



Isolated Nodular Ischemic Infarcts: A Central Lesion That Presents as Peripheral Vertigo

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Authors' contributions

This work was carried out in collaboration between all authors. Author LLY study concept and design, Table, chart review, drafting the manuscript and literature search. Author HLT literature search, manuscript review. Author RR manuscript review and editing. Authors GH and ET Interpreting neuroimaging studies, critical revision of the manuscript. Author VKS Conceptualize and supervise the study. Review and editing of the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims and Objective: Giddiness is one of the commonest presenting complaints to the emergency physicians. Differentiation between 'peripheral' and 'central' etiologies is important to avoid unnecessary investigations and avoid missing a potentially serious diagnosis such as an ischemic stroke. Isolated nodular infarction can present with clinical signs that mimic a peripheral vestibular cause. We present the clinical findings in 14 cases of isolated nodular infarction and discuss their differentiating features.

Study Design: Retrospective case series.

Place and Duration: Tertiary care university hospital in Singapore between January 2007 to September 2012.

Methods: We evaluated the clinico-radiological findings of all the patients diagnosed with isolated nodular infarction at our center during the study period. Their clinical presentations were extracted from the case records. We combined our cases to an

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existing series of 8 patients from Korea to strengthen the findings.

Results: Of the 286 acute posterior circulation ischemic stroke patients admitted to our tertiary care center during the study period, 6 (2.1%) were found to have isolated nodular infarction. They typically presented with acute severe giddiness. Nystagmus was seen in all, which was unidirectional and beating towards the side of the lesion with no latency or fatigability. Walking was usually severely impaired due to imbalance and all patients had a negative head impulse test. All patients at our center achieved complete recovery at 3-months.

Conclusions: We present the clinical spectrum of isolated nodular infarction. In addition to a high index of suspicion in patients with multiple vascular risk factors, a negative head impulse test despite severe vertigo and imbalance can help in establishing the correct diagnosis.

Keywords: Acute ischemic stroke; cerebellum; nodulus; vestibular; vertigo.

1. INTRODUCTION

Giddiness is a common presenting complaint to the emergency physicians. One of the primary aims of the initial clinical evaluation in patients with vertigo is the differentiation between 'peripheral' and 'central' etiologies. By adopting this approach, the treating clinician aims at limiting the advanced investigations in most cases while 'not' missing a potentially serious diagnosis such as an acute posterior circulation ischemic stroke. An isolated infarction of the cerebellar nodulus (nodular infarction) is one entity that can present with clinical signs mimicking a peripheral vestibular cause. We present the spectrum of clinical findings in 14 cases of isolated nodular infarction and discuss their differentiating features.

2. MATERIALS AND METHODS

In this retrospective single center study, we evaluated the case records of all the patients admitted to our tertiary care center between January 2007 and September 2012. All patients with posterior circulation stroke underwent magnetic resonance imaging (MRI) and angiography (MRA) of the brain at our center. Information regarding their demographic characteristic, vascular risk factors, presentations, clinical finding, course and outcome at 3 months (measured by modified Rankin scale) was extracted from the chart reviews. In addition to the 6 patients from our center, we included 8 patients from a recently published case series from Korea [1] for further elaboration of the clinical spectrum of isolated nodular infarction. Data for the patients from Korea were extracted from the published manuscript [1].

3. RESULTS AND DISCUSSION

Of the 286 acute posterior circulation ischemic stroke patients admitted to our tertiary care center during the study period, 6 (2.1%) were found to have isolated nodular infarction. Demographic characteristics, vascular risk factors, clinical presentations and outcome data are presented in Table 1.

Similar to other ischemic strokes, nodular infarcts occurred in all age-groups (mean age 66.5 years; range 37-88) and most of the cases suffered from various cardiovascular risk factors. None of the patients suffered from hearing difficulties, tinnitus, pain or ear discharge. Absence of dysarthria, cranial nerve palsy, long tract signs and truncal ataxia were striking

features. All cases presented with severe acute giddiness and walking was severely impaired due to imbalance. Only case-3 could stand unaided. Most of the cases demonstrated nystagmus at rest that became worse on head-shaking. Although nystagmus at rest was not seen in cases-3 and 11, it could be evoked with head shaking, beating in the direction of the nodular infarction. Importantly, none of the cases demonstrated dysmetria or other cerebellar signs.

Acute cerebellar nodulus infarctions were noted on diffusion-weighted MRI in all cases. However, MR angiography did not reveal significant arterial stenosis in the vertebro-basilar circulation in any patient. There was no relationship between the side of hypoplastic vertebral artery and nodular infarction. All cases at our center recovered completely at 3-months from symptom-onset and received aspirin (100mg daily) for secondary stroke prevention.

The typical characteristics of one case are presented below-

Case 1, a 77-year old man with well controlled diabetes mellitus (glycosylated hemoglobin 6.7%) presented with severe vertigo of sudden-onset. On arrival to hospital, he was fully conscious and orientated, with a regular pulse at 67 beats/minute and blood pressure 123/65 mmHg. He was unable to stand without support and tended to fall to his right side. Speech, limb power and coordination were normal and there was no truncal ataxia. Interestingly, a left-beating nystagmus was observed at rest, which was accentuated with head-turning to the left. Extra-ocular movements revealed normal saccades and smooth pursuits. Head-impulse test was negative. Brain computed tomography (CT) was unremarkable. Owing to the persistent symptoms, magnetic resonance imaging (MRI) of the brain was performed on day-3 that revealed restricted diffusion in the left cerebellar nodulus (Fig. 1). No flow limiting stenosis in the intracranial arteries was noted on MR angiography. Aspirin was commenced for secondary stroke prevention. The patient recovered completely within 2 weeks.

Table 1. Clinical features and outcomes in 14 patients with nodular infarcts

	Age/ Sex	Risk Factors	Present -ation	Able to stand or walk	Side of nodular infarct	Ocular Saccades and pursuits	Nystagmus		Head- impulse test	Falling while attemp t to walk	Modified Rankin scale at 3 months
							Spontaneous	Head- shake			
Case 1	77/M	DM	vertigo	No	Left	Normal	Left	Left	Negative	Right	0
Case 2	88/M	HTN, DM	vertigo	No	Left	Normal	Left	Left	Negative	Right	0
Case 3	65/F	HTN, DM	vertigo	Able to stand but not walk	Right	Normal	None	Right	Negative	Left	0
Case 4	82/M	AF, Lipid	vertigo	No	Right	Normal	Right	Right	Negative	Left	0
Case 5	82/M	AF	vertigo	No	Right	Normal	Right	Right	Negative	Right	0
Case 6	52/M	Lipid	vertigo	No	Right	Normal	Right	Right	Negative	Left	0
Case 7*	56/M	Lipid, Smoking	vertigo	No	Right	Unknown	Right	Right	Negative	Right	Unknown
Case 8*	67/M	Smoking	vertigo	No	Both	Unknown	Right/ Down	Right/ Down	Negative	Left	Unknown
Case 9*	66/F	HTN	vertigo	No	Right	Unknown	Right	Right/ Down	Negative	Left	Unknown
Case 10*	51/M	Nil	vertigo	No	Left	Unknown	Left	Left	Negative	Right	Unknown
Case 11*	64/F	Nil	vertigo	No	Left	Unknown	Nil	Left	Negative	Right	Unknown
Case 12*	69/M	HTN	vertigo	No	Both	Unknown	PAN	Down	Negative	NA	Unknown
Case 13*	37/M	HTN	vertigo	No	Left	Unknown	Left /CCW	NA	Negative	Right	Unknown
Case 14*	75/F	Nil	vertigo	No	Right	Unknown	Right	Nil	Negative	Both	Unknown

*HTN- hypertension; AF- atrial fibrillation; DM- diabetes mellitus; Lipid- hyperlipidemia; PAN-
perverted alternating nystagmus; CCW- counter-clockwise nystagmus; NA- not available
*patients from Korean series

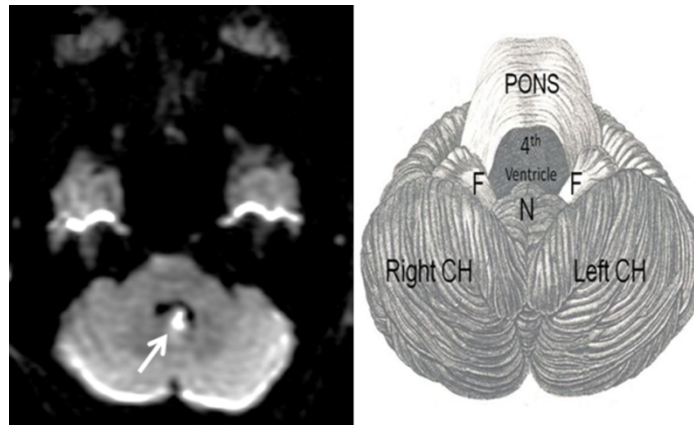


Fig. 1. Diffusion-weighted Magnetic resonance imaging in case 1 shows an acute infarction in the region of left nodulus (A). Panel B shows a schematic diagram to represent various structures in the posterior cranial fossa. CH-cerebellar hemisphere; F- flocculus; N- nodulus

Vertigo of sudden-onset, without accompanying focal neurological deficits is often diagnosed as acute vestibulopathy, especially if only computed tomography of the brain is performed and the symptoms resolve. The advent of MRI has facilitated the diagnosis of small ischemic infarctions in the brain. Nodulus is a small area of cerebellum, just adjacent and posterior to the 4th ventricle and plays an important role in maintaining balance. Isolated vertigo is the commonest presentation in patients with isolated acute nodular infarction, which may easily be dismissed as vestibulopathy. Such a mis-diagnosis might deny the benefits of antithrombotic agents for secondary prevention of cerebral ischemia in these patients.

3.1 Anatomical Considerations

The nodulus and flocculus make up the vestibulocerebellum and help fine-tune the eye movement with the inputs from the vestibular system [2]. In addition to modulating eye movements, these structures help in spatial proprioception of the body and head [3].

The flocculus derives its blood supply from the anterior inferior cerebellar artery while the nodulus is perfused by the posterior inferior cerebellar artery. Nodular infarcts seldom occur in isolation and are more commonly associated with other ischemic infarctions within the vascular territory of the medial branch of posterior inferior cerebellar artery.

3.2 Etiopathogenic Considerations

MRI scans in all the patients demonstrated nodular infarcts. No relevant steno-occlusive lesions were noted in the vertebrobasilar system in any patient in our series, suggesting small vessel disease as the likely mechanism. However, atrial fibrillation was also noted in 2 cases that could also have contributed to the stroke etiology.

3.3 Nystagmus

Differentiating between the peripheral and central nystagmus is a pivotal step in the evaluation of a patient with vertigo. Ischemic infarcts have a hyperacute onset while peripheral vestibular lesions tend to have a subacute onset that can take minutes to few hours. Nystagmus from a 'peripheral' vestibular cause is predominantly horizontal with increasing intensity when the gaze is turned in the direction of fast phase. It is typically direction-fixed with a short latency at the onset. A key sign of vestibular dysfunction is the suppression of unidirectional nystagmus with visual fixation, representing an intact central mechanism.

An important feature of nystagmus that can help in differentiating between the central and peripheral lesions is the habituation. Nystagmus from a central lesion does not habituate as compared to a vestibular lesion in which it tends to gradually desist. Owing to the prolonged nystagmus, cerebellar infarctions can lead to some unusual ocular signs such as periodic alternating nystagmus (in which the eyes undergo a horizontal jerk nystagmus that periodically reverses direction) and perverted head shaking nystagmus (nystagmus occurs in a plane other than that being stimulated) [4].

Unidirectional nystagmus is usually believed to be 'vestibular' in origin. However, nodular infarctions often defy this principle, as evident in 11 out of the 14 patients in this series. The nystagmus beats towards the side of the lesion, possibly due to be the loss of inhibition from the ipsilateral vestibular nucleus [5]. Cerebellar flocculus is important for suppressing the vestibular nystagmus by visual fixation. Therefore, in the isolated infarctions of nodulus (with sparing of the flocculus), ocular fixation is intact and the nystagmus from a 'central' cause might mimics a peripheral vestibular lesion [6]. Finally, nodular lesions usually present with direction-fixed horizontal nystagmus. However, down-beat nystagmus may also be seen rarely [1]. In some cases, even body tilting contralateral to the direction of the nystagmus may occur in nodular infarcts, which mimics an acute pathology of the contralateral labyrinth.

In summary, isolated nodular infarcts present with a hyperacute onset of giddiness accompanied by a horizontal nystagmus. The nystagmus has a fast component in the direction of the side of lesion and has no latency or fatigability. Interestingly, the nystagmus can be suppressed with visual fixation due to an intact flocculus.

3.4 Bedside Tests

Head-shake and head-impulse tests for nystagmus are the two bedside maneuvers frequently used to screen for unequal vestibular function due to vestibulopathy rather than a central cause. Although the head shaking test is used to detect a unilateral vestibulopathy, this test is frequently positive in patients with isolated nodular infarcts. This occurs because nodular connections to the vestibular nuclei apply constraints to the velocity-storage mechanism in the vestibular-ocular reflex [7]. Hence, unilateral nodular lesions cause unequal asymmetrical velocity storage mechanisms and might enhance the spontaneous nystagmus, as seen in case-3 in our cohort.

In patients with intact vestibular-ocular reflex, when the head is rotated during the head-impulse test, the eyes remain fixated on the examiner's nose. If the vestibular-ocular reflex is unilaterally impaired, patient's eyes will momentarily lose the fixation during the head rotation. The head impulse test has been described as a reliable method to detect a

unilateral peripheral vestibulopathy, especially sensitive during the acute stage [8]. In patients with spontaneous nystagmus resembling acute vestibulopathy, a negative head-impulse test is suspicious of a central lesions [9], as seen in all patients of our cohort.

Patients with pure vestibulopathy are able to stand and walk due to the intact proprioception and visual inputs. Inability to stand serves as an important clue to identify a central lesion. Except case-3, none of our patients could stand. Patients with nodular dysfunction tend to fall towards the side opposite of the spontaneous nystagmus, noted in 8 out of 14 patients in our series.

Thus, patient with isolated nodular infarction are unable to stand and tend to fall away from the side of nystagmus. Negative head impulse test is a typical finding. However, the head-shake test does not help in differentiating between isolated nodular infarction from a vestibular pathology (Table 2).

Table 2. A comparison of peripheral vestibulopathy against nodular infarcts

Signs	Peripheral vestibular lesion	Nodular lesion
onset	Subacute onset over hours, of severe vertigo. Occasionally the onset is over minutes	Hyperacute onset severe vertigo
Nystagmus at rest	Predominantly Horizontal	Predominantly horizontal
Suppression with visual fixation	Yes	Depends on floccular integrity
Latency	Yes	No
Fatigability	Yes	no
Head impulse test	Impaired	intact
Falls	Away from side of nystagmus	Away from side of nystagmus

Arboix et al described a series of 39 patients that presented with atypical lacunar syndrome [10]. However, none of their patients presented with isolated vertigo and no nodular infarcts were described. Perhaps, some of the patients with isolated vertigo, especially if mild and short-lived did not undergo MRI of the brain. In a recent study, patients presenting with vertigo, considered due to stroke underwent MRI of the brain. Of the 28 patients, 11 (39%) showed small diffusion restricted lesion on MRI of the brain. However, their patients with stroke on MRI of the brain presented with vertigo that was accompanied by other neurological symptoms also [11]. Our patients presenting with isolated vertigo could be classified as atypical lacunar strokes and serve as a reminder that patients presenting with isolated vertigo, especially when associated with negative head impulse test should undergo MRI of the brain to exclude a posterior circulation stroke.

4. CONCLUSION

The appearance of a peripheral localization of giddiness can be misleading in the case of nodular infarcts. A high index of clinical suspicion is required, especially in patients with multiple cardiovascular risk factors. A negative head impulse test despite severe vertigo and imbalance are important clinical discriminants to help establish the correct diagnosis. The importance of distinguishing a peripheral lesion from stroke lies not only in overlooking a serious diagnosis and exposing these patients to subsequent ischemic strokes, but also in avoiding unnecessary investigation.

CONSENT

Not applicable.

ETHICAL APPROVAL

The study was approved by the institutional review board at our institution.

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COMPETING INTERESTS

None of the authors declare any competing interests exist related to this manuscript.

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