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Receive Accepte Publishe	Case Report of False-Negative Diffusion- Weighted Image of Brain Magnetic Resonance Imaging (MRI) in Acute Ischemic Stroke		gative Diffusion- n Magnetic Resonance Ischemic Stroke		
Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G		B 1 CEF 2 F 2 E 3 A 1	Wei-Lun Chang* Ji-Ching Lai* Rong-Fu Chen Han-Hwa Hu Chau-Shiung Pan	<ol> <li>Department of Neurology, Chang Hua Show Chwan Memorial Hospital, Changhua, Taiwan</li> <li>Research Assistant Center, Chang Hua Show Chwan Health Care System, Changhua, Taiwan</li> <li>Graduate Institute of Clinical Medicine and Department of Neurology, College of Medicine, Taipei Medical University and Hospital, Taipei, Taiwan</li> </ol>	
Corresponding Author: Conflict of interest: Source of support:		Author: iterest: upport:	* Wei-Lun Chang and Ji-Ching Lai contributed equally to this work, and both should be considered as first authors Chau-Shiung Pan, e-mail: a0920968108@gmail.com None declared This work was supported by the Changhua Show-Chwan Memorial Hospital, Taiwan, ROC		
Patient: Final Diagnosis: Symptoms: Medication: Clinical Procedure: Specialty:		tient: nosis: toms: ation: edure: :ialty:	Male, 75 Acute ischemic stroke Dizziness • unsteady gait — None Radiology		
Objective: Background:		ective: ound:	<b>Challenging differential diagnosis</b> Acute ischemic stroke is a major cause of mortality and morbidity in Taiwan. Diffusion-weighted image (DWI) is a sensitive and common strategy used for imaging acute ischemic stroke.		
Case report:		eport:	We present a case of a negative DWI MRI for detecting acute ischemic stroke in a clinical setting. A 75-year- old male had a DWI performed after onset of symptoms suggesting acute ischemic stroke. The initial DWI re- sult was negative at 72 hours of presentation. The neurological symptoms of the patient persisted and DWI was repeated. After 14 days, the DWI data confirmed and demonstrated an acute ischemic stroke. The delay in DWI confirmation, from symptom onset until DWI diagnosis, was 336 hours.		
Conclusions:		sions:	DWI may not have 100% sensitivity and accuracy in early stages of acute ischemic stroke. The time course to the development of abnormalities detected by DWI may be longer than anticipated.		
MeSH Keywords		vords:	Diffusion Magnetic Resonance Imaging • Neurologic Examination • Stroke		
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# Background

Stroke is a leading cause of disability and the second leading cause of death in Taiwan [1]. An acute ischemic stroke occurs when an artery supplying the brain becomes occluded, leading to the death of brain tissue and focal neurological deficits [2]. Magnetic resonance imaging (MRI) provides important information to distinguish between hemorrhagic and ischemic stroke [3]. Recently, diffusion-weighted imaging (DWI) has been shown to be an excellent tool for the detection of acute stroke; early DWI has been used as an independent predictor for favorable outcomes in ischemic stroke patients [4]. Importantly, the presence of an intracranial hemorrhage can be excluded, and imaging can help classify the stroke subtype by determining the site and size of the ischemic lesion, which may help predict the functional consequences of the event [5]. Among MRI intensity studies, most of studies have showed DWI and fluid-attenuated inversion recovery (FLAIR) imaging were more sensitive for early ischemic changes than T2-weighted imaging (T2-WI) in the acute stage after stroke [6,7].

Here we report a case of a 75-year-old man who was admitted for dizziness, unsteady gait, and had abnormal white blood cell counts. Initially, the patient's brain lesion was not found on DWI MRI by using 1.5 Tesla superconducting system. After two weeks, DWI MRI showed restricted water distribution in the left side of midbrain and left cerebellar hemisphere. Additionally, low-apparent diffusion coefficient (ADC) pattern plus long T2 appearance was compatible with acute infarction. This report presents an interesting case of false-negative DWI of brain MRI in acute ischemic stroke.

## **Case Report**

A 75-year-old male presented on March 9, 2015 to our General Neurology Service with intermittent dizziness for five days, cold sweating, nausea with vomiting, and poor appetite. The patient's past history included: diabetes mellitus type 2 treated with oral antidiabetic agents (OAD) for one year, benign prostatic hypertrophy (BPH), hypertension, hyperglycemia, and hyperlipidemia for one year. The unsteady gait was observed and a cerebellar infarction suspected. He was admitted to our ward for further evaluation and management. Immediately, a brain computerized tomography (CT) scan and then MRI were performed to check the status of the brain. There was no visible abnormal intracranial space-occupying lesion found in the CT and MRI analysis (Figures 1A, 2A). Subsequently, DWI and magnetic resonance angiography (MRA) were arranged for further analysis. Unfortunately, the DWI and MRA data revealed no atherosclerotic narrowing of bilateral carotid siphons (March 9, 2015). In the meantime, the clinical status of the patient was not improving, and the blood examination showed abnormal white blood cell counts (WBCs, 14,500/µL), Hb 18.2 g/dL, and HcT 54.8%, normality of creatinine (CREA, 0.78 mg/dL), glomerular filtration rate (GFR) (103.41 mL/min), high density lipoprotein cholesterol (HDL-C, 42 mg/dL), low density lipoprotein cholesterol (LDL-C, 81 mg/dL), and electrocardiography (ECG) data. There were no symptoms such as chills, fever, headache, shortness of breath, dyspnea with exertion, chest pain, chest tightness, rhinorrhea, hemiparesis, blurred vision, double vision, dysarthria, dysphagia, aphasia, dysuria, or swelling. After three days (March 12, 2015), the patient was transferred to the intensive care unit (ICU) due to right facial palsy and progressive gait disturbance. We arranged brain MRI and DWI procedures (March 18, 2015). The CT and DWI reports showed left midbrain and left cerebellar infarction (Figures 1B, 2B, respectively). Furthermore, the MRA report revealed posterior cerebral artery (PCA) lesion, spinocerebellar artery (SCA) and basilar artery (BA) lesion. Subsequently, we used enoxaparin via subcutaneous injection and added symptomatic control. On day 7 in the ICU, the gait of the patient was significantly improved, and there were no abnormal values reported from the laboratory data.

## Discussion

DWI is widely used for the diagnosis of acute ischemic stroke, but increasing evidence has reported DWI failure to detect acute stroke lesions. One study found that the delayed DWI time for detecting lesions ranged from 8 hours to 144 hours [8]. In our case report, the delayed DWI time (after symptom onset) was 336 hours (two weeks); such an extreme delayed DWI time appears to be rare. However, our case demonstrated that DWI performed early may fail to reveal a small lesion located in the area of the brain supplied by posterior circulation. This finding suggests that routine use of DWI-MRI for making clinical decision and guiding aggressive therapy in acute ischemic stroke patients may not always reliable.

There are several technical reasons that may have contributed to the early false-negative DWI in our case study. First, the lesion was too small for the resolution of DWI analysis. Second, a low sign noise ratio was observed in the first 24 hours after symptom onset. Third, the DWI of the brainstem was distributed by magnetic susceptibility artifact. Another important factor was the time elapsed from ictus at which the DWI was performed. Within 24 hours may not be sufficient for observing the alteration of DWI. However, our patient had a prolonged neurological deficit for 14 days and DWI failed to diagnosis the disease.

The prevalence rate of false-negative DWI is 1.5-25.6% [8–11]. Sylaja et al. reported that of 401 patients, 25.6% had falsenegative DWI results; and the final clinical diagnosis was transient ischemic attack (61.2%), stroke (25.2%), and non-ischemic causes (13.6%). Lesions located in the brainstem had a



Figure 1. CT images. (A, B) The CT image at 24 hours and 192 hours, after symptom onset, respectively. The white arrow denotes new infarction at the left cerebellar hemisphere.



Figure 2. Diffusion weighted images. (A) Diffusion weighted images (DWI) MRI done day 3 after symptom onset shows no lesion. (B) DWI done after 14 days; the thin white arrow denotes acute infarction over left midbrain and left cerebellar hemisphere.

high prevalence for false-negative DWIs (50% of patients) [11]. Oppenheim et al. found the rate of false-negative DWI was 5.8% (8/139) of patients with ischemic stroke. Several studies reported that false-negative DWI results may correlate with the location of the lesion and MR latency [8–12]. DWI has been correlated with the severity of artery lesions [13]. In our case study, the infarction lesion was located at the region of

posterior circulation (left side midbrain and cerebellum) and the results were consistent with previous studies [11].

## Conclusions

DWI has been an excellent tool for early diagnosis of acute ischemic stroke, however, false-negative DWI is not uncommon for

small ischemic stroke, especially lesions located within areas of posterior circulation. This report found that acute ischemic stroke could not be ruled out on the basis of a negative DWI. Accordingly, a patient with a false-negative DWI who has persistent neurological deficits requires follow-up DWI examination.

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#### **Conflicts of interest**

No potential conflicts of interest were disclosed.

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