Plus-minus lid syndrome with ataxia and severe apathy—A rare manifestation of midbrain infarct

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ABSTRACT

Plus-minus lid syndrome is a rare manifestation of midbrain infarct, characterized by ptosis of one eye and lid retraction in the other eye. It has also been described in ocular myasthenia gravis, orbital myositis, or after lesions of the oculomotor nerve. Our patient was a 55-year-old man with hypertension and atrial fibrillation, who presented to us with acute onset left-sided ptosis and right-sided eyelid retraction. He was apathic and had right-sided ataxia. His MRI of the brain showed acute infarct involving the paramedian midbrain. To our knowledge, severe apathy and resultant executive function disorder have not been described previously in a patient having plus-minus lid syndrome with ataxia.

KEY WORDS: Apathy, ataxia, midbrain, plus-minus lid syndrome

Introduction

Midbrain infarcts can present with a wide variety of symptoms. Particular syndromes associated with midbrain infarction include the Weber, Claude, Benedikt, Nothnagel, and Wernekink commissure syndromes. Plus-minus lid syndrome, a rare manifestation of midbrain infarct, is characterized by unilateral ptosis and contralateral lid retraction. Plus-minus lid syndrome associated with ataxia has been previously reported in midbrain infarcts. An extensive PubMed search revealed only three reported cases of plus-minus lid syndrome with ataxia due to midbrain infarction. However, to the best of our knowledge, severe apathy and resultant executive function disorder have not been described previously in a patient having plus-minus lid syndrome with ataxia.

Plus-minus lid syndrome is an acquired neurological abnormality of eyelid position, characterized by unilateral ptosis and contralateral lid retraction. It was originally described as a palpebral plus-minus syndrome by Gaymard et al. in 1992, in a patient with midbrain infarct. It is usually caused by injury to the third nerve fascicle and the nucleus of the posterior commissure, although it has also been described in ocular myasthenia gravis. It has been previously described in paramedian mesencephalic-diencephalic lesions. We hereby report the case of a 55-year-old man who presented with plus-minus lid syndrome with ataxia, severe apathy and resultant executive function disorder.

Case History

A 55-year-old man, with a background history of systemic hypertension, who was working abroad was found lying on the floor in a drowsy state by his roommates. He was noted to be slow to respond to their queries and would reply only on repeated coaxing. He was noted to have drooping of the left eyelid and squint. When made to walk, he was swaying to the right side. He complained of binocular diplopia with a vertical separation of images. There was no history of headache, vomiting, fever, or limb weakness. After an initial evaluation...
abroad, he was brought to Kerala, his hometown, for further evaluation.

On examination in the neurology ward, he was conscious, had severe apathy and had to be coaxed to answer queries. His comprehension was normal. His attention was impaired. On neuropsychological evaluation, he was noted to have an impaired fund of knowledge, problem-solving, abstract-thinking, and motor Luria test. Trail A test was abnormal, as was the graphic Luria test [Figure 1]. All these abnormalities were indicative of a frontal lobe dysfunction. Cranial nerve examination revealed ptosis of the left eye (indicating weakness of levator palpebrae superioris), with retraction of the right eyelid [Figure 2]. The retraction, however, did not reduce when the left eyelid ptosis was manually raised. Bell’s phenomenon was not noted. The adduction, elevation, and depression of the left eye was abnormal, suggestive of the involvement of the third cranial nerve. Pupils were bilaterally equal in size and reacting to light. There was no papilledema. Examination of other cranial nerves and as motor and sensory systems were normal. He had right-sided cerebellar signs, evidenced by right finger nose incoordination, impaired right heel-knee test and swaying to right on tandem walking. He was detected to be in atrial fibrillation at admission. MRI of the brain was done and he was detected to have a paramedian midbrain infarction [Figure 3]. He was started on an antiplatelet, statin, and supportive physiotherapy at admission. He was initiated on oral anticoagulants after a week in view of atrial fibrillation. He improved symptomatically after a week, with a modified Rankin score of 2 at discharge. On follow-up, 2 weeks later, his apathy had improved, however, eye signs were persisting.

**Discussion**

Unilateral ptosis and contralateral eyelid retraction were originally described as plus-minus lid syndrome by Gaymard et al. in 1992.\(^1\) It has also been previously described in ocular myasthenia gravis, orbital myositis, or after lesions of the oculomotor nerve.\(^3,4\) The muscles mediating the elevation of the eyelids are the Muller’s muscle, supplied by the sympathetic and the levator palpebrae superioris, supplied by the oculomotor nerve.\(^3\) The oculomotor fascicles supplying the levator palpebrae superioris arise from a single medial nucleus called the central caudal nucleus, a subdivision of the oculomotor nuclear complex, located ventral to the aqueduct in the midbrain.\(^5\) The nucleus of the posterior commissure, located in the dorsal midbrain, sends inhibitory fibers to the central caudal nucleus, thus preventing retraction of the eyelids. Lesions of this structure result in disinhibition of levator palpebrae superioris bilaterally, resulting in eyelid retraction.\(^6\) When the oculomotor fascicle is also involved, the ipsilateral eyelid retraction is masked by the ptosis resulting in a plus-minus lid syndrome. Yet another mechanism for contralateral lid retraction has been explained by the Hering’s law of equal innervation. Here, the retraction occurs as a mechanical effect secondary to ipsilateral ptosis; in such case, on raising the ptotic lid manually the contralateral retraction corrects itself, which was not the case in our patient.\(^6\) The contralateral ataxia was attributed to the involvement of the superior cerebellar peduncle (Claude syndrome).\(^1\)

Our patient had severe apathy and executive function disorder. Apathy is usually associated with disruption particularly of medial frontal circuit/the anterior cingulate circuit. However, task-based fluorodeoxyglucose positron emission tomography studies have shown that patients with apathy had lower activation of the ventromedial prefrontal cortex, striatum, amygdala, and midbrain. The midbrain is the site of the ventral tegmental area (VTA), a key source of dopaminergic projections to the nucleus accumbens and to the prefrontal cortex.\(^7\) Hence, lesions affecting the midbrain can result in amotivational syndrome and apathy. Hoffman et al., in their study on cognitive dysfunction in isolated brainstem strokes,
using single-photon emission computerized tomography identified that frontal lobe dysfunction was seen in 5 out of 73 patients, of which only one had infarct involving the midbrain.\[8\] In the study by Fu et al., data from 34 patients with isolated brainstem infarction revealed that mild cognitive impairment (MCI) was noted in all, and that visuospatial, attention, linguistic, and emotional disturbances may occur after an isolated brainstem stroke.\[9\] Garrad et al. have reported that in seven consecutive patients referred to a neurological rehabilitation unit with lesions limited to brain stem structures, all were shown to exhibit deficits in at least one domain of cognition.\[10\] To the best of our knowledge, such presentation of the plus-minus syndrome with contralateral ataxia and severe apathy has not yet been reported.

Figure 3: Diffusion-weighted MRI brain sequences showing acute infarct involving paramedian midbrain

Declaration of patient consent
The authors certify that appropriate patient consent was obtained.

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Conflicts of interest
There are no conflicts of interest.

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