Isolated sixth nerve palsy: An unusual presenting diagnosis of multiple sclerosis

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Learning Points

- Multiple sclerosis can present as isolated sixth nerve palsy especially in younger patients
- Timely MRI should be performed in young patients with sixth nerve palsy to detect any brainstem lesions or demyelinating lesions
- Careful history, examination and radiological evidence are important to establish a diagnosis of MS

Case Presentation

A woman in her 30s presented to the ophthalmology department with new onset painless visual disturbance. She reported an eight-day history of acute onset horizontal diplopia on right lateral gaze. There was no further focal neurology reported. There were no red-flag symptoms for raised intracranial pressure suggestive of space-occupying lesion.

She had a known history of sensorineural hearing loss which was investigated as a child, and the cause of it was thought to be hereditary. She does not take any current medications. Family history revealed that her maternal grandmother experienced symptoms suggestive of rheumatoid arthritis. She does not smoke or drink alcohol.

On examination, her visual acuity was 6/6 in both eyes. She did not have a relative afferent pupillary defect or colour vision deficiency. She had a right head turn with a small right esotropia. There was a large abduction deficit of the right eye on right gaze. There was no evidence of optic nerve swelling or atrophy. A full neurological examination was unremarkable. Limitation of right abduction on dextroversion was suggestive of right lateral rectus underaction.

From the history and examination, a clinical diagnosis of isolated right sixth nerve palsy was made.

Investigations

Blood tests demonstrated normal full blood count, coagulation screen, inflammatory markers, and renal function.
Immunology screening tested negative for connective tissue disease and neuromyelitis optica. Immunoglobulins blood test did not demonstrate any positive findings. Atypical infection screen tested negative. Protein electrophoresis did not demonstrate any monoclonal bands.

Magnetic resonance imaging (MRI) head in FLAIR sequences demonstrated multiple hyperintense plaques (see figures 1-6). There was no evidence of infarct or haemorrhage. The findings were highly suggestive of demyelinating disease.

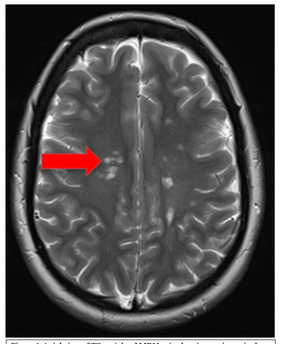


Figure 1: Axial view of T2-weighted MRI brain showing periventricular plaques (red arrow)in bilateral cerebral hemispheres, juxtacortical plaques in bilateral front and left anterior temporal areas.

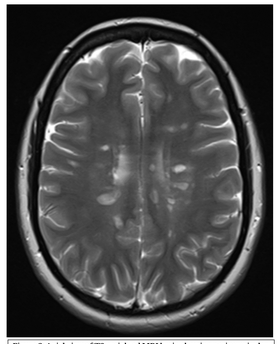


Figure 2: Axial view of T2-weighted MRI brain showing periventricular plaques in bilateral cerebral hemispheres, juxtacortical plaques in left parietal area.

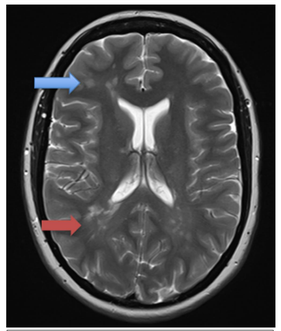


Figure 3: Axial view of T2-weighted MRI brain showing juxtacortical plaques in left parietal (blue arrow) and left anterior temporal (red arrow) areas.

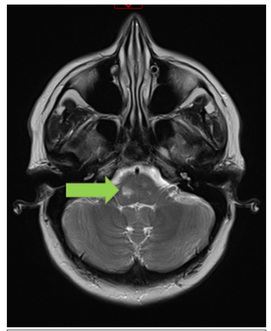


Figure 4: Axial view of T2-weighted MRI brain showing bilateral pontine lesions(Green Arrow).

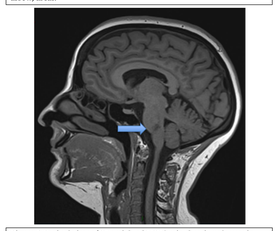


Figure 5: Sagittal view of T1-weighted MRI brain showing plaques in splenium of corpus callosum, left cerebral peduncle and left pons (blue arrow).

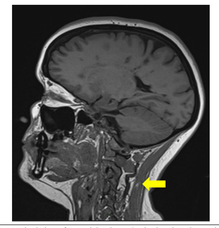


Figure 5: Sagittal view of T1-weighted MRI brain showing plaques in upper cervical cord (yellow arrow).

Differential Diagnosis

Sixth (abducens) nerve palsy is an ocular clinical finding with varied aetiology including stroke, trauma, infection, vascular disease, to space-occupying lesions.(1)(2)

Initial fundoscopy and ocular computed tomography (OCT) are useful investigations to investigate for papilloedema or evidence of retinopathy. There was no evidence of papilloedema or retinopathy suggestive of raised intracranial pressure in intracranial disease or underlying vascular disease respectively.

Baseline bloods including inflammatory markers were requested to screen for infection. Clinical observations and findings did not suggest intracranial or systemic infection. The baseline bloods demonstrated normal inflammatory markers. Atypical immune screen was undertaken to test for Lyme's disease as patient reported prior tick bite in previous 12 months; Borrelia burgdorferi antibodies were negative.

Patient had no history of migraines. There was no evidence of prodrome or headache prior to visual disturbances. There were no additional focal neurological deficits. There was no history of acute head trauma.

There was no personal or familial autoimmune history. There was no indicative signs or symptoms of connective tissue disease prior to symptom onset.

Cross-sectional imaging was then requested to assess for acute organic disease. MRI head was completed and did not demonstrate any evidence of infarct or haemorrhage.

In a young patient, female, European descent, with new onset of ocular disease with no evidence of ocular pathology on fundoscopy or OCT, demyelinating disease must be excluded. Further cross-sectional imaging in MRI head demonstrated multiple widely disseminated plaques. The demonstrable clinical episode coupled with the MRI head findings would be consistent with a diagnosis of multiple sclerosis.

Treatment

The patient was subsequently started on a five-day oral course of 500mg Methylprednisolone on the recommendation of the Neurology team. Intravenous (IV) steroids were not started given her symptoms were not severe enough requiring admission and IV treatment. She was additionally referred to orthoptics for co-supportive care of sixth nerve palsy with optical prisms.

The patient was followed up by the Neurology team, a week following discharge from ophthalmology, who agreed on the working diagnosis of multiple sclerosis..
She was commenced on a further short course of high dose oral steroids. Her sixth nerve palsy had resolved after completion of the steroid course.

Discussion

Brainstem involvement is not uncommon in MS. Isolated sixth nerve palsy as the presenting symptom or sign for MS is quite rare, with a prevalence of 0.4% to 3.2%[3, 4].

Annual incidence of sixth nerve palsy is 11.3/100000[5]. A review by Elder et al showed high frequencies of traumatic (5–20 %), microvascular (8–36 %) and undetermined (22-30%) causes[6].

In patients older than 50 years old, microvascular causes such as hypertension, diabetes and atherosclerosis are usually attributed to the cause of sixth nerve palsy. However, in patients younger than 50 years old, a wider differential diagnosis including MS, sarcoidosis, vasculitis, infections (viral, Lyme disease, syphilis), nasopharyngeal carcinoma should be considered[6-10]. In a case series, 8% of the new sixth nerve palsy were associated with MS, only 3.2% of the cases were presenting symptoms in MS and two patients were younger than 50 years old[5]. In a retrospective, non-comparative case series of 45 patients, aged 20 to 50 years old with non-traumatic, sixth nerve palsies, 33% of patients had a central nervous system mass lesion, 24% had MS, 13% are idiopathic, and 9% are due to viral infection. Among the 11 patients who had MS, 8 of them presented initially with sixth nerve palsy associated with facial numbness and optic atrophy[11].

Our patient presented with right sixth nerve palsy with no brainstem or cerebellar symptoms. MRI showed demyelinating lesion in the pons with other demyelinating lesions disseminated in space. The location of the lesion in the pons was consistent with her sixth nerve. The nucleus of the sixth nerve is in the pons near the floor of the fourth ventricle. It runs anteriorly and medially as a compact bundle containing motor neurons, where the nerve exits the pons. It then projects to the contralateral medial rectus subdivision of the oculomotor nerve nuclear complex via the medial longitudinal fasciculus[4, 12]. On MRI, our patient's lesion appeared to be in the fibre tract of the sixth nerve as it emerges from its nucleus, which would explain her lateral gaze palsy. In this case, there was a pontine lesion seen alongside with demyelinating lesions disseminating in space.

In conclusion, isolated sixth nerve palsy as the presenting sign of MS is rare. There is an extensive list of differential diagnoses of non-traumatic sixth nerve palsy. A diagnosis of MS should be suspected in all patients with this presentation, particularly in those under the age of 50. We recommend performing timely MRI can help to clarify the aetiology in such cases.

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