also noticed occasional ptosis, especially in the afternoons and evenings. Family history was noncontributory.

The present episode started with difficulties in swallowing and speaking which rapidly developed into extreme generalized muscular weakness and acute respiratory distress. On admission the child

Fig. 1. Patient 1. Four hours after 60 mg of oral pyridostigmin.
was lethargic, cyanotic and febrile with severe dyspnea and muscular weakness. Ptosis was not immediately observed because of his apathy. It was not possible to elicit any tendon reflexes. Other than these, there were no contributory diagnostic findings in the neurological, cardiovascular, gastrointestinal, and hematologic examinations. Anterior and posterior segments of the eyes were normal. Due to his general condition, it was not possible to perform ocular motility investigation. Blood, urine, and sputum cultures were negative as was chest radiography.

Laryngeal intubation was performed and the child was given intermittent positive pressure assisted respiration with the resulting improvement in his general condition and the state of his awareness. Then it became apparent that he flexed his neck muscles in order to be able to look around. The diagnosis of MG was suspected and a Tensilon test was performed and was strongly positive. The laryngeal tube was removed and therapy with progressively increasing doses of pyridostigmine bromide was started until a dosage of 60 mg, four times daily was reached. Each dose was effective for five to six hours as judged by the recurrence of the ptosis (Fig. 2).

**Patient No. 2**

A one-year-old female child was sent to the pediatric department of the Hadassah University Hospital, Jerusalem, for evaluation. Her parents gave a history of normal pregnancy, labor, and delivery. Her development was normal until the age of nine months when she was hospitalized elsewhere because of pyrexia, dyspnea and dysphagia. Pneumonia was diagnosed and she recovered rapidly when given antibiotic treatment. During the following few months she was recurrently hospitalized because of pneumonia.

The main complaint when examined by us was dysphagia. When the parents were asked about the obviously present ptosis, they said that it was present intermittently for the last few months but they ascribed it to the weakness resulting from her frequent illness. It was reported that the patient’s mother has a first cousin suffering from intermittent ptosis. The cousin was not available for examination. Physical examination revealed no cardiovascular, respiratory, or intestinal anomalies. No ocular or neurological anomalies were found except for the bilateral ptosis; motor and sensory functions were intact, reflexes and muscle tone were normal and there were no fasciculations, tremor or ataxia. Skull x-ray, electroencephalogram, electromyogram of arm muscles, and cerebro spinal fluid were within normal limits. Since the only anomalies present were the dysphagia and ptosis, she was given one mg Tension intramuscularly and within 90 seconds the ptosis disappeared completely. The diagnosis of MG became apparent and she was given maintenance of

**DISCUSSION**

The two children described in this report probably represent the two types of MG described by Bundy. Case 1 is of the juvenile type with onset over two years of age which resembles the adult type of MG. This type has no clear-cut inheritance pattern, is probably autoimmune in origin, and is associated with increased incidence of thyroid dysfunction, although this facet of the disease was not demonstrated in our case.

Case 2 represents the milder infantile type which is thought to have either an autosomal recessive or multifactorial genetic combined with environmental etiology. Unfortunately, we were not able to examine the mother’s first cousin who was described to have similar symptoms.

Both cases, however, have some features in common. They were treated incorrectly for a considerable part of their life because their disease was not diagnosed due to the rarity of

![Fig. 2. Patient 2. Eight months of age before diagnosis was made. The ptosis is obvious.](image-url)
MG in children and because the ptosis was not noticed or taken into account. Both had myasthenic crises, either precipitated or complicated by respiratory tract infections. This crisis was especially severe in Patient 1 who had to be given intensive respiratory care and was apparently saved by timely diagnosis, suggested by his ptosis.

The first symptoms and signs of MG in children are often ocular and thus the ophthalmologist should always consider this disease in the differential diagnosis of ptosis and external ophthalmoplegia. The hallmark of MG is, of course, its exacerbation with fatigue and therefore detailed history taking is of paramount importance. Any mentioning by the parents of worsening of the condition in the evening should raise the suspicion of MG. A useful procedure is to examine the patient both in the morning and afternoon and compare the results.

No clear-cut guide lines can be given for the diagnosis of myasthenic external ophthalmoplegia since this condition can mimic any type of oculomotor disturbance. However, accurate measurements of the diurnal variation of the angle of heterotropia and in older children the diplopia should raise the suspicion of MG when other types of intermittent and cyclical heterotropias were ruled out. When dealing with a case of ptosis, the absence of furrowing of the forehead, so typical of other patients with ptosis, is a useful sign of MG, as is the lid twitch sign. 10 However, in cases of myasthenic ptosis the main diagnostic feature is the diurnal fluctuation of the width of the palpebral fissure.

In any case, whenever there is any suspicion of MG in a child, the Tensilon test should be performed by intravenous injection of 0.5 to 1.0 mg of edrophonium chloride and observing the resultant changes in the patient’s muscular activity. Electromyography 10 is rarely required.

The cases described in this report serve to call the attention of pediatric ophthalmologists to the vital importance of early diagnosis of MG, the possibility that ptosis and external ophthalmoplegia can be caused by MG, the relatively simple diagnosis of this disease, once considered, and to his ability to save the child and his family a lot of unnecessary suffering by accurate and timely diagnosis.

SUMMARY

A boy aged five and a girl aged one year suffering from myasthenia gravis are described. Both cases had respiratory complications and were treated erroneously until their ptosis was noticed and the diagnosis of myasthenia gravis confirmed.

The etiology, types, symptomatology, and treatment of the disease are described. Attention of the pediatric ophthalmologists is called to the fact that they should consider myasthenia gravis in the differential diagnosis of ptosis and external ophthalmoplegia.

REFERENCES


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