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Ear or brain: the hyperacute vestibular syndrome

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In 1998, Hotson and Baloh[1] detailed the clinical acute vestibular syndrome (AVS), consisting of severe vertigo, nausea and vomiting, spontaneous nystagmus, and postural instability, caused by a rapid unilateral injury to either peripheral or central vestibular pathways. Differentiating between a peripheral vestibular injury and a central, potentially life-threatening disease such as stroke, represents a clinical challenge for clinicians 25 years on. Indeed, a quarter of patients with risk factors for stoke who present with an isolated AVS have posterior circulation strokes, but these are missed in up to 60% of cases.[2]

Several diagnostic algorithms, focusing on history (TiTRATE, ATTEST) or eye movements (HINTS-plus) with gait assessment (STANDING) have been proposed to facilitate detection of stroke in patients with acute vertigo.[3] These algorithms have been mostly evaluated in specialist units, and exclusively in patients with AVS for whom symptoms have been present for a minimum of 24 h. The greatest diagnostic challenge lies closest to the symptom onset (<24 h), when decisions regarding acute imaging, reperfusion treatment, or safe hospital discharge are made. Focus on the hyperacute vestibular syndrome has been conspicuously absent in clinical research, perhaps precisely because determining an accurate diagnosis is particularly challenging.

In the setting of an ongoing acute vertigo study embedded within the emergency department (final dataset not published), we have observed patients presenting within a few hours of symptom onset, with an isolated hyperacute vestibular syndrome and evolving ocularmotor signs suggestive of a peripheral vestibular nystagmus to that suggestive of central nystagmus (figure).

A 75-year-old female with a background of breast cancer (treated with total mastectomy several years prior) presented with an acute onset of rotational vertigo whilst in the shower. This was associated with vomiting, and oscillopsia (causing blurring and jumping of vision, without diplopia). She was unsteady but initially managed to walk from the bathroom to her bedroom, holding onto furniture. A few minutes later was unable to stand due to severe unsteadiness. She did not report any other neurological symptoms. On arrival to the emergency room 2 hours later her blood pressure was 230/120mmHg. A 12-lead electrocardiogram was normal. She had unidirectional third degree right-beating nystagmus (figure 1A). There was a subtle right over left skew deviation. Pursuit movements were interrupted by the nystagmus. The head impulse test was abnormal to the left. There was loss of hearing to finger rub on the left (that the patient had not been previously aware of hearing loss) and grade 2 ataxia. Laboratory investigations including blood count, renal, liver, and bone profiles were normal. Total cholesterol was elevated at 7.0 (HDL 1.7, LDL 4.5). A CT head performed within 5 hours of symptom onset was normal. CT angiography revealed a short segment of severe stenosis of the left terminal internal carotid artery only. An MRI brain scan, including diffusion weighted images, was normal (within 24 hours of symptom onset). The National Institutes of Health Stroke Scale (NIHSS) score was 1, suggesting very mild disability. In the clinical context, a stroke affecting the anterior inferior cerebellar artery (AICA) was suspected so the patient was given dual antiplatelet therapy (aspirin and clopidogrel), atorvastatin and labetalol to control the elevated blood pressure.

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Audiovestibular assessment 24h after symptom onset revealed gaze-evoked nystagmus (figure 1B) and unilateral hearing loss on left. An MRI scan performed 5 days after symptom onset revealed an acute infarct in the left lentiform nucleus but no evidence of a posterior circulation infarct. Transthoracic echocardiography and 72-hour Holter monitor were normal. AICA-territory strokes often present as a pseudo-labyrinthitis, where ocularmotor features and ipsilateral hearing loss mimic a peripheral audiovestibular syndrome. As in this case, there may be other subtle central eye movement findings, such as skew deviation in patients with stroke, although skew deviation can also be seen in patients with an acute peripheral vestibulopathy as part of an ocular tilt reaction.. Brain imaging can be normal, particularly where the area of ischaemia is small[2]. The evolution of peripheral ocularmotor features (spontaneous unidirectional horizontal-torsional nystagmus) to central (gaze-evoked nystagmus) and acute hearing loss were red flags for a brain pathology. It should be noted that a thorough assessment must therefore include other ocularmotor signs (e.g., skew deviation), and an assessment of hearing and gait.

Presumably the changes in oculomotor signs are the consequence of the evolving ischaemia and infarction, challenging the dogma that the natural history of an acute ischaemic stroke is characterised by a sudden onset of acute neurological symptoms, peaking within a few minutes and persisting (unchanged) for 24h or more.[4]

These changing clinical signs might be responsible for a proportion of misdiagnosis in the emergency setting, where peripheral nystagmus can develop into central nystagmus over subsequent minutes or hours, even in the presence of normal brain imaging. The use of infrared or video technology to capture this evolution could help us to better identify central eye movement features to improve diagnosis, triage, and treatment. Moreover, we recognise that a minority of patients will present with central hyperacute vestibular syndrome and gait ataxia but without nystagmus or other neurological signs,[5] blunting the utility of algorithms such as HINTS and highlighting the need for hyperacute vertigo algorithms to include assessment of gait ataxia, such as the STANDING algorithm[3].

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References

1. Hotson JR, Baloh RW. Acute vestibular syndrome. *N Engl J Med* 1998; **339:** 680-5.
2. Saber Tehrani AS, Kattah JC, Mantokoudis G, et al. Small strokes causing severe vertigo: frequency of false-negative MRIs and non-lacunar mechanisms. *Neurology* 2014; **83**: 169–173.
3. Nakatsuka M, Molloy EE. The HINTS examination and STANDING algorithm in acute vestibular syndrome: a systematic review and meta-analysis involving frontline point-of-care emergency physicians. *PLoS One* 2022; **17**: e0266252.
4. Campbell BCV, Khatri P. Stroke. *Lancet* 2020; **396:** 129-142.
5. Carmona S, Martínez C, Zalazar G, Koohi N, Kaski D. Acute truncal ataxia without nystagmus in patients with acute vertigo. *Eur J Neurol* 2023; published online Feb 8. doi: 10.1111/ene.15729. doi: 10.1111/ene.15729.

Figure: A) Third-degree unidirectional right beating horizontal nystagmus (arrows) conforming to a peripheral vestibular syndrome in a patient with acute prolonged vertigo, vomiting, and grade 2 ataxia, examined in the hyperacute phase. B) 24 h later the nystagmus evolved to bi-directional gaze-evoked nystagmus (arrows) of central type. We propose this was due to an anterior inferior cerebellar artery stroke of embolic origin given an acute lentiform nucleus infarct. Note that strokes affecting the posterior circulation can be missed on MRI scans, as in this case. Written informed consent to publish clinical data was obtained from the patient.