Paradoxical reversal of ptosis in myasthenia gravis by edrophonium administration

Sir: Paradoxical responses, worsening and reversal of ptosis, in myasthenia gravis can sometimes be seen following administration of edrophonium chloride (Tensilon), but their precise mechanisms are not fully understood. We report two patients with ocular myasthenia gravis whose ptosis reversed paradoxically by the intravenous administration of edrophonium, and discuss the possible mechanisms.

**Patient 1.** A 44 year old woman, had a left severe ptosis which developed about a year after thymectomy. Both anticholinesterase (AChR) antibody and anti-striational antibody tests were positive. Early in the morning she always found her right eyelid transiently ptotic, which later in the day became seemingly normal, and left severe persistent ptosis developed. We also confirmed such a spontaneous reversal of ptosis even during examination. Neurological examination did not reveal other muscle weakness except for that of the left eyelid closure. The intravenous administration of 5 mg edrophonium resulted in a paradoxical reversal of ptosis. The elevation of the eyebrow was also reversed (fig). She did not receive any anticholinesterase medication.

**Patient 2** was an 11 year old girl who had developed left ptosis, diplopia and photophobia since the age of 5 years. Neurological examination at the time of onset revealed bilateral ptosis and left pseudointernuclear ophthalmoplegia. These signs were relieved by edrophonium injection. Furthermore, the cold test also alleviated her ptosis. Prednisolone therapy (20 mg every other day) improved her ocular symptoms moderately. At the age of 11 an exacerbation of left ptosis and limited ocular movement developed following physical exertion. She was aware that her right eyelid was ptotic when she awoke in the morning and that soon after the ptosis shifted from right to left spontaneously. By the intravenous administration of 2 mg edrophonium, her left eyelid became rather retracted and her ptosis shifted from left to right. She did not receive any anticholinesterase medication. The intravenous methylprednisolone pulse therapy led to a marked improvement of her ocular abnormalities.

Worsening of ptosis after the injection of edrophonium has generally been considered to be a negative response. Reversal of ptosis was interpreted as follows: the ptotic eyelid developed retraction and the normal eyelid became ptotic. In our patients, however, the eyelid which became ptotic after the edrophonium injection was not normal but was the affected one which drooped early in the morning and after a short sleep. Spontaneous shift of ptosis could be explained by Hering’s law of bilateral and equal levator innervation: fatigability of one eyelid was greater than that of the other, thus resulting in persistent ptosis of one eye and the other eyelid became seemingly normal because of the central compensation for the ptosis.

When the edrophonium test was performed at this point, its effect was more prominent on the eyelid with an active lesion, leaving the other eyelid with a relatively inactive lesion ptotic. The edrophonium-induced eyelid retraction in patient 2, possibly associated with increased presynaptic ACh release to compensate for the impaired AChR prior to the test, may partially be responsible for the contralateral eyelid dephosphatase by Hering’s law. The ptosis of our patients was not induced by an overdose of anticholinesterase since they received no oral anticholinesterase medication. We believe that the present observation may provide one of the plausible explanations for the edrophonium-induced reversal of myasthenic ptosis.

**References**