CEREBELLAR INFARCTS VS ACUTE PERIPHERAL VERTIGO: HOW TO AVOID MISDIAGNOSIS- A REVIEW OF LITERATURE

Shaveta Yadav1, Narendra Singh Rathore2, Guang Yao Wu3 and Ning Tu4

1MD, Department of Radiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, P. R. China.
2MD, Department of Radiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, P.R.China.
3MD, Ph.D. Department of Radiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, P.R.China.
4PhD. Department of Radiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, P. R. China.

*Corresponding Author: Guang Yao Wu
MD, Ph.D. Department of Radiology, Zhongnan Hospital of Wuhan University, Wuhan 430071, P.R.China.
Email ID: wuguangy2002@163.com.

ABSTRACT
Cerebellar infarcts account for between 1.5% and 3% of all ischemic strokes. Vertigo and imbalance are the most common symptoms in patients with isolated cerebellar infarctions1,2 and they appear without any other signs of cerebellar dysfunction in approximately 38% of patients.3 Cerebellar infarcts are one of the common causes of vascular vertigo. APV is a clinical disorder caused by acute unilateral damage of the peripheral vestibular structures, which is characterized by long-lasting (more than 24 hours) rotary vertigo, spontaneous nystagmus, postural instability, and neurovegetative symptoms without signs of cochlear and brain stem involvement.4 The diagnosis of cerebellar infarctions can be challenging, as the commonly associated clinical signs and symptoms and the unfound reliance on a negative CT scan5 may not necessarily alert a physician to a stroke. Misdiagnosis of cerebellar infarct (CI) has not been well documented.6 There are very few reports regarding the misdiagnosis of cerebellar infarct (CI).7 Study by Norrving8, found that approximately one-fourth of patients with vascular risk factors who presented in an emergency medical setting with isolated severe vertigo, nystagmus, and postural instability had an infarct in the territory of the mPICA. Kuroki,9 reported that 4 of 18 (22%) patients with CI were not diagnosed at first and were misdiagnosed as patients with vertigo. The goal of the present review article is to study how to avoid the misdiagnosis of cerebellar infarct. Diffusion Weighted Imaging (DWI) is considered better than computed tomography (CT) for the diagnosis of infarct but in some cases even DWI may fail to predict an acute infarct and its sensitivity is lower in the posterior fossa as compared to the anterior fossa. A focused bedside HINTS (head impulse, nystagmus, test of skew) examination can identify stroke with high sensitivity and specificity in patients presenting to the emergency department with acute isolated vertigo and is superior to diffusion-weighted magnetic resonance imaging (MRI) during the acute phase.  

KEYWORDS: *Cerebellar infarction *MRI *Misdiagnosis.

INTRODUCTION
Cerebellar infarcts account for between 1.5% and 3% of all ischemic strokes. Vertigo and imbalance are the most common symptoms in patients with isolated cerebellar infarctions1,2 and they appear without any other signs of cerebellar dysfunction in approximately 38% of patients.3 Cerebellar infarcts are one of the common causes of vascular vertigo. The differentiation between acute peripheral vertigo (APV) and pseudo-APV can be challenging, because the commonly presenting signs and symptoms might not necessarily alert a physician to a stroke. Cerebellar infarcts (CIs) are one of the most common causes of vascular vertigo. It is usually accompanied by other neurological symptoms or signs, but a small infarct in the cerebellum can present with vertigo without other localizing symptoms. Vertigo caused by CI is associated with a poor prognosis compared with vertigo related to other causes. Therefore, early diagnosis and treatment are very much necessary in patients with acute CI.

CLINICAL PRESENTATION
A) SYMPTOMS
Cerebellar infarct typically presents with non-specific symptoms such as headache, dizziness, nausea, vomiting and unsteady gait. It may mimic benign conditions such as viral gastroenteritis or labyrinthisis. Vertigo and lateropulsion are the most commonly seen symptoms seen in cases of isolated cerebellar infarction. Patients having stroke in the posterior circulation present with headache complaint more often as compared to patients presenting with strokes in the anterior circulation and more often with cerebellar infarction. Although the most common causes for dizziness are benign10,11 such as...
vestibular neuritis in which is not accompanied by hearing loss or labyrinthitis which is accompanied by hearing loss, the differential diagnosis for dizziness includes potentially life-threatening stroke. On the other hand, an acute imbalance without vertigo or dizziness is usually caused by a cerebellar stroke, particularly within the superior cerebellar artery distribution[12] and is not the result of a peripheral vestibular disorder. The medial branch of posterior inferior cerebellar artery (mPICA) infarcts are mostly associated with dizziness. A physician should think of stroke by looking for gait disturbance and assessment of eye movements. Some case reports and small series have shown that dizziness can also be the principal or only complaint in patients with stroke.[8,13,21]. In some cases, nausea and vomiting may be the only presenting symptom.

B) SIGNS

Neurological signs seen in cases with cerebellar infarcts include nystagmus, dysmetria, dysarthria and ataxia. Dysarthria is seen in about half of the cases of cerebellar stroke. Dysarthria with dizziness always suggest a central lesion. The motor deficits seen are ipsilesional. A lateral medullary syndrome namely Wallenberg's syndrome can be seen in PICA infarct. Limb ataxia is characterised by dysmetria, dysynergia and intention tremor, and is clinically assessed by the finger-to-nose and heel-to-toe tests 15]. It is classically associated with hemispheric cerebellar lesions[16] and rarely with brainstem lesions.[17] Limb ataxia is a sign of infarction of the lateral branches of superior cerebellar artery (SCA) and PICA. However, limb ataxia may even be absent in some cases with extensive cerebellar infarcts or can be seen in cases with supratentorial lesions. Thus, the patients presenting with vertigo or lateropulsion with stroke risk factors require special attention whether or not any other cerebellar symptoms or signs are present or not. In rare cases, the presentation of cerebellar infarction can be severe (e.g., coma and quadriplegia), particularly in association with incipient basilar artery thrombosis. Nystagmus can also be seen with peripheral vestibulopathies very commonly. The patients with infarcts in the cerebellum can also present with the cerebellar cognitive affective syndrome, which includes visual, executive, spatial, and linguistic impairments, and affective dysregulation in addition to the cerebellar motor syndrome. Some small cerebellar infarcts, occurring within the territory of the posterior cerebellar artery, may be silent or present with only subtle cerebellar findings. The cerebellar infarctions can be subclinical as well and, therefore, small incidental infarct cavities are frequently found in the cerebellum, especially in elderly and patients with cardiovascular disease, who do not have a known history of cerebellar transient ischemic attack (TIA) or stroke. If the stroke is unilateral, most of the patients fall towards the side of the lesion. Vertigo and imbalance are the most frequently seen symptoms in patients with isolated cerebellar infarctions[13,12], and they appear alone without any other signs of cerebellar dysfunction in approximately 38% of patients.[8] Several recent papers[18,19,20] have shown that how closely a cerebellar stroke may mimic an acute peripheral vertigo (APV). Usually when a cerebellar stroke mimics APV clinically, the infarct is located in the territory supplied by the medial branch of PICA.[18,21] This territory includes structures like nodulus and uvula connected with the ipsilateral vestibular nuclei and receives projections from the labyrinth.[22,23] Patients may have isolated vertigo, hearing loss with or without tinnitus (similar to Meniere's disease) as the initial symptoms 1–10 days prior to the permanent infarction. Orthostatic hypotension (OH), the most incapacitating sign of an autonomic failure, is defined as a decrease in systolic BP (SBP) of greater than 20 mmHg or a decrease in diastolic BP (DBP) of greater than 10 mmHg on standing or head-up tilt.[24] In the study done by Hyun[25], OH was found in 31% of the patients and the most common pattern of OH was early OH, which was observed in approximately 80% (7 out of 9) of the patients with OH. The medial part of the superior semilunar lobule and tonsil were more commonly damaged in the cerebellar OH group than in no cerebellar OH group. It was surprising that approximately 30% of the patients with isolated cerebellar infarction showed OH during tilting.

NEUROIMAGING

A) CT

The most commonly used imaging test for stroke is CT. CT is widely available, quick to perform and excludes acute haemorrhage. Cerebellar infarcts present as areas of hypodensity on CT. But CT is usually negative in the first few hours of acute ischaemic stroke and further because of the artifacts, CT has even lower sensitivity in the posterior fossa. Clinicians must understand this intrinsic limitation of CT in case they don't have access to MRI and avoid misdiagnosis.

B) MRI

Acute cerebellar infarcts are usually readily recognised as bright areas on DWI with low signal on apparent diffusion coefficient (ADC) maps due to restricted diffusion, although it should be noted that infarcts in the posterior circulation may be more often DWI negative than those in the anterior circulation.[26,27,28] DWI becomes positive within minutes after the onset of infarction because of cytotoxic oedema.[29,30] In the following hours, infarcts become hyperintense on FLAIR and T2-weighted images (T2WI). On MRI, small cerebellar infarcts are more conspicuous on T2WI than they are on fluid-attenuated inversion recovery images. DWI has increased the conspicuity of MRI in detecting small acute infarcts and is positive just within minutes after onset. DWI can also help differentiate between recent and older infarcts. But even DWI can be falsely negative in some cases of acute ischemic stroke. In the study Jorge et al[31], by DWI was found to be 88% sensitive overall and 72% sensitive for the infarctions in the lateral medulla and the lateral pons with vertebrobasilar strokes in these areas very frequently found to mimic APV closely. These results are almost
the same as the results from 2 prior studies of early DWI that reported on 206 vertebralbasilar strokes and found 77% sensitivity within 24 hours of symptom onset. CT is known less accurate in detecting an acute ischemic lesion within the posterior fossa but DWI can also be misleading in quite a few number of cases in the first 24-48 hours after symptom onset which makes MRIs less potent for diagnosing stroke than the composite HINTS examination.

MISDIAGNOSIS

Misdiagnosis of cerebellar infarct (CI) has not been well documented. There are very few reports regarding the misdiagnosis of CI. Kerber et al. [31] reported that stroke or transient ischemic attack was diagnosed in only 3.2% (553/1666) of the patients presenting with dizziness. Miyashita [34] reported that stroke was diagnosed in 7.4% (23/309) of patients admitted with complaint of vertigo. Approximately one-fourth of patients with vascular risk factors who presented in the emergency department with isolated severe vertigo, nystagmus, and postural instability had a CI in the territory of the mPICA [8]. Kuroki [18] reported that 4 of 18 (22%) patients with CI were not diagnosed at first and were misdiagnosed as patients with vertigo. Misdiagnosis of strokes in the posterior circulation presenting with dizziness is very common, occurring in about 35% of cases [33] and can result in high morbidity and mortality. The differentiation between APV and pseudo-APV can be challenging, because the commonly presenting signs and symptoms might not necessarily alert a physician to a stroke. Cerebellar infarcts are one of the most common causes of vascular vertigo. It is usually accompanied by other neurological symptoms or signs, but a small infarct in the cerebellum can present with vertigo without other localizing symptoms. Vertigo caused by CI is associated with a poor prognosis compared with vertigo related to other causes. Therefore, early diagnosis and treatment are very much necessary in patients with acute CI. Approximately 11% of the patients with isolated cerebellar infarction simulated acute peripheral vestibulopathy (APV). APV is a clinical disorder characterised by long-lasting (>24hours) rotatory vertigo, spontaneous nystagmus, postural instability and neurovegetative symptoms without signs of cochlear and brain stem involvement and is caused by acute unilateral damage of the peripheral vestibular structures. The most frequent cause of APV is vestibular neuritis [4,35]. An ischemic cause can also lead to APV [36,37] as frequent association of APV with blood hyperviscosity has been seen [38] also with alterations of the hemostatic system [39], or dysfunction or microvascular endothelium [40].

Mostly, patients with vertigo and headache are seen by physicians for their first medical examination rather than neurologists and this leads to mis-diagnosis in the very first place. If a presents with vertigo and nausea, general physicians might avoid neurologic examination in such patients which will again, lead to mis-diagnosis of CI. Insufficient examination and imaging can result in misdiagnosis. Savitz et al. [41] have reported a relationship of 15 cases of misdiagnosed CIs and they found that misdiagnosis was more frequent in younger patients and those with incomplete or poorly documented neurologic examinations and a normal initial CT scan. Misdiagnosis may be more likely in younger patients who are not generally considered to be at risk for stroke. Vertebral artery dissections, the leading identifiable cause of posterior circulation stroke among young adults [42], can present with an APV mimic. Saito et al. [43] reported that 5 of 22 patients with CI were not initially diagnosed with CI, even though the main complaint of all the 5 patients was vertigo. Therefore, they recommended that the stroke team should be involved in the diagnosis of patients with vertigo or vomiting so as to avoid misdiagnosis of CI. Lee et al. [44] reported that 10.4% (25/240) of patients with isolated CI clinically resembled vestibular neuritis. A normal head impulse and caloric test could differentiate between isolated vertigo associated with mPICA infarction from acute peripheral vestibulopathy.

Following are the consequences of missed cerebellar infarction.

a) Not recognizing dissection
b) Missing other vascular occlusive lesions that predispose to recurrent strokes
c) Missing a cardiac thrombus
d) Life-threatening edema
e) Morbidity (permanent deficits)
f) Death

BEDSIDE DIAGNOSIS OF STROKE IN ACUTE ISOLATED VERTIGO:

A) HIT

It is believed that the bedside head impulse test (HIT) is very useful for differentiating acute vascular vertigo from that due to pathology involving the inner ear. The Head Impulse Test (HIT) is a widely used clinical tool used to look for the angular vestibulo-ocular reflex (aVOR). During the HIT, the patient is asked to fix his or her eyes on a target (e.g. the examiner’s nose). The examiner generates a rapid head impulse and looks for a corrective or compensatory saccade (CS) response. The individuals with normal vestibular function keep their eyes fixed on the target even after the head impulse by the examiner and therefore the head impulse is negative in patients with normal vestibular function. Patients with vestibular hypofunction may generate a corrective saccade (CS) after the head impulse towards the affected (pathological side) & this is considered a +ve HIT test. The rapid rotation of the head toward the affected side will result in loss of fixation and movement of the eyes.
away from the target in cases of peripheral vertigo (where vestibulo-ocular reflex is impaired). This is followed by a corrective saccade as the subject looks back towards the target. This finding of corrective saccade is abnormal, and considered a positive test. In patients with central vertigo, there is no corrective saccade (the vestibulo-ocular reflex usually remains intact). The clinical HIT is not scored per se, aVOR function is evaluated as normal or abnormal (i.e., hypofunctional) by noting the presence (+ finding) or absence (-finding) of a compensatory saccade.

a) Pros of HIT
1. It is a very quick way to detect a unilateral loss.
2. HIT is also poorer than the vibration test as it can fail (especially in compensated patients) and also vulnerable to bias. But in uncompensated vestibular loss, HIT is more specific than vibration test and head shaking.
3. HIT is the most consistent bedside predictor of central isolated vertigo of a vascular cause and a normal HIT indicates an absence of vascular pathology.
4. A -ve h-HIT strongly suggests a central lesion with a pseudo-labyrinthine presentation.
5. If a patient has all the three tests-HIT, head-shaking nystagmus and vibration induced nystagmus tests positive, one can be certain that there is highly significant unilateral vestibular weakness.

b) Cons of HIT
1. It is well documented that the sensitivity of the HIT depends on the degree of canal paresis, as well as on the phase of the disease and is 100% only in the case of complete vestibular loss and in the acute phase of AVS, and also more than 50% of canal paresis is needed for the HIT to be positive.
2. Furthermore, small fast corrective saccades which could occur during the head rotation are impossible to detect with the naked eye (covert saccades).
3. Patients with infarcts in the cerebellum and lateral pons may also show a +ve horizontal head impulse test (h-HIT) so we cannot rely that a +ve HIT implies a benign pathology.
4. HINTS might be negative during the acute phase of APV as well and a careful interpretation of HINTS requires high degree of skill. Therefore, HINTS cannot be considered as a single predictor to diagnose central lesions.
5. False positives HIT may be seen with (+) findings reported in patients with acute cerebellar and brainstem strokes unrelated to peripheral vestibular dysfunction.
6. HIT may be positive in infarcts involving AICA territory(flocculus) and in brainstem stroke involving the vestibular nucleus.
7. It does not replace electronystagmogarn (ENG) which is sensitive to even 35% weakness) or vibration or rotatory chair (which can check the low frequencies).

B) HINTS
Another rapid test HINTS has been proposed to differentiate central from peripheral vertigo. HINTS stand for Head Impulse, Nystagmus and Test of Skew. If any single test out of these three is positive, the HINTS test is considered positive and further evaluation for stroke or any other central pathology should be done.

Study by Jorge et al[31], also proves that a presence of even one of the three oculomotor signs of HINTS examination (normal h-HIT or horizontal nystagmus that changes direction in eccentric gaze or skew deviation) is more sensitive than the combined presence of all other traditional neurological signs for identifying stroke as a cause of AVS. Most importantly, they showed that a benign H.I.N.T.S. exam result at the bedside “rules out” stroke better than a negative MRI with DWI in the first 24–48 hours after symptom onset, with acceptable specificity (96%).

Table 1: To differentiate central from peripheral vertigo using HINTS test.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CENTRAL VERTIGO</th>
<th>PERIPHERAL VERTIGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>HEAD IMPULSE</td>
<td>Normal</td>
</tr>
<tr>
<td>2.</td>
<td>NYSTAGMUS</td>
<td>Gaze-evoked/ Bidirectional</td>
</tr>
<tr>
<td>3.</td>
<td>TEST OF SKEW</td>
<td>Refixation/Vertical Strabismus</td>
</tr>
</tbody>
</table>

The three components of the examination are as follows.

1- Head impulse test
Discussed above.

2- Nystagmus
Patients with peripheral vertigo will have a horizontal-beating, unidirectional nystagmus which beats away from the affected side and increases in intensity when the patient looks in the direction of the fast phase. Vertical or horizontal nystagmus indicates a central pathology but these patients may also show a horizontal nystagmus, thus making diagnosis difficult. These case can be judged by looking at the direction of the fast phase which may change on eccentric gaze, this means, if the fast phase beats in a particular direction when the patient is looking towards left, it will beat in opposite direction when patient looks to the right (on returns to the midline). This direction-changing nystagmus reliably excludes a peripheral etiology.

3- Skew deviation
Patients presenting with vertigo because of a central pathology will have a vertical misalignment of eyes (one
eye’s gaze slightly higher than the other) as a result of right-left imbalance in otolith (gravity-sensing) function. In this test, the patient is asked to focus on a fixed target and the eyes are closed alternatively. The cover is moved from one eye to the other, and the uncovered eye at that point of time corrects for the misalignment by looking up or down to focus back on the target. The eye which is covered this time, will be uncovered next time and the uncovered eye at that point of time will correct for misalignment. The cover is moved back and forth over the two eyes and this slight correction is noted. Patients with peripheral vertigo show no skew deviation or ocular tilt in majority of the cases whereas patients with posterior fossa abnormalities/brainstem strokes show such misalignment and skew deviation (with or without an associated head tilt and ocular fundus torsion).

a) Pros of HINTS
1. Skew predicts brainstem involvement in AVS and can identify stroke when we have an abnormal h-HIT which is falsely suggesting a peripheral lesion.
2. Most patients with central vertigo lack an objective finding. In such cases, HINTS exam will be an added benefit to detect the central pathology who would otherwise be discharged home otherwise.
3. Although physicians rely on MRI to diagnose acute stroke, care should be taken not to use DWI alone to rule out stroke in AVS in first 24-48 hours after symptom onset.
4. A benign HINTS exam rules out stroke much better than a -ve MRI in the first 24-48 hours after onset of the symptoms.
5. Cases with stroke in the posterior fossa may have -ve MRI but +ve HINTS examination. These cases should be admitted for further testing and evaluation.
6. A bed-side evaluation of HINTS test showing abnormal head- impulse test, a unidirectional nystagmus and absence of skew deviation has high specificity than MRI to exclude stroke and strongly predicts peripheral pathology. DWIs may be false-negative in the first 24-48 hours of symptom onset.
7. Bedside HIT may be the best tool among the three signs in HINTS for differentiating isolated vertigo due to cerebellar stroke (particularly within the territory of the posterior inferior cerebellar artery, PICA) from acute peripheral vestibulopathy as mild degree of skew deviation may go unnoticed during the examination and Gaze Evoked Nystagmus (GEN) might be absent in some cases of cerebellar stroke.

b) cons of HINTS
1. This test should be performed only on patients with continuous vertigo. Head impulse will be normal in patients without active, continuous vertigo as they have the intact vestibulo-ocular reflex so no corrective saccade will be observed. This holds for both patients with BPPV and in those without vertigo at all. Such a finding is misleading, as it indicates a central pathology. This leads to unwanted tests or hospital admission in such patients.
2. Although a normal h-HIT is the single best bedside predictor of stroke[19] and the test properties of h-HIT are also comparable to those of early diffusion weighted MRIs but even then if the other findings are not considered, about one in ten strokes might still be missed. The dangerous signs can be remembered using the acronym I.N.F.A.R.C.T. (Impulse Normal, Fast-phase Alternating, Refixation on Cover Test).
3. The HINTS exam is very sensitive in distinguishing central from peripheral vertigo but studies till now have judged its importance in the hands of neuro-otologists and neuro-ophthalmologists who are much more familiar with each component of the HINTS examination than the emergency physicians who are the ones who have to examine the patient in the emergency department. Studies on HINTS have not been done in the hands of emergency physicians and additional training might be necessary before this test can be routinely used in the emergency setting.
4. Most of the emergency physicians are either completely unaware of the importance of the HINTS examination or are unfamiliar about how to perform it and interpret it.
5. Some argue that in patients in whom stroke is considered should be advised MRI or be admitted for further evaluation by a neurologist. But HINTS examination is considered reliable when performed carefully and in skilled hands and a -ve test should obviate the need for further testing in almost all but the highest- risk patients.

When Does a Patient with Isolated Vertigo Need an Urgent Brain Scan?
An urgent brain scan should be done in:
1. older patients with isolated spontaneous prolonged vertigo
2. any patient with isolated spontaneous prolonged vertigo having vascular risk factors who had a normal HIT
3. any patient with isolated spontaneous prolonged vertigo with severe gait ataxia with falling at upright posture or had direction-changing GEN
4. any patient presenting with acute spontaneous vertigo and new-onset headache, especially occipital,
5. any patient with vascular risk factors and acute onset of vertigo and hearing loss without a history of Meniere’s disease.

CONCLUSION
CT is less sensitive than MRI in the posterior fossa but diffusion-weighted MRI can also be misleading in quite a few number of cases especially in the first 24-48 hours after symptom onset. Screening AVS patients for HINTS (normal h-HIT, direction-changing nystagmus, skew deviation) appears to be more sensitive than MRI with
DWI in detecting acute stroke in the first 24–48 hours after symptom onset. The presence of skew deviation may help in identifying a stroke when a positive h-HIT is falsely suggesting a peripheral lesion. These “H.I.N.T.S. approach could help prevent misdiagnosis of patients with stroke in AVS and are also cost-effective against neuroimaging by diffusion-weighted MRI.

CONFLICTS OF INTEREST
The authors have no conflict of interest.

REFERENCES
6. Yoko Masuda, MD,* Hideaki Tei, MD,† Satoru Shimizu, PhD,‡ and Shinichiro Uchiyama, MD* Factors Associated with the Misdiagnosis of Cerebellar Infarction Journal of Stroke and Cerebrovascular Diseases, October 2013; 22(7): 1125-1130.
28. Makin SD, Doubl F, Dennis MS, Wardlaw JM: Clinically confirmed stroke with negative diffusion-weighted imaging magnetic resonance imaging: longitudinal study of clinical outcomes,


31. Jorge C. Kattah, MD; Arun V. Talkad, MD; David Z. Wang, DO; Yu-Hsiang Hsieh, PhD, MS; David E. Newman-Toker, MD, PhD HINTS to Diagnose Stroke in the Acute Vestibular Syndrome Stroke, 2009; 40: 3504–3510.


