CLINICAL VIGNETTE

Cranial nerve VI palsy as a presentation of Myasthenia Gravis

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A 53-year-old, right-handed male presented for evaluation after onset of cranial nerve VI (abducens nerve) palsy. He developed acute onset of double vision while driving three weeks before. Only his left eye was affected. He could see clearly if he covered his left eye and denied eye pain or photophobia. He saw an ophthalmologist and was diagnosed with a cranial nerve VI palsy. At that time, the patient also developed shooting pains down his left arm and paresthesia in digits two, three, and four on the left hand. The left upper arm and hand felt mildly weak. He denied any injuries to the neck.

The patient also reported intermittent changes in phonation with prolonged talking. He developed a more nasal quality to his speech during these episodes. He also noted mild, intermittent dysphagia over the previous month.

On physical exam, he was alert and fully oriented. Vital signs were within normal limits. His speech was fluent, and he was able to recall 3/3 items at one and five minutes. On cranial nerve examination, both pupils were 3mm in size and were equal and reactive to light. (CNII) Fundoscopic exam was normal and showed sharp discs bilaterally. Cranial nerves III and IV were intact except for mild ptosis of the bilateral upper eyelids. The patient had difficulty abducting the left eye, which worsened with distance fixation. (CNVI) Corneal reflexes were present bilaterally. (CNV) Cranial nerve VII testing revealed normal strength of the orbicularis oculi muscles along with a symmetric smile. Cranial nerves IX and X were intact with normal gag reflex and normal elevation of the palate. Cranial nerves VIII, XI, and XII were also intact.

He had normal muscle tone and bulk of the upper and lower extremities. On the left arm, triceps muscle strength was 4-/5, wrist extension was 4+/5, and finger extension was 4+/5. Biceps, brachioradialis, patellar, and ankle reflexes were 1+ bilaterally. The triceps reflex was 0 on the left and 1+ on the right. Romberg's sign was negative, and he had a normal gait. His sensation to light touch was symmetric and intact on bilateral upper extremities. He had normal range of motion in the cervical spine. Cardiovascular, respiratory, and abdominal exams were normal.

Labs and Studies

The initial lab results included a mildly elevated sedimentation rate of 29mm/hr, Hgb A1c of 6.4%, and a fasting glucose of 105 mg/dL. TSH was normal. The acetylcholine receptor antibody was positive at 0.80 nmol/L (positive range > or =0.50nmol/L). The assay for antibodies to muscle-specific tyrosine kinase was negative. Antibodies to striated muscle were detected with a titer of 1:40 (the positive range is $\geq$ 1:40).

MRI of the orbits was normal. Cerebral MR angiogram showed a 2.5mm aneurysm of the posterior communicating artery. The MRI of his brain was normal, and bilateral carotid dopplers were negative for signs of significant carotid stenosis. An MRI of his chest was negative for thymoma.

The MRI of his cervical spine showed a dessicated C5-6 disc space with a 2-3mm right lateral bridging osteophyte and moderate to severe right C6 foraminal stenosis. At the C6-C7 disc space there was a 2mm right proximal foraminal protrusion with moderate to severe right C7 foraminal stenosis and mild to moderate left foraminal stenosis. There was no central canal stenosis.

Initial Treatment Course

The patient was diagnosed with myasthenia gravis and a separate C7 radiculopathy. He was started on pyridostigmine, 60mg three times a day. The C7 radiculopathy improved with naproxen and physical therapy with decreased arm pain and improved muscle strength. On follow up, left triceps muscle strength was 5-/5 and left wrist extension and finger extension 5/5. The left triceps reflex remained absent.

Discussion

Myasthenia gravis (MG) is an autoimmune condition that attacks the neuromuscular junction.[1] Antibodies at the postsynaptic membrane lead to crosslinking of antigens, activation of complement, and degradation of proteins to ultimately cause muscle weakness and fatiguability.[2] Approximately 80% of patients with myasthenia gravis have antibodies to nicotinic acetylcholine receptors (AChR-Ab).[3] AChR-Ab testing has high specificity of .97 to .99 for ocular and generalized myasthenia gravis.[4] Of the 20% of individuals with MG who are not seropositive for acetylcholine receptor antibodies, many have antibodies against muscle-specific receptor tyrosine kinase (MuSK).[3] An individual with myasthenia gravis who lacks AChR-Abs is considered antibody negative or seronegative.[5]

Our patient was seropositive for AChR-Abs and negative for MuSK Abs, which is the classic presentation of myasthenia gravis. MG is further divided into early-onset MG if symptoms start before age 50 or late-onset MG if symptoms develop at age 50 or later.[6] Our patient had late-onset MG. Late-onset MG presents certain challenges as patients are

more likely to have comorbidities such as diabetes and osteoporosis, which can increase the adverse effects of treatments such as corticosteroids.[7] However, the risk of myasthenic crisis appears to be similar between early-onset MG and late-onset MG.[7]

Our patient had an atypical presentation because his initial symptom was an isolated cranial nerve VI palsy. Cleary et al[8] examined the pattern of extraocular muscle impairment for 49 patients with MG. They found that 72% of patients had involvement of bilateral extraocular muscles (EOM) and the majority of patients had weakness of both horizontal and vertical eye movements.[8] Only 4% of patients presented with a cranial nerve VI palsy.[8]

Nontraumatic cases of cranial nerve VI palsy are more likely to have a vasculopathic etiology.[9] Nair et al[9] reviewed 95 nontraumatic cases of cranial nerve VI palsy. More than 50% were secondary to vasculopathic causes with underlying diabetes or hypertension.[9] The remaining cases that were not congenital were secondary to aneurysm, tumor, tuberculosis, idiopathic intracranial hypertension, or Tolosa-Hunt syndrome.[9]

In addition to the atypical presentation of an isolated cranial nerve VI palsy, our patient subsequently developed left arm symptoms including involvement of proximal and distal muscles. MG is more likely to present with proximal weakness than distal weakness, but when distal weakness is present, it is more likely to impair the finger extensors.[10] Our patient had weakness of the finger extensors on the left hand in addition to proximal weakness of the triceps muscle. However with the decreased triceps tendon reflex and the findings on the MRI of his cervical spine, some of his arm symptoms are likely related to cervical foraminal stenosis.

Fifty to sixty percent of individuals who present with ocular symptoms will progress to have generalized MG within 2 years.[11] Treatments such as azathioprine, acetylcholinesterase inhibitors, thymectomy, and corticosteroids are used to manage symptoms and try to prevent the progression to generalized MG.[11]

Our patient was treated with an acetylcholinesterase inhibitor. Acetylcholinesterase inhibitors improve visual impairment in 20-40% of individuals with ocular myasthenia.[11] However, they do not prevent the disease from becoming generalized.[11] Corticosteroids and azathioprine may reduce the risk of progression to generalized MG.[11] There is still debate regarding thymectomy treatment for individuals who have late-onset MG but without a thymoma on imaging.[12] However, Uzawa et al[12] showed higher remission rates and better symptom control after thymectomy particularly when histopathology of the thymus showed thymic hyperplasia. Randomized controlled trials regarding treatment options for myasthenia gravis are lacking,[11,13] and we eagerly await further research to help manage this difficult disease.

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