Letters to the Editor

Bilateral INO in PSP

The diagnosis of internuclear ophthalmoplegia (INO) hinges on the disturbance of ocular motility which leads to adduction deficit on the affected side and abduction nystagmus on the contralateral side.\[1\] If the adduction deficit is seen bilaterally along with bilateral abduction nystagmus, then it is called a bilateral INO (BINO).\[1\] Frequently, BINO is associated with exotropia in the primary gaze which gives an appearance as if the eyes are looking sideways called as wall-eyed bilateral INO (WEBINO).\[1\]

A 79-year-old right-handed man presented with a 5-year history of symptoms suggestive of Parkinsonism. His initial symptoms included slowness in daily tasks, difficulty turning while walking, small handwriting, a decrease in the volume of voice, and dysphagia which required the placement of a PEG tube. His other symptoms included constipation, urinary urgency, and drooling. His wife mentioned short-term memory loss, and he would forget conversations. The dose of carbidopa/levodopa was increased gradually to 1000 mg a day which did not lead to any improvement. Recently, he complained of double vision especially when reading and was using prism glasses.

The patient’s visual acuity with correction was 20/200 in the right eye (improving with a pinhole to 20/60-2) and 20/50 in the left eye (no improvement with pinhole). His color vision was normal. Pupils were equal and reactive to light with no relative afferent pupillary defect, and eyelid blinking rate was severely reduced. His eye movement testing showed slowed adduction saccades bilaterally with bilateral abducting nystagmus, but with no visible exotropia in primary position. There was slowing of vertical saccadic eye movements as well. Oculocephalic reflex (VOR) revealed a full range of eye movements. The conjugate up gaze was severely impaired, square-wave jerks were present, and convergence was intact [Video 1]. He had a mild cognitive impairment with a MoCA (Montreal Cognitive Assessment) score of 23/30 (losing 2 points for visuospatial, 1 point for naming, 1 point for attention, 1 point for language, and 2 points for delayed recall).

Brain MRI with contrast did not show any parenchymal lesion but showed reduced midbrain to pons ratio of 0.50 [Figure 1]. A midbrain to pons ratio of less than 0.52 is quite specific for progressive supranuclear palsy (PSP) based on a study of pathologically confirmed PSP cases.\[2\] Thus, this patient met the diagnostic criteria for probable PSP based on the signs seen on examination.\[3\]

A thorough eye movement exam is prudent in the clinical diagnosis of PSP. In the initial stages, there is impairment in the vertical eye movements, particularly downgaze and slowing of vertical saccades. However, in the later stages, complete ophthalmoplegia can be seen. In the initial description of PSP, degeneration in superior colliculi and pretectal regions were attributed as a cause of vertical gaze impairment.\[4\] Due to the involvement of supranuclear pathways, the term PSP was used.\[5\] Another reason proposed for a supranuclear etiology of impaired vertical eye movements was an intact VOR.\[5\] In the initial description of PSP, mild demyelination of medial longitudinal fasciculus (MLF) was also seen but attributed to

Figure 1: MRI brain shows reduced midbrain to pons ratio of 0.50 on the sagittal T1 image

---

References:

1. Choi HS, Oh HJ, Choi H, Choi WH, Kim JG, Kim KM, et al. Vitamin D insufficiency in Korea--a greater threat to younger generation: The Korean national health and nutrition examination survey (KNHANES) 2011;7:337-45.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Executive summary: guidelines for preventing and treating vitamin D deficiency: for the National Institutes of Health Consensus Development Conference on Prevention of Vitamin D Deficiency and Bone Loss with Advancing Age: October 22-23, 2001. JAMA 2001;9:164-73.
3. Chung K, Song C. Clinical usefulness of fatigue severity scale for patients with fatigue, and anxiety or depression. Korean J Psychosom Med 2001;9:164-73.
4. Aurora SK, Brin MF. Chronic migraine: An update on physiology, imaging, and the mechanism of action of two available pharmacologic therapies. Headache 2017;57:109-25.
Impaired Clinical diagnosis of progressive supranuclear palsy: Preserved
Impaired Intact M Impaired
72 Impaired Impaired Orthotropic Bilateral exotropia Impaired F Impaired Impaired Impaired Preserved
Orthotropic 72 Impaired Impaired Convergence 60 Impaired Preserved Vertical eye Preserved 71 Impaired Impaired Impaired M 72 Exodeviation of the right eye Sex F Preserved Absent 73 Absent Normal of bilateral INO with PSP, out of which one was BINO and three were WEBINO[8-10] [Table 1].

The possible explanation behind the development of exotropia seen in bilateral INO is not entirely known.[1] Some studies have suggested the involvement of medial rectus neurons in the MLF while others have suggested a lesion of the oculomotor nucleus in the midbrain.[1] Bilateral exotropia seen with BINO is usually related to the involvement of rostral midbrain.[9]

Convergence commands do not pass through the MLF and are sent from the midbrain direct to the medial rectus motor neurons.[11] Convergence is usually preserved in unilateral INO but may be affected in WEBINO or BINO.[11] In the presence of bilateral INO, convergence has limited localizing value because it is variable. Vertical nystagmus is common in WEBINO because of damage to the vestibulo-ocular motor pathways passing through the MLF.[11]

In our case, the likely localization of BINO is caudal midbrain or pons because exotropia was not seen in the primary position and convergence was intact. The involvement of bilateral MLF is the most likely explanation for BINO. MLF is considered as a common pathway for conjugate gaze. It is possible that there are separate pathways for VOR and saccadic or pursuit eye movements within the MLF. An ischemic stroke or a demyelinating plaque involves a larger area and involve all the pathways within the MLF leading to impaired VOR, saccadic, and pursuit eye movements. On the other hand, a degenerative condition such as PSP may involve selective pathways within the MLF responsible for saccadic or pursuit eye movements and spares the pathway responsible for VOR. Another possible reason could be a different pathway for VOR which is not properly understood and MLF may not be a part of it at all.

In summary, we are reporting a unique case of BINO with intact convergence and absence of exotropia in the primary position. This case expands the spectrum of oculomotor abnormalities seen with PSP.

Table 1: Clinical features of patients with bilateral INO in PSP

| Age | Sex | Convergence | Vertical eye movements | Horizontal eye movements | Oculo-cephalic reflex | Primary position |
|-----|-----|-------------|------------------------|--------------------------|----------------------|------------------|
| Case 1 | 49 | M | Impaired | Impaired | Impaired | Preserved | Orthotropic |
| Case 2 | 72 | F | Impaired | Impaired | Impaired | Preserved | Orthotropic |
| Case 3 | 73 | F | Impaired | Impaired | Impaired | Preserved | Orthotropic |
| Flint AC 2005[7] | 71 | M | Intact | Impaired | Impaired | Preserved | Exodeviation of the right eye |
| Ushio M 2008[8] | 72 | M | Absent | Impaired | Impaired | Preserved | Bilateral exotropia |
| Matsumoto H 2008[9] | 72 | M | Impaired | Impaired | Impaired | Preserved | Exotropia of one eye |
| De Souza LC 2017[10] | 60 | F | Impaired | Impaired | Impaired | Preserved | Bilateral exotropia |

Declarations of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Wu YT, Cafiero-Chin M, Marques C. Wall-eyed bilateral internuclear ophthalmoplegia: Review of pathogenesis, diagnosis, prognosis and management. Clin Exp Optom 2015:98:25-30.
2. Massey LA, Jäger HR, Pavour DC, O’Sullivan SS, Ling H, Williams DR, et al. The midbrain to pons ratio: A simple and specific MRI sign of progressive supranuclear palsy. Neurology 2013;80:1856-61.
3. Höglinger GU, Respondek G, Stamolou M, Kurz C, Josephs KA, Lang AE, et al. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord 2017;32:853-64.
4. Steele JC, Richardson JC, Olszewski J. Progressive Supranuclear Palsy. A heterogeneous degeneration involving the brain stem, basal ganglia, and cerebellum with vertical gaze and pseudobulbar palsy, nuchal dystonia, and dementia. Arch Neurol 1964;10:333-59.
5. Mastaglia FL, Grainger KM. Internuclear ophthalmoplegia in progressive supranuclear palsy. J Neurol Sci 1975;25:303-8.
6. Friedman DI, Jankovic J, McCrory JA 3rd. Neuro-ophtalmic findings in progressive supranuclear palsy. J Clin Neuroophthalmol 1992;12:104-9.
7. Flint AC, Williams O. Bilateral internuclear ophthalmoplegia in progressive supranuclear palsy with an overriding oculocephalic maneuver. Mov Disord 2005;20:1069-71.
8. Ushio M, Iwasaki S, Chihara Y, Murofushi T. Wall-eyed bilateral internuclear ophthalmoplegia in a patient with progressive supranuclear palsy. J Neuroophthalmol 2008;28:93-6.

The involvement of the oculomotor nucleus.[4] It is now widely believed that the defects in oculomotor control seen with PSP can occur because of nuclear or supranuclear pathways.[6] The presence of bilateral INO in PSP (3 out of 4 cases) was first described in 1975.[11] There have been four other case reports of bilateral INO with PSP, out of which one was BINO[7] and three were WEBINO[8-10] [Table 1].

De Souza LC 2017
Matsumoto H 2008
Ushio M 2008

There have been four other case reports of bilateral INO with PSP, out of which one was BINO[7] and three were WEBINO[8-10] [Table 1].

It is now widely believed that the defects in oculomotor control seen with PSP can occur because of nuclear or supranuclear pathways.[6] The involvement of the oculomotor nucleus.[4] It is now widely believed that the defects in oculomotor control seen with PSP can occur because of nuclear or supranuclear pathways.[6] The involvement of the oculomotor nucleus.

Letters to the Editor

De Souza LC 2017
Matsumoto H 2008
Ushio M 2008

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Wu YT, Cafiero-Chin M, Marques C. Wall-eyed bilateral internuclear ophthalmoplegia: Review of pathogenesis, diagnosis, prognosis and management. Clin Exp Optom 2015:98:25-30.
2. Massey LA, Jäger HR, Pavour DC, O’Sullivan SS, Ling H, Williams DR, et al. The midbrain to pons ratio: A simple and specific MRI sign of progressive supranuclear palsy. Neurology 2013;80:1856-61.
3. Höglinger GU, Respondek G, Stamolou M, Kurz C, Josephs KA, Lang AE, et al. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord 2017;32:853-64.
4. Steele JC, Richardson JC, Olszewski J. Progressive Supranuclear Palsy. A heterogenous degeneration involving the brain stem, basal ganglia, and cerebellum with vertical gaze and pseudobulbar palsy, nuchal dystonia, and dementia. Arch Neurol 1964;10:333-59.
5. Mastaglia FL, Grainger KM. Internuclear ophthalmoplegia in progressive supranuclear palsy. J Neurol Sci 1975;25:303-8.
6. Friedman DI, Jankovic J, McCrory JA 3rd. Neuro-ophtalmic findings in progressive supranuclear palsy. J Clin Neuroophthalmol 1992;12:104-9.
7. Flint AC, Williams O. Bilateral internuclear ophthalmoplegia in progressive supranuclear palsy with an overriding oculocephalic maneuver. Mov Disord 2005;20:1069-71.
8. Ushio M, Iwasaki S, Chihara Y, Murofushi T. Wall-eyed bilateral internuclear ophthalmoplegia in a patient with progressive supranuclear palsy. J Neuroophthalmol 2008;28:93-6.

The involvement of the oculomotor nucleus.[4] It is now widely believed that the defects in oculomotor control seen with PSP can occur because of nuclear or supranuclear pathways.[6] The involvement of the oculomotor nucleus.

Letters to the Editor

De Souza LC 2017
Matsumoto H 2008
Ushio M 2008

There have been four other case reports of bilateral INO with PSP, out of which one was BINO[7] and three were WEBINO[8-10] [Table 1].

It is now widely believed that the defects in oculomotor control seen with PSP can occur because of nuclear or supranuclear pathways.[6] The involvement of the oculomotor nucleus.

Letters to the Editor

De Souza LC 2017
Matsumoto H 2008
Ushio M 2008

There have been four other case reports of bilateral INO with PSP, out of which one was BINO[7] and three were WEBINO[8-10] [Table 1].
Acute Flaccid Myelitis Caused by Japanese Encephalitis Virus: A Rare Association

Sir,

Acute flaccid myelitis (AFM) is a rare clinical entity characterized by acute onset flaccid paralysis involving one or more limbs and involvement of spinal cord grey matter on magnetic resonance imaging (MRI). [1]

It is known to be associated with several antecedent viral infections. [2]

We report a 13-year-old female with Acute flaccid myelitis caused by Japanese encephalitis virus (JEV). AFM was confirmed with clinical examination, MRI imaging and exclusion of other causes. There have been reports of AFM in association with various viral infections, commonest being the Enterovirus. [2] However, this may be a rare case report of AFM caused by JEV.

A 13 year-old-girl presented with sudden onset weakness of both upper and lower limbs. The weakness which was proximal at the beginning, progressed to involve distal muscles within one hour of onset. Patient had history of upper respiratory tract infection one week prior to this presentation. There was no history suggestive of seizures, altered sensorium or any similar complains in past. The clinical examination revealed flaccid quadriplegia with power of 0/5 in all limbs along with areflexia without any cranial nerve, sensory or bladder and bowel involvement. Rest of the clinical examination was normal. On investigations, MRI brain and spine showed linear intensity involving bilateral anterior horn cells in cervical cord extending from C4-5 to D1-2 vertebrae with subtle patchy enhancement [Figure 1a and b] Cerebrospinal fluid (CSF) analysis revealed mild increase in protein at 720 mg/L and 0.030 × 10^9/mcL cells all of which were lymphocytes. IgM antibody to Japanese encephalitis was detected both in CSF and serum using ELISA (enzyme-linked immunosorbent assay). Rest of the CSF evaluation for other viruses and mycobacterium tuberculosis and neuromyelitis optica antibody were found to be negative. Nerve conduction velocity (NCV) was suggestive of motor axonal polyneuropathy. Electromyography was normal. A CSF Polymerase chain reaction panel for various bacteria and viruses including cytomegalovirus, Herpes simplex, Varicella Zoster, Parecho and enterovirus was found to be negative. Stool examination for poliomyelitis was also found to be negative. A diagnosis of definitive case of AFM was thus made based on CDC definition. [1]

Patient was treated IV immunoglobulin, fluoxetine and other supportive measures. The repeat MRI and CSF examination done four weeks later was found to be normal. Patient could be discharged after five weeks with power of 3/5 in lower limbs and 4/5 in upper limbs.

Acute flaccid myelitis is a rare clinical syndrome reported commonly in western countries with few cases reported in India. AFM actually is a subset of acute flaccid paralysis in which cord myelitis is documented, by magnetic resonance imaging (MRI). The exact cause and pathophysiology have not been elucidated till date. However, an autoimmune etiology has been postulated, although the clinical presentation of sudden onset limb weakness and predominant radiological findings involving the gray matter and not the white matter are more suggestive of a neuro-invasion by the culprit viruses. Lack of response to response to various immunosuppressive agents also discredits the autoimmune pathophysiology. [3]

The commonest agent in various case series is believed to be viral infections, of which enteroviruses are the commonest culprits. [2]

Poliomyelitis is an important differential.

Submitted: 16-Apr-2019    Revised: 02-May-2019    Accepted: 02-May-2019
Published: 25-Feb-2020

Video available on: www.annalsofian.org

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

DOI: 10.4103/aian.AIAN_216_19