



The use of video-oculography to assist in diagnosis of subtle inter-nuclear ophthalmoplegia

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ABSTRACT

Inter-nuclear ophthalmoplegia (INO) may not always have overt or obvious clinical signs during bedside examination. In patients presenting with mild/subtle INO with no focal neurological deficits or cerebellar signs, an unremarkable radiographic imaging and blood work, diagnosis will be challenging. Results of bedside head thrust tests will also be confounded and difficult to interpret, leading to discordant impressions among physicians of different specialties. Patients with mild INO will still require active surveillance to watch for any progression and development of clinical signs and should be managed by neuro-ophthalmology specialty. Video-oculography can assist with the interpretation of bedside head thrust and reveal slowing of adduction that is otherwise not obvious bedside. This has downstream implications on the management of patients with mild INO as they may be “volleyed” among different medical specialties if covert bedside signs are overlooked. Greater caution is needed on interpreting positive head thrust/video head impulse test as a peripheral vestibular sign in the presence of disconjugate oculomotor movements. Patients with mild INO may be relatively asymptomatic but may still have some functional impairments that should be addressed appropriately.

1. Introduction

Inter-nuclear ophthalmoplegia is characterized by limited or slowing of ipsilesional adduction with abducting nystagmus in contralateral gaze [1]. It is one of the most common neuro-ophthalmologic syndromes due to lesions in the medial longitudinal fasciculus (MLF) [2]. Aside from these deficits, the vestibular-ocular reflex (VOR) can also be affected since the semi-circular canals and otoliths neural projections are conveyed by ascending or descending MLF tracts [3,4]. The head impulse test, first described more than three decades ago, [5] still remains as one of the most important bedside tests of VOR integrity. It is also widely used as part of a three step Head Impulse, Nystagmus, Test of Skew (HINTS+) to distinguish between peripheral and central vestibular disorders [6] and is more sensitive than diffused weighted radiographic imaging in the first 48 hours of an acute vestibular syndrome [7]. At times, quantification of the VOR may be needed especially when bedside signs are covert or subtle. The recently introduced Video Head Impulse test (vHIT) is a useful non-invasive lightweight device, embedded with high-speed infrared video camera(s) and inertial accelerometers to measure eye and head movements respectively [4].

2. Case study

We present a case of a young 40-year-old woman with hypertension as the only known medical history, when she presented to the Otorhinolaryngology-Head & Neck Surgery specialist outpatient clinic in June this year. There were no other cardiovascular risk factors or previous thromboembolic events. The patient noted an acute non-vertiginous dizziness for the past week, accompanied with imbalance and visual surround movements whenever she turned her head to either side while ambulating. Beside examination revealed a bilateral abducting nystagmus that was disconjugate with greater velocity on rightward gaze. Convergence was preserved, there was no diplopia, ptosis or skew deviation, and extraocular movements were full. Hence, the patient was preliminary diagnosed with suspicion of a unilateral left INO and asked to go to the emergency department (ED) for a stroke workup and admission to the general wards for observation. At the ED, physical examination of the heart, lungs and abdomen and calves were unremarkable, the pupils were equal and reactive to light (PEARL 3 mm) with no relative afferent pupil defect (RAPD). Extraocular movements (EOM) were also full, with cranial nerves grossly intact. There were also no focal neurological deficits or cerebellar signs. The rest of the physical

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examination was unremarkable. The patient was scheduled for a Computer Tomography (CT) of the brain with complete blood count and an urgent brain Magnetic Radiographic Imaging (MRI) with Magnetic Resonance Angiogram (MRA) to rule out central causes. Radiographic imaging (CT) and blood count including Troponin levels, Liver function tests, and urine full and microscopic examination were unremarkable. The patient also had a negative syphilis screen with unremarkable autoimmune markers. The patient was subsequently admitted seeing an internist as planned and to keep in view a referral to neurology after MRI. Incidental findings during admission include hypovitaminosis D and hyperlipidemia for which, the patient was treated pharmacologically. A positive head thrust to the left with rightward gaze evoked abducting nystagmus were consistent findings when the patient was reviewed during the inpatient ward rounds. On occasions, bilateral positive head thrusts were noted, also with a mild left-beating abducting nystagmus. Such conflicting observations bedside led to suspicion of a peripheral vestibulopathy and even on one account, suspicion of a bilateral vestibulopathy by the internist. Balance assessment by an inpatient-trained physiotherapist was however unremarkable with an excellent Berg Balance Scale (BBS) of 53 points out of 56. As clinical impressions were discordant, the Otolaryngologist decided to employ the use of vestibular function test with video-oculography for objective quantification and visual recording of ocular movements. The results are presented below.

2.1. Video-oculography

Spontaneous: No spontaneous nystagmus was noted in vision or vision denied conditions.

Gaze: Significant right-beating nystagmus on rightward gaze. Mild left-beating nystagmus on leftward gaze with rebound. Nystagmus is disconjugate (Fig. 1).

Smooth Pursuit: Asymmetrical gain of the smooth pursuit in either direction of pursuit (Fig. 2).

Saccade: Bilateral slowing of adduction with delayed latencies and accuracy (Fig. 3).

Optokinetic: Abnormal optokinetic reflexes in either direction (Fig. 4).

Post Headshake Test: Unremarkable for any asymmetry in the velocity storage or cross coupling of vestibular ocular reflex.

Positional Test: Direction fixed positional nystagmus noted, which is suppressible with fixation.

Video Head Impulse Test (vHIT): Bilaterally low gains of the lateral and posterior canals with atypical catch-up saccades. However, results should be interpreted cautiously as a peripheral finding in lieu of central indicators (Figs. 5 and 6).

Cervical Vestibular Evoked Myogenic Potential (cVEMP): Bilaterally absent VEMP despite palpable sternocleidomastoid in optimal recording position. This may be suggestive of a lesion in the descending MLF tract.

Bi-thermal Caloric: Symmetrical VOR response to bi-thermal caloric irrigations suggesting intact low-frequency labyrinthine function.

Overall impression: The vestibular function test with video-oculography revealed an absent cVEMP response, slowing of adducting saccades, poor optokinetic reflexes and asymmetrical smooth pursuit bilaterally. These findings are disproportionate to the patient's age and intact labyrinthine status and suggests that a CNS involvement cannot be definitively ruled out.

3. Discussion

Signs of INO and potentially important diagnoses may be very subtle during bedside examination especially when there are no other focal neurological deficits or remarkable radiographic imaging. Gaze-evoked nystagmus may also be an end-point nystagmus that is non-pathological but interpreted otherwise. Subtle or sub-clinical INO may hence be missed without any objective recording of the eyes. Video-oculography can therefore value-add by providing an objective quantification, recording and analyses of oculomotor movements. This has implications on the interpretation of bedside tests such as the Hamalgyi-Cuthoys head thrust, which should be cautiously interpreted as a peripheral finding in view of the disconjugate oculomotor test results. One such useful test is the vHIT, which can record individual eye movements in response to bi-directional head thrust. In this case study, when left eye was recorded (Fig. 5), the abducting saccades were more prominent (due to higher velocities) on right head thrusting as compared to left head thrusting (corresponding adducting saccade). Conversely, saccade velocities were much higher in abduction of right eye during leftward thrusting as compared to adducting saccades during rightward thrusting when the right eye was recorded (Fig. 6). This is due to "slowing" of bilateral adduction, which is congruent with findings of lower adduction velocities in the video-oculography saccade test. Lower abduction eye gains during head thrusting can be explained by the failure of disfacilitation of medial rectus motor neurons by the excitatory abducen interneurons, which are usually inhibited by type 1 vestibular neurons [4]. In INO, Contralateral Posterior Semi-Circular Canals (SCC) are selectively impaired due to contralateral projections from the posterior SCC that ascends via ipsilesional Media-Longitudinal Fasciculus (MLF) [2]. However, anterior SCC are spared due to secondary neurons in the superior vestibular nucleus that receive projections from anterior SCC travelling outside the MLF tracts. These extra-MLF tracts are believed to be in the branchium conjunctivum or crossed central tegmental tracts [8]. Overall, the patient is relatively asymptomatic, aside from

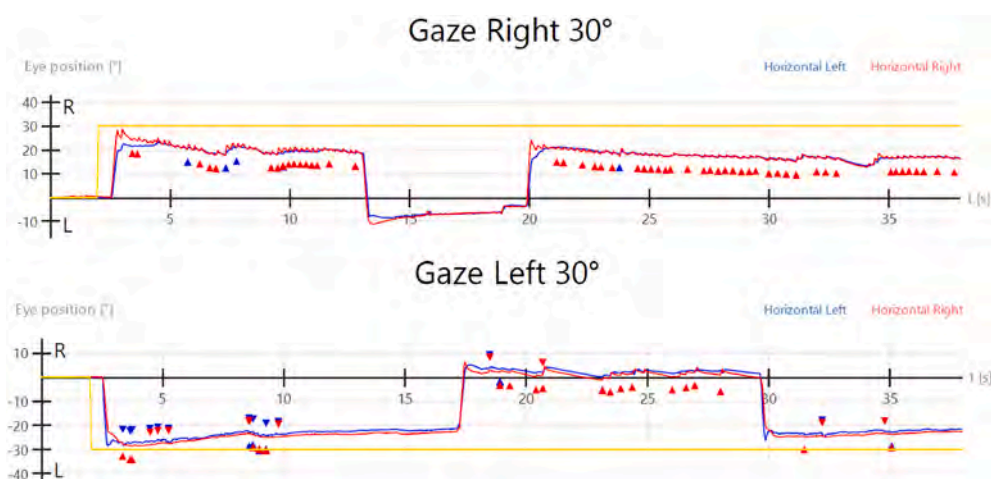


Fig. 1. Gaze evoked nystagmus.

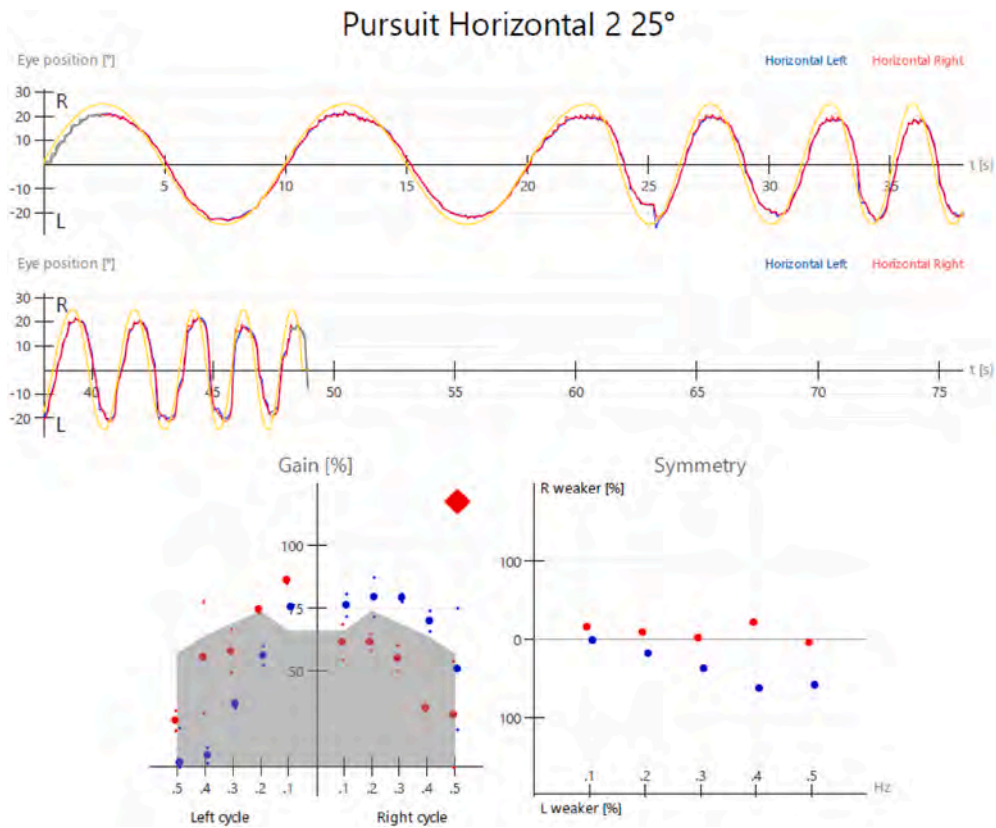


Fig. 2. Smooth pursuit.

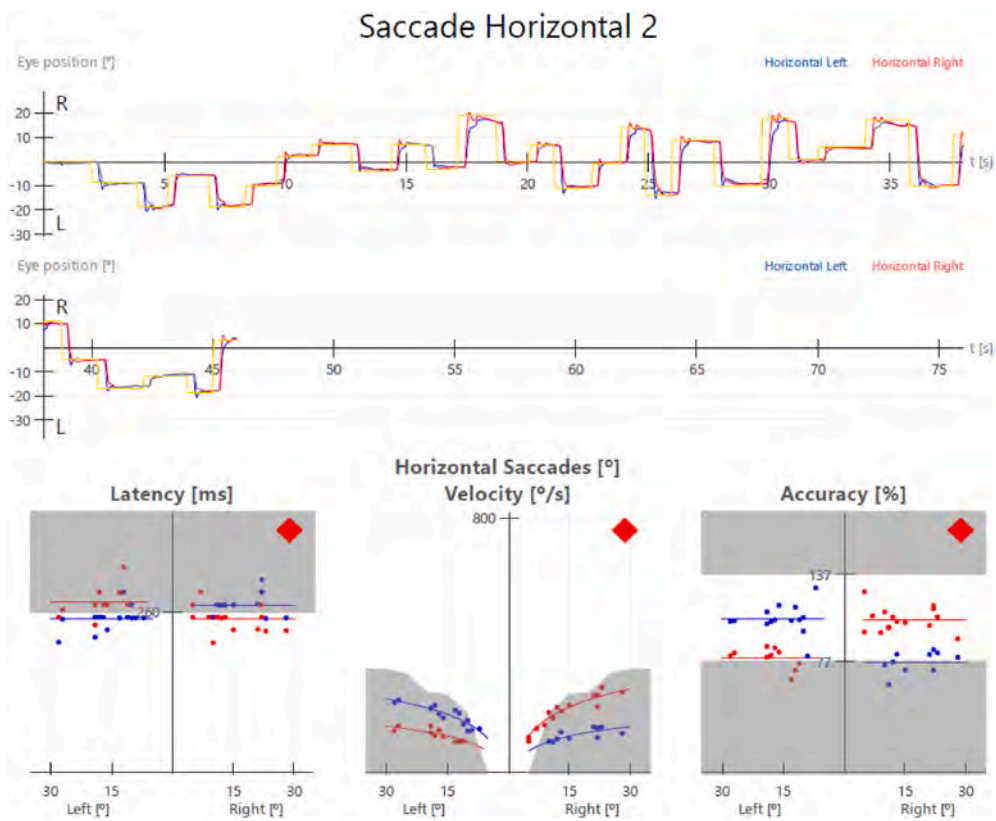


Fig. 3. Saccades.

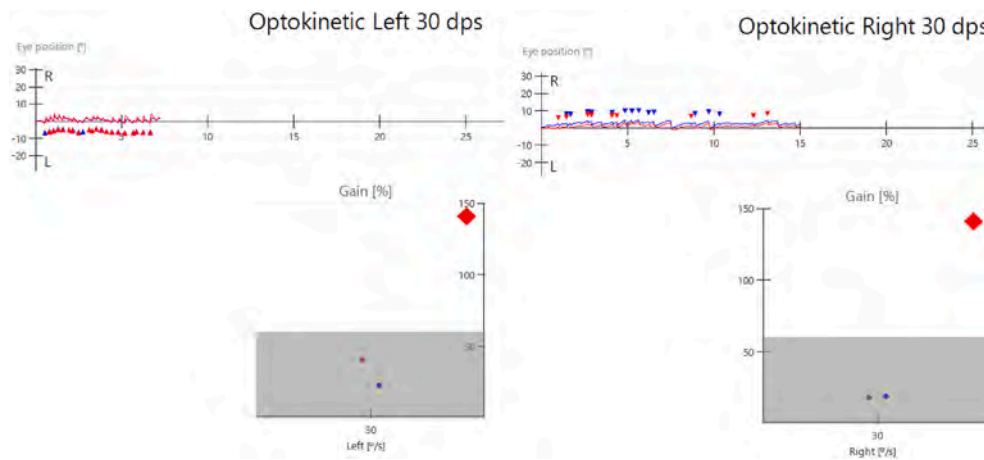


Fig. 4. Optokinetic nystagmus.

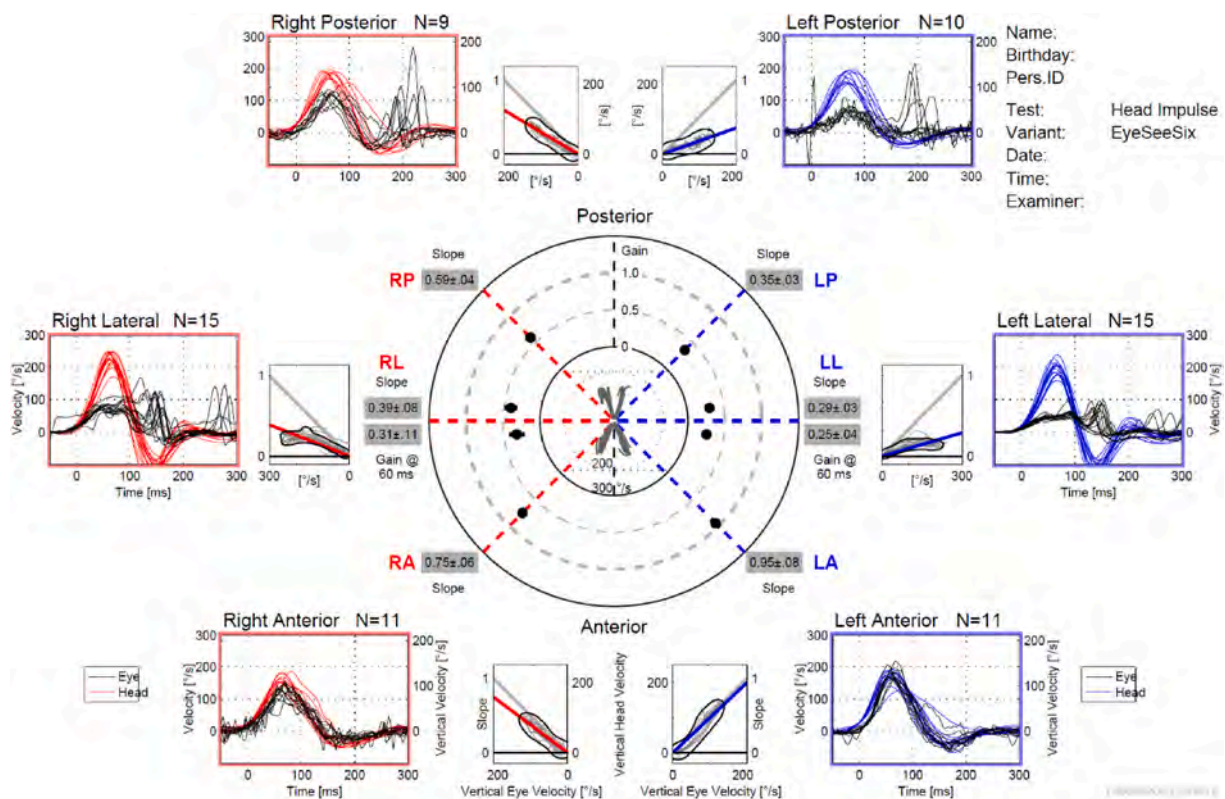


Fig. 5. Left eye recording of Video Head Impulse test (all paired canals).

complains of “shakiness” in her vision with head turns to either side while ambulating. Though there are no overt neurological signs and radiographic imaging are unremarkable, the patient still has functional impairments namely, with dynamic head movements due to disconjugate oculomotor movements. Such functional impairments should be focused on [9], with rehabilitation of central vestibular function showing promising results in small studies [10]. When radiographic imaging studies are negative but there are vHIT supporting signs of INO, patients should still be treated the same as those with overt INO. Active surveillance is hence, needed to watch for progressive demyelinating disease such as multiple sclerosis (MS) or less commonly encountered progressive supranuclear palsy (PSP). When INO is of a vascular cause, it is usually unilateral in most of cases [11]. Especially in the older age group with significant vascular risk factors, the focus is on ischemic

stroke as an underlying cause. On the contrary, bilateral INO are usually seen in demyelinating diseases [11] such as MS that needs to be ruled out, especially when it affects patients of a younger age group, with no significant vascular risk factors.

4. Conclusion

Clinical impressions for this case study were different and confusing because of peripheral vestibular and subtle neurological signs bedside. In this case study with a subtle bilateral INO, it was difficult to see the covert neurological signs such as slowing of adduction bilaterally. The employment of video-oculography will assist in visualizing and quantifying the oculomotor movements to assist in the diagnosis and management of INO. Ultimately, neuro-ophthalmology physicians should

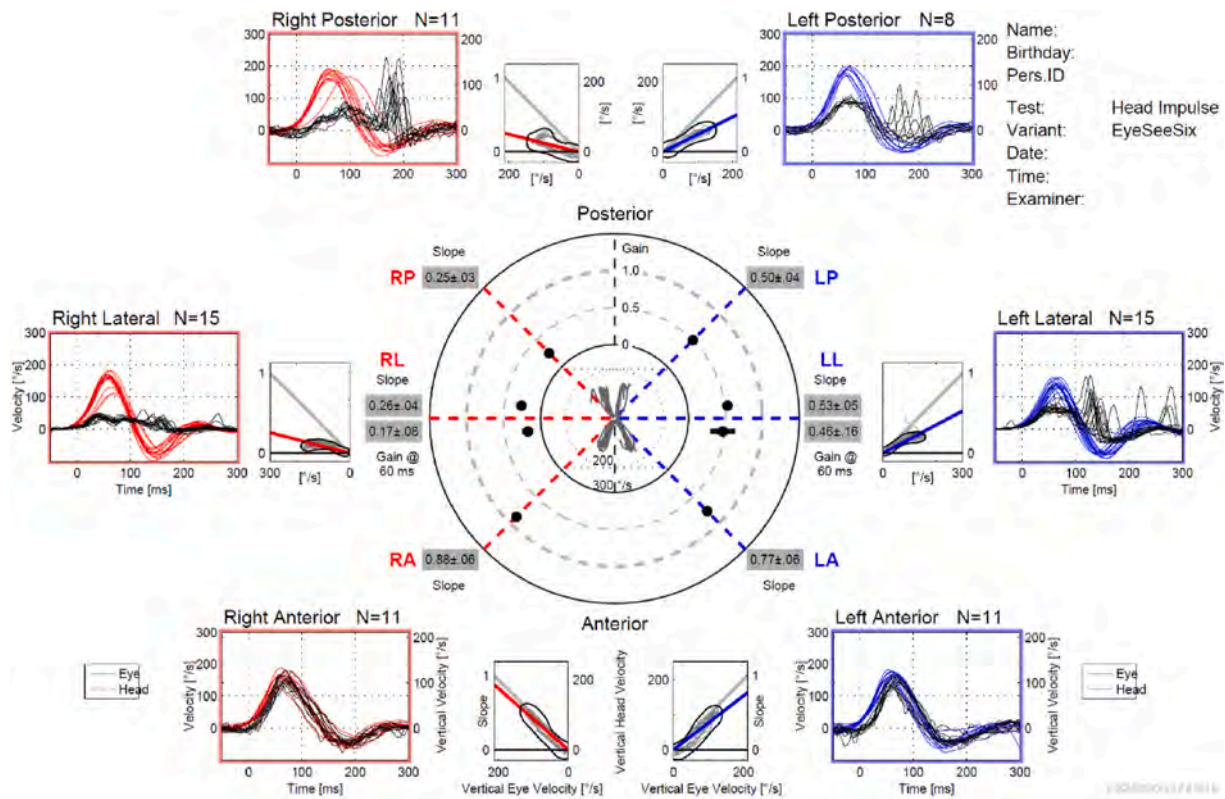


Fig. 6. Right eye recording of Video Head Impulse Test (all paired canals).

actively survey such patients even with subtle clinical signs, as it may be in the early stages of a progressive sinister disease such as MS or PSP.

5. Clinical PEARL

- 1) Interpret bedside head thrust with caution as a peripheral sign when nystagmus or eye movements are disconjugate.
- 2) Subtle clinical signs may require video-oculography to assist in the diagnosis and management of INO patients especially in the absence of other neurological signs.
- 3) Multi-disciplinary team of health professionals needed with good conceptual and procedural knowledge of INO needed to minimize “patient volleying” among departments.
- 4) Mild/subtle INO requires active surveillance and should be treated similarly to patients with overt INO.

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Ethical statement

Kenneth Chua: Conceptualization, Methodology, Software, Data curation, Writing- Original draft preparation, Visualization, Investigation, Validation, Writing- Reviewing and Editing.

Huang Xin Yong: Investigation, Validation, Paper Reviewing, final approval of manuscript.

David Low: Investigation, Validation, Paper Reviewing, final approval of manuscript.

Informed consent: Informed consent was obtained from the patient who consented to the use of data for the purpose of this case report.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.\

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