Original Article

Various Clinical Presentations of Nystagmus: Case Series and Review of Literature

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Abstract

Introduction: Nystagmus is a rhythmic regular oscillation of the eyes. In this case series, we present four cases who presented to the emergency department different clinical complaints and had nystagmus on examination.

Methodology: The patients presented to the D.Y. Patil Medical College & Hospital, Navi Mumbai, India with varied clinical presentations and on ophthalmologic examination had nystagmus. The data presented in this article were obtained from the retrospective review of the medical records of the patient.

Results: One patient, recently diagnosed with seizure disorder, presented with decreased vision and slurred speech. Horizontal nystagmus with fast component to the left was observed on ophthalmologic examination and serum phenytoin levels were more than 40 µg/ml. Final diagnosis of phenytoin diagnosis was made. One hypertensive patient with giddiness and loss of balance presented with blood pressure of 170/100 mm Hg. Vertical nystagmus with positive Romberg sign was noted. Magnetic Resonance Imaging (MRI) revealed an infarct on the right hemi-pons. Another patient with no significant past medical history presented with headache, slurred speech and blurred vision. Nystagmus and impaired cerebellar signs were noted. MRI revealed an infarct in the right middle cerebellar peduncle. Last patient with history of hypertension had ptosis, ophthalmoplegia and vertical nystagmus, who had an ischemic stroke of ventromedial portion of bilateral thalami and peri-aqueductal grey matter.

Conclusions: Nystagmus can present with various clinical conditions. Eliciting relevant past medical history, understanding present illness in detail and correlating with laboratory and imaging studies is necessary to make a correct and timely diagnosis.

Keywords: Seizure; Stroke; Nystagmus.

Introduction

Nystagmus is a rhythmic regular oscillation of the eyes. It may consist of alternating phases of a slow drift in one direction with a corrective quick "jerk" in the opposite direction, or of slow, sinusoidal, "pendular" oscillations to and fro. Jerk nystagmus occurs most often when there is an imbalance in the activation of the semicircular canals because
of either peripheral vestibular disease or disruption of central vestibular pathways in the brainstem. There are numerous conditions in which patients can present with nystagmus along with other clinical symptoms. Reaching the final diagnosis can be challenging for a physician and a delayed diagnosis may prove fatal for the patient. In this case series, we present four cases who presented to the emergency department different clinical complaints and had nystagmus on examination.

Methodology
The patients presented to the D.Y. Patil Medical College & Hospital, Navi Mumbai, India. These cases presented with varied clinical presentations and on ophthalmologic examination had nystagmus. The data presented in this article were obtained from the retrospective review of the medical records of the patient. The personal identifiers of the patients were not noted to maintain confidentiality and thus informed consent of the patients was not required.

Case Series
Case 1
A 15 years old male presented to the OPD with complaints of decreased vision, slurred speech with swelling and pain in right side of neck. The patient gave no history of loss of consciousness, vomiting, lacrimation, chemosis, any other neurological deficit, chest pain or breathlessness. Patient was diagnosed with seizure disorder approximately 15 days ago, and was taking oral phenytoin thrice a day since then. No history of Koch’s or Koch’s contact could be elicited. On examination the patient was conscious, cooperative well oriented to time, place and person, with normal vitals and examination of respiratory, cardiovascular and abdominal systems were within normal limits. Central nervous system examination revealed a horizontal nystagmus (Grade II) with fast component to the left. Higher functions, other cranial nerves, motor, sensory and cerebellar system were within normal limits. Based on the examination findings and past medical history, a differential diagnoses of phenytoin toxicity and brainstem lesion were made and investigated further. Hemogram and electrolytes were within normal range, while erythrocyte sedimentation rate was raised (40 mm/hour). Plain and contrast Magnetic Resonance Imaging (MRI) of the brain revealed well defined altered signal intensity lesion in the left parafalcine parietal lobe of size 6 x 4 mm with no perilesional edema, which were suggestive of infective granuloma. Ultrasonography of the neck found right sided cervical lymphadenopathy with largest measuring 2.1 x 0.9 mm in cervical II region. Abnormal awake electroencephalogram (EEG) was recorded. Serum phenytoin levels were raised (more than 40 μg/ml). Patient was put on levetiracetam, calcium and folic acid. And because of the infective granuloma and cervical lymphadenopathy, anti-tubercular therapy was started according to weight of the patient.

Case 2
A 70 year old female presented with complaints of giddiness and loss of balance since two days. Giddiness was described as spinning of surroundings which was more on looking up and also associated with blurring of vision. She also complaints of loss of balance towards back on attempting to get up from sitting position however, no history of loss of conscious, vomiting, seizure, diplopia, squint, ear discharge, earache, hearing loss, tinnitus or any other cranial nerve involvement or neurological deficit was given by the patient. She was known case of hypertension since three years and was taking amlodipine 5mg once a day. On examination, the vitals and systemic examination were within normal range. Higher functions, power, tone, reflexes were normal and a vertical nystagmus with fast component upwards was observed. On performing the Romberg’s test, patient was swaying towards the back with eyes open as well as closed. No other cerebellar signs were noted. Based on the clinical presentation and past
medical history, differentials of brainstem stroke or cervical spondylosis were listed. Her hemogram was normal, thyroid stimulating hormone was raised, lipid profile was deranged. Electrocardiography and echocardiography were suggestive of left ventricular hypertrophy (ejection fraction 55%) and fundoscopy revealed Grade I hypertensive retinopathy. Cervical X-ray AP/Lateral view was suggestive of loss of cervical lordosis and osteophytes arising from the anterior end plates at C5-C6 levels. MRI brain plain revealed an acute non-hemorrhagic infarct involving right hemi pons. Mild generalized cerebral atrophy with chronic ischemic changes in bilateral fronto-parietal and periventricular white matter. Patient was started on ecosprin, atorvastatin (40mg), amlodipine (5mg), betahistine (8mg), prochlorperazine and Gingko biloba as and when required for persistent giddiness. Limb physiotherapy and cervical strengthening exercises were advised as well.

Case 3
A 43 year old male presented with headache, difficulty in walking on one side, slurring of speech, blurring of vision since 6 hours. The patient was apparently alright 6 hours back when he started having headache while working, then after 2 hours when he attempted to walk, he noticed that he’s losing balance towards right side of the body and he also had slurred speech as he couldn’t pronounce the syllables clearly as well as blurring of vision with diplopia. The patient gave no history of loss of consciousness, vomiting, seizures, any other cranial nerve involvement, any motor or sensory deficit or involvement of bowel and bladder. The patient was not a known case of Diabetes Mellitus, Hypertension, Tuberculosis or had a history of Tuberculosis contact. Vitals except for blood pressure (170/100 mm Hg), respiratory, cardiovascular and per abdominal examinations were within normal range. Higher mental functions, power, tone were normal with scanning speech. Nystagmus was observed with fast component on the right and no other cranial nerve involvement was noted. Reflexes were diminished bilaterally and a pendular knee jerk was observed. Cerebellar signs like dysdiadokinesia, finger nose test and heel shin test were impaired on the right side. High stepping gait with swaying towards the right was observed and Romberg’s test demonstrated swaying on right on standing with eyes open and closed. A clinical diagnosis of right sided cerebellar stroke was made. Computed tomography of the head was done immediately at presentation to rule out bleed and it revealed an ill defined hypodense area in left frontal lobe predominantly involving the white matter suggestive likely of ischemic changes. Blood pressure monitoring was done 4 hourly but due to persistently high blood pressure even after 24 hours of developing stroke, the was started on telmisartan + chlorthalidone (40/12.5 mg) once a day, metoprolol and amlodipine (25/5 mg) once a day, ecosprin, atorvastatin and citicholine 500mg twice a day. After 36 hours, power decreased in the right upper and lower limbs. This was followed by MRI Brain and an angiogram, which was suggestive of an acute non hemorrhagic infarct involving the right middle cerebellar peduncle. A diagnosis of infarct on the right middle cerebellar peduncle was made. Chronic ischemic changes in bilateral fronto-parietal and periventricular white matter were seen. Atherosclerotic plaque involving the distal cervical portion of right internal carotid artery causing 30-40% luminal compromise, eccentric atherosclerotic plaque in the right carotid bulb causing 20-30% luminal compromise were revealed as well. The patient was started on enoxaparin 60mg subcutaneously twice a day for 5 days and clopidgrel75mg was started in addition to the above drugs after consulting the neurologist. Patient’s power improved in the next 24 hours, and limb physiotherapy was advised.

Case 4
A patient 44 year old female was brought by relatives in the casualty with decreased responsiveness since morning. The patient was
apparently alright until morning when she started to experience giddiness and then fell unconscious on the bed. The patient had irrelevant talks, only responded with agitation to painful stimuli and was taken to local hospital and computed tomography (CT) scan was suggested. She was a known case of hypertension since one year, was started on Amlodipine 5 mg once a day, but she was not taking medications for past 6 to 7 months. She had no significant past medical problems and addictions. There was no history of fever, headache and vomiting and she was apparently fine on the previous night. Examination revealed an afebrile, deeply drowsy, confused and aphasic lady (Glasgow Coma Scale score: 8/15), with regular heart rate of 84/min, blood pressure of 130/90 mm Hg and respiratory rate of 12/min. She had bilateral ptosis and external ophthalmoplegia, vertical nystagmus with fast component downwards. Pupils were 3 mm, with sluggish reaction to light and there was no weakness of limbs. Plantar responses were flexor on both sides. Optic fundi were normal. Cardiovascular and other systemic examination was unremarkable. Biochemical laboratory tests and blood counts were normal. Electrocardiogram and two dimensional echocardiography was within normal limits. Initial CT of the brain at admission was unremarkable. MRI of the brain revealed infarct. Angiography done later revealed an acute non-hemorrhagic infarct involving ventromedial portion of bilateral thalami and periaqueductal grey matter- with possibility of artery of Percheron infarct is likely.

Table 1 Description of clinical cases

| Cases | Presenting complaints | Past history | Differential diagnosis | Examination finding | Specific investigations | Final diagnosis |
|-------|-----------------------|--------------|------------------------|---------------------|------------------------|----------------|
| 1     | Decreased vision, slurred speech with swelling and pain in right side of neck | Recently diagnosed seizure disorder | 1) Phenotoin toxicity 2) Brainstem lesion | Horizontal nystagmus with fast component to the left | Serum phenotoin levels more than 40 µg/ml | Phenotoin toxicity |
| 2     | Giddiness and loss of balance since two days | Hypertension since three years | 1) Brainstem stroke 2) Cervical spondylosis | 1) Vertical nystagmus with fast component upwards 2) Positive Romberg test | MRI brain: acute non-hemorrhagic infarct in right hemi-pons | Brainstem stroke |
| 3     | Headache, difficulty in walking on one side, slurring of speech, blurring of vision since 6 hours | None | Stroke | 1) Nystagmus was observed with fast component on the right 2) Diminished reflexes 3) Dysdiadokinesia, finger nose test and heel shin test impaired on the right side 4) Rombergs test demonstrated swaying on right | 1) CT head: ill defined hypodense area in left frontal lobe 2) MRI brain: non-hemorrhagic infarct in right middle cerebellar peduncle 3) Angiography: 30 to 40% compromise of the right carotid artery | Ischemic stroke in right middle cerebellar peduncle |
| 4     | Decreased responsiveness, irrelevant talk | Hypertension since one year | Stroke | Bilateral ptosis, External ophthalmoplegia, Vertical nystagmus with fast component downwards | MRI brain: infarct Angiography: acute infarct with possibility of artery of Percheron infarct. | Ischemic stroke of ventromedial portion of bilateral thalami and peri-aqueductal grey matter |
Discussion

The present study describes four patients who presented to the emergency ward of our hospital with varied clinical presentations, with a common finding of nystagmus. One patient was diagnosed with phenytoin toxicity and two patients with non-hemorrhagic stroke. Nystagmus is a rhythmic regular oscillation of the eyes. The rhythmic nature and slow speeds of nystagmus distinguish it from a number of other abnormal involuntary eye movements. Since its introduction, Phenytoin has been known to effect ocular motility. Gaze-evoked horizontal nystagmus and impaired smooth pursuit eye movements are frequently observed with phenytoin use. Rarely, abduction paresis, oculogyria, alternating nystagmus and divergent nystagmus have also been associated with the use of phenytoin.2 Additionally, total external ophthalmoplegia to command and pursuit, as well as to doll’s head manoeuvre and caloric stimulation, may occur with toxic blood levels.3

A downbeat nystagmus may be observed in numerous clinical conditions. Structural lesions at the craniocervical junction like Arnold-Chiari malformation, arachnoid adhesions, neck injury and aneurysm; diseases of cerebellum like tumor, stroke, multiple sclerosis, syphilis and metabolic disorders like hypomagnesemia, phenytoin or carbamazapine can present with nystagmus. Wheeler et al described downbeat nystagmus in a patient receiving phenytoin and phenobarbital in addition to carbamazepine.4 The authors correlated the resolution of the nystagmus with a decreasing carbamazepine-free fraction despite an increasing total serum carbamazepine. Though the phenytoin level in their patient was 22.2/μg/ml, the authors did not comment on its possible contributory role. In addition, color vision discrimination has also been well documented with the conventional use of anti-epileptics.5 Phenytoin exhibits non-linear pharmacokinetics because of its saturable liver metabolism. This results in a non-linear relationship between doses and the plasma concentrations achieved. It is for this reason that excessive increase in daily dosage, rapid loading, medication abuse, alcohol abuse and concomitant liver disease may result in toxic phenytoin plasma concentrations, often associated neurologic and non-neurologic manifestations.6 Apart from nystagmus, other dose-related neurologic manifestations include movement disorders, external ophthalmoplegia, ataxia, hallucinations and paradoxical seizures.

Three patients in our series with nystagmus were diagnosed as non-hemorrhagic strokes. One had nystagmus with fast component upwards, other one to the right and one downwards. Both the patients had a positive Romberg’s test. Acute vestibular syndrome (AVS), characterized by sudden onset of dizziness/vertigo, nausea/vomiting, and gait unsteadiness, results from static and dynamic imbalance in the discharge of the vestibular systems on both sides. AVS of central origin have mostly been found in strokes involving the caudal cerebellum or the dorsal portions of the lower brainstem.7 The vertebrobasilar artery system accounts for 20% of cerebral perfusion and provides vascular supply to both central and peripheral vestibular organs. It has been demonstrated that the peripheral vertigo may be the initial symptom when the blood flow slows down or is disturbed in the vertebrobasilar artery system, before the posterior fossa stroke becomes symptomatic.8 Several studies correlated reduced caloric test responses in cases of vascular lesion. As a result of prolonged vasoconstriction leading to hypoperfusion of the vestibular labyrinth, approximately half of all patients with migraine reported unilateral caloric hypofunction.9 Further, it was reported that 42% of the patients with vertigo of vascular origin displayed unilateral caloric hypofunction and attributed the selective vulnerability of the vestibular labyrinth to ischemic insults.10 Thus, normal caloric test reflects an intactvestibulo-ocular reflex, which passes through the upper brainstem, including the vestibular and oculomotor components, and is regulated through the cerebellar circuitry.
Conclusion
Our series of clinical cases demonstrate that patients presenting with nystagmus and other complaints should be thoroughly investigated. Eliciting relevant past medical history and describing the history of present illness in detail is very important to lead the investigation. Correlating information obtained from clinical, laboratory and imaging studies helped us in correctly diagnosing the patients in a timely manner.

Study Funding: None
Conflict of interest: None

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