

Isolated abducens nerve palsy with hyperhomocysteinemia: Association and outcomes

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Ischemic abducens nerve palsy usually presents as isolated cranial nerve palsy in the middle aged and elderly patients with known risk factors such as diabetes mellitus,

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hypertension, dyslipidemia, carotid artery disease, etc., In this report, we describe four patients with isolated abducens nerve palsy who presented with an acute onset diplopia whose detailed history and examination were suggestive of an ischemic etiology. Detailed systemic and laboratory evaluation revealed hyperhomocysteinemia as the only potential risk factor. To the best of our knowledge this is the first report of association of hyperhomocysteinemia and isolated abducens nerve palsy.

Key words: Abducens nerve palsy, hyperhomocysteinemia, isolated abducens nerve palsy, nontraumatic

Isolated abducens nerve palsy is the most common form of cranial nerve palsies encountered in neuro-ophthalmology clinics and may be idiopathic or due to head trauma,

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intracranial space occupying lesions, vascular diseases, inflammatory conditions (postviral fever, postinfectious, post-vaccinal) or demyelinating disorders in young patients (<50 years).^[1] Hyperhomocysteinemia has been reported as an independent risk factor for systemic and ocular vaso-occlusive disorders, especially in young patients.^[2-4] In this case series, we describe four patients with isolated abducens nerve palsy where hyperhomocysteinemia was the sole risk factor.

Review of Cases

Between November 2008 and October 2010, 27 patients with isolated abducens nerve palsy presented to our clinics. All of these patients underwent evaluation for potential predisposing factors like viral fever, trauma, diabetes, hypertension, collagen vascular disorders, and dyslipidemia. Serum homocysteine levels were determined in those patients without any obvious history of ocular trauma, with or without presence of other risk factors like diabetes, hypertension, and dyslipidemia. Our series comprises of four patients who were found to have hyperhomocysteinemia as the sole risk factor.

Three patients were female and one was male. Details of the cases are shown in Table 1. The mean age of patients was 25 years (range: 6-52 years). All patients presented with complaints of double vision and mean duration of symptoms was 29 days (range: 3-90 days).

All patients had a -4 to -3 limitation of abduction where -4 limitation implied no movement of the eyeball beyond

the midline and -1 limitation of abduction referred to limitation of abduction only in extreme abduction. The mean amount of esotropia [Table 1] in primary gaze was 20 prism diopters (range: 12-30 PD, standard deviation (SD) =7.48 PD). Greatest deviation was noted in direction of limitation of movement [Fig. 1a]. Anterior segment and fundus examination was unremarkable. All patients underwent magnetic resonance imaging (MRI) brain with contrast [Fig. 2] which showed only the presence of ischemic lesions in two patients [Table 1]. The erythrocyte sedimentation rate (ESR), C-reactive protein, lipid profile, blood glucose levels, blood pressure, echocardiogram, and carotid Doppler were normal for all patients.

However, all patients were found to have elevated serum homocysteine. Mean serum homocysteine level was 19.20 $\mu\text{mol/L}$ (range: 16.07-20.50, SD: 2.09 $\mu\text{mol/L}$, normal: 3.9-13.9 $\mu\text{mol/L}$, chemiluminescence method). The patients were treated with vitamins B6 (250 mg), B12 (1,500 μg), and folic acid (5 mg). Two patients were given injection botulinum toxin (BOTOX, Allergan, 2.5 IU) in the medial rectus muscle of the affected eye to relieve diplopia while the other two were observed. After 2 months, all patients showed complete resolution with orthotropia in primary gaze and complete recovery of extraocular motility [Fig. 1b].

Discussion

Hyperhomocysteinemia is characterized by an elevation of serum homocysteine, an intermediate metabolite in methionine

Table 1: Clinical and laboratory features of patients with isolated lateral rectus palsy

Age (years)	Gender	Presenting complaints	Duration	Risk factors	Eye	Clinical features	Diagnosis	Investigations*	Serum homocysteine level ($\mu\text{mol/L}$)
18	F	Diplopia	7 days	Nil	OD	18 PD, -3 abduction	OD LR palsy	Normal	20.1
6	F	Diplopia	3 days	Nil	OS	12 PD, -3 abduction	OS LR Palsy	Normal	20.1
52	F	Diplopia	15 days	Nil	OD	20 PD, -3 abduction	OD LR Palsy	Normal	20.50
25	M	Diplopia	3 months	Nil	OS	30 PD, -4 abduction	OS LR Palsy	Normal	16.07

*M: Male, F: Female, OD: Right eye, OS: Left eye, PD: Prism diopters, LR: Lateral rectus. Risk factors include: Hypertension, diabetes mellitus, dyslipidemia, trauma, connective tissue disorders. Investigations include: Hemogram with erythrocyte sedimentation rate (ESR), C-reactive protein, 2D echocardiography of heart, serum lipid profile, carotid doppler, blood sugar, and rheumatologist evaluation for collagen vascular disorders



Figure 1: (a) Nine gaze ocular motility showing incomitant esotropia and limitation of abduction in the right eye in patient 1 at initial visit and (b) at 3 months follow-up showing orthotropia and complete recovery of abduction

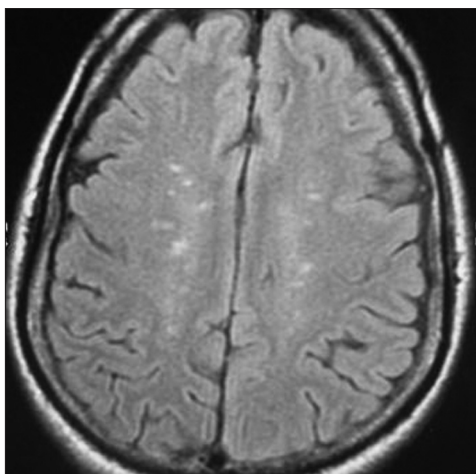


Figure 2: Magnetic resonance imaging brain showing the presence of bilateral white matter hyperintense lesions suggestive of ischemia in patient 2

metabolism. Homocysteine is a potent atherosclerotic risk factor that leads to formation of the free radicals and promotes smooth muscle proliferation. This promotes thrombus formation and increases the risk of vascular occlusion. Hyperhomocysteinemia is reported as an independent risk factor for systemic and ocular vaso-occlusive disorders, including nonarteritic ischemic optic neuropathy (NAION), central retinal artery occlusion (CRAO), and central retinal vein occlusion (CRVO), especially in young patients.^[2-4]

It has been reported that as many as 17% of young patients with NAION may have isolated hyperhomocysteinemia as the risk factor.^[3]

We have previously reported a case of combined cilioretinal artery obstruction and NAION in a young patient with hyperhomocysteinemia.^[4] In another study by Kalita *et al.*,^[5] 60.6% of the patients with ischemic strokes had hyperhomocysteinemia. A 5 $\mu\text{mol/L}$ elevation of homocysteine has been reported to increase risk of vaso-occlusive diseases by 60% in males and 80% in females with an increased odds ratio of 1.4–1.7.^[6]

Similar to the previous reports, patients in our series were young with a mean age of 25 years (range: 6–52 years). In our series, all patients presented with isolated abducens nerve palsy without any other known risk factor apart from hyperhomocysteinemia. The presence of the ischemic lesions on MRI in two patients prompted us to think of hyperhomocysteinemia as a possible risk factor. Since we found elevated homocysteine levels in these patients, we investigated for hyperhomocysteinemia in the other patients as well, despite a normal neuroimaging. Abducens nerve involvement in these cases could be attributed to microvasculopathy induced damage similar to that found in diabetic patients with abducens palsy.

Hyperhomocysteinemia is a potentially modifiable risk factor. Dietary supplementation of 250 mg of vitamin B₆, 5 mg of folic acid and vitamin B₁₂ daily has been shown to lower serum homocysteine levels.^[5] Complete resolution, either

spontaneous or following single botulinum injection and oral vitamin supplementation, was noted in all patients as is seen in patients with microvasculopathy as seen in diabetes mellitus.

Although hyperhomocysteinemia has been reported with various vaso-occlusive diseases; however, causal association is still not proven. Population based randomized trials such as CARDIOVIT study,^[7] are underway to investigate the association of hyperhomocysteinemia with systemic vaso-occlusive diseases. Until conclusive data is available it is recommended to investigate and treat for hyperhomocysteinemia in cases of vaso-occlusive diseases.

The main limitation of our series is its retrospective nature with limited size. However, this is an uncommon condition and to the best of our knowledge, this is the first reported association of hyperhomocysteinemia with isolated cranial nerve palsy. Based on our findings we recommend estimation of serum homocysteine in the work up of young patients with nontraumatic isolated abducens nerve palsy in the absence of other risk factors.

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