Plus Minus Syndrome – A case report

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Introduction

Plus minus lid syndrome originally described by Gaymard et al as palpebral plus minus syndrome is an acquired neurological abnormality of eyelid position which is associated with unilateral ptosis with contralateral eyelid retraction. This association has been described in ocular myasthenia, after lesions of oculomotor nerve, ocular myositis and paramedian mesencephalic-diencephalic lesions. Contralateral retraction may also occur as a mechanical effect secondary to ipsilateral ptosis (Hering’s Law). In such cases on raising the ptotic lid manually the contralateral retraction corrects itself.

Plus minus syndrome associated with Wernicke’s encephalopathy is an unusual presentation. In 1881 Carl Wernicke described an illness of sudden onset of ophthalmoplegia, mental confusion and gait ataxia in three of his patients, out of which two were alcoholics and one was a young female who had persistent vomiting. This was associated with optic disc swelling and retinal haemorrhages. All the three patients died and their autopsy confirmed haemorrhages affecting the grey matter around the third and fourth ventricles and aqueduct of sylvius. Later this syndrome was named as Wernicke’s encephalopathy precipitated by acute thiamine deficiency.

Case report

A 44 year old male with history of chronic alcoholic cirrhosis and portal hypertension was admitted under gastroenterology department in our hospital with haemetemesis and hepatic precoma. He was treated with anti coma measures and banding for oesophageal varices. When he recovered from precoma stage he complained of diplopia and decreased vision in left eye. Hence he was referred to ophthalmologist for evaluation.

On examination the patient was in a confused state with gait ataxia, and complained of diplopia on looking down. Vision in the right eye was 6/60 and left eye was less than 2/60. There was mild ptosis in right eye and left eye showed lid retraction with hypo and exotropias. In primary position and on vertical gaze there was upbeat nystagmus. Vertical eye movements were restricted but horizontal eye movements were normal. Vertical gaze palsy was noted for both down and up gaze. Right pupil was 3mm sluggishly reacting to light, left pupil was 5mm in size and showed afferent pupillary defect. Anterior and posterior segment examinations were otherwise normal. No light near dissociation was noted. Colour vision was defective.
MRI showed the following findings. Focal altered signal intensity was noted in both basal ganglia in midbrain superior to aqueduct with sparing of red nucleus appearing heterogeneous on T2 and FLAIR sequences (peripheral hyper intense with central hypo intensity)

Based on the history, clinical findings and MRI report patient was diagnosed to have Wernicke’s encephalopathy with plus minus syndrome and treated with injection IV thiamine 100mg in 100ml normal saline for 3 days followed by oral thiamine 75mg one tab twice daily for four weeks. He was also given nutritional therapy including folate and Vitamin B12 injections.

Patient improved symptomatically in a week’s time there was no obvious ptosis in right eye on discharge but nystagmus, gaze palsy and pupillary abnormalities persisted even after fourth week. Vision improved to 6/6 partial in right eye and with pin hole 6/6 partial in left eye. Colour vision improved to normal.

**Investigations**

Wernicke’s encephalopathy is a clinical diagnosis though brain MRI can be very helpful. MRI show signal abnormalities on T2 weighted, fluid attenuated inversion recovery (FLAIR) and diffusion weighted images in the periaqueductal regions, medial thalami and bilateral mamillary bodies. The lesions sometimes show contrast enhancement. The signal abnormalities typically resolve completely with treatment but shrunken mamillary bodies may be seen as a residual finding. The CSF is either normal or show mild elevation in protein.

In the case discussed the patient had elevated liver function tests, increased mean corpuscular volume, raised uric acid and triglycerides with low serum potassium and magnesium showing chronic alcoholic syndrome. In non alcoholic patients measurement of erythrocyte transketolase activity coefficient greater than 15-20% suggesting thiamine deficiency or urinary thiamine excretion can be used for confirmation.

**Discussion**

Midbrain lesions can follow many causes like hydrocephalus, stroke, tumours, encephalitis, trauma, AV malformations, multiple sclerosis and Wernicke’s encephalopathy. The common ocular findings include weakness of abduction, gaze evoked nystagmus, primary position vertical nystagmus, impaired vestibular responses, INO, horizontal and vertical gaze palsies that may progress to total ophthalmoplegia. Imaging studies show unilateral paramedian lesions, usually infarctions, dorsal and rostral to the red nucleus in
the area of the nucleus of posterior commissure, extending ventrocaudally to the fascicle of the oculomotor nerve on the ptotic side. The affected areas of the brain stem contain neurons that use high amount of glucose. Thiamine pyrophosphate is an essential coenzyme for glucose metabolism. Impairment of aerobic glucose metabolism can affect the nervous system quickly. In the reported case the eye signs can be explained as a right paramedian lesion leading to right ptosis with left eyelid retraction. Nucleus of posterior commissure provide inhibitory input to the central caudal nucleus (LPS Nucleus) of oculomotor nuclear complex of opposite side. Each nucleus of posterior commissure is connected with its contralateral counter part through the posterior commissure. The eye lid retraction was possible due to failure of inhibition of contralateral levator palpebrae resulting in its over action.

Loss of vision is uncommon in Wernicke’s encephalopathy[1]. Visual impairment in this case has to be explained as due to Nutritional optic neuropathy which responds to injection B12 and folate along with general nutritional therapy. Fixed non reactive pupil is commonly reported in thiamine deficiency but in that case colour vision will not be affected.

Thiamine is a water soluble vitamin which is not stored in the body. Daily requirement in an adult is 0.8-1mg/day; thirty times the requirement circulates in the tissues as functional enzyme bound vitamin. Deficiency starts after about a month on thiamine free diet. Wheat flour, legumes, nuts, fortified breakfast cereals are some of the common sources of thiamine. In addition to heavy alcohol in take the other causes of Wernicke’s encephalopathy are hyperemesis, systemic malignancies, gastro intestinal surgeries, prolonged intravenous feeding, high carbohydrate diet, hemodialysis, peritoneal dialysis, refeeding after prolonged fasting, AIDS etc.

**Course and prognosis**

Treatment should be started immediately and gradual return of motor & sensory function can be expected after thiamine replenishment. Mildly affected patients experience considerable improvement after a few weeks of treatment. In severe case the improvement may take many months and may be incomplete.

**References**

1. Walsh & Hoyts’ clinical Neurophalmology. The essentials 5th edition page 297,611,733