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Stroke with persisting false-negative diffusion-weighted imagings: A case report

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ABSTRACT

Rationale: Diffusion-weighted imaging (DWI) is a cardinal tool for detecting acute brain ischemia; however, recent studies have shown that DWI may not show the ischemic lesion during the hyperacute period.

Patient concerns: A 76-year old male patient was admitted due to an acute onset of dysarthria and right lower paresis which progressed on the second day of admission.

Diagnosis: The preliminary diagnosis was an ischemic stroke and the final diagnosis was left medullary stroke.

Interventions: Antiaggregant and anticoagulant therapies were initiated after excluding hemorrhagic stroke by cranial computed tomography. However, DWIs, which were recorded on the 6th hour and 19th hour after the symptom onset, were in normal ranges. Hence, the patient was referred to a senior hospital for further etiological investigations.

Outcome: The patient was discharged after treatments with aspirin and atorvastatin, and the neurological examination showed mild-moderate dysarthria and moderate right-sided paralysis (3/5).

Lessons: Clinicians should pay more attention to stroke patients with negative DWI and perform DWI several times when the diagnostic is unclear.

KEYWORDS: Stroke; Diffusion-weighted imaging; Diagnosis; Diffusion-negative stroke

1. Introduction

Early recognition, diagnosis, and appropriate therapy is extremely critical for the treatment of patients with acute stroke[1]. After its first introduction in the early 1990s, diffusion-weighted imaging (DWI) is quickly adopted in the detection of suspected ischemic stroke and has become a vital tool for the diagnosis of ischemic stroke. However, in some circumstances particularly cases with

false-negative DWI results, the diagnosis may be strictly challenged. Herein, we reported a stroke patient presenting with persisting false-negative DWIs results, and discussed the reliability of DWI for diagnosis of stroke.

2. Case report

The informed consent has been obtained from the patient and his relatives. A 76-year-old male patient with a medical history of hypertension and diabetes mellitus was admitted due to dysarthria and right lower extremity paresis which had abruptly started 5 h prior to the admission. Neurological examination showed mild dysarthria and right-sided mild paresis, prominent in the lower extremity (Medical Research Council grade 4/5) [National Institutes of Health Stroke Scale (NIHSS): 3]. Laboratory examinations including complete blood count, serum biochemistry, B12, folic acid, thyroid function tests were in normal limits, except mild anemia [Hb: 12.9 g/dL (13.0-17.5g/dL), WBC: 5.6 / μ L (4.5-11.0 / μ L), thrombocytes: 310.0/ μ L (150.0-450.0/ μ L)]. Cranial DWI (using the 3-T-MRI device) performed 6 h after the onset of symptoms was within normal limits (Figure 1A). Although DWI findings were normal, he was provisionally diagnosed as stroke with negative DWI and after initiation of treatment with aspirin, he was hospitalized for further etiological investigations. However,

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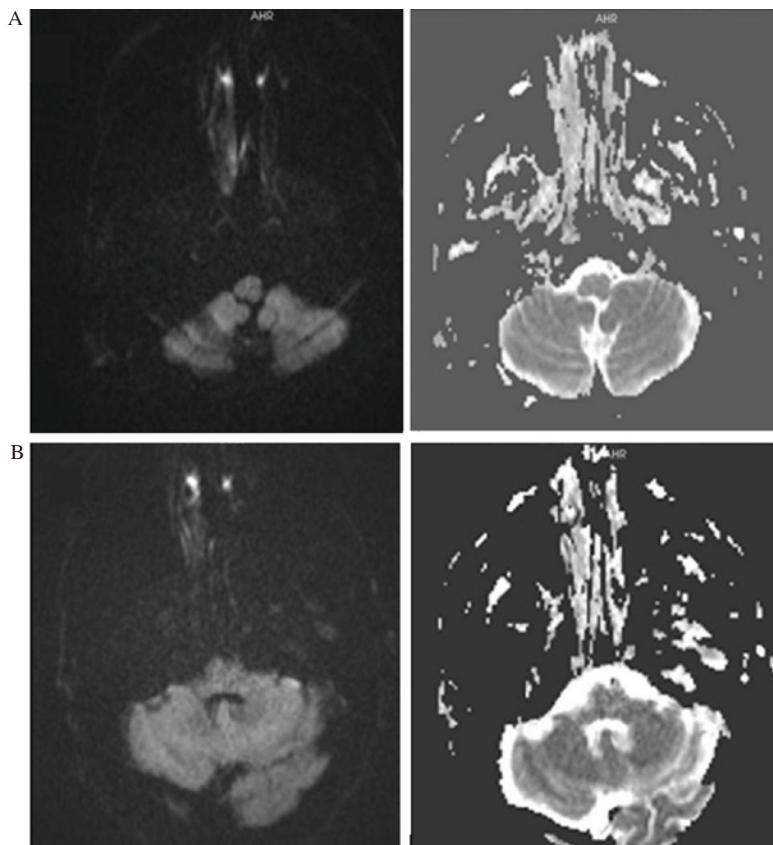


Figure 1. 3-T-diffusion-weighted imaging results. A: performed six hours after the onset, showing normal findings. B: performed nineteen hours after the first symptoms, showing normal findings [diffusion-weighted imaging (upper images) and apparent diffusion coefficient images (lower images)].

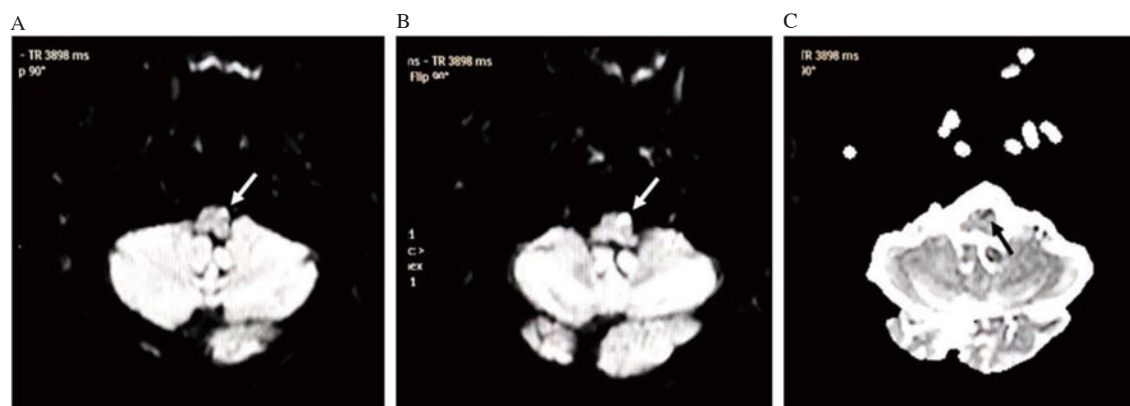


Figure 2. 1.5-T-diffusion-weighted imaging results. A and B: 1.5-T-diffusion-weighted imaging; C: Apparent diffusion coefficient images recorded 180 h after the first symptoms, showing diffusion restriction in the left medial medullary localization (arrows).

the neurological examination, performed on the second day of admission, showed a mild deterioration in the right-sided paralysis (from 4/5 to 3/5) and dysarthria (NIHSS: 6, 5B: +2, 6B: +2, 10: +2). Besides, difficulties in swallowing fluid nutrients had newly occurred. Anticoagulant therapy was carried out; however, repeated 3.0 T DWI (19 h after the symptom onset) was still within normal limits (Figure 1B). Therefore, the patient was re-evaluated. Detailed neurological examination showed widespread diminished deep tendon reflexes. Taken together with the negative repeated DWI results and progressive clinical course, the pre-diagnosis of Guillain-

Barre syndrome was considered and the patient was referred to a senior hospital for further electromyographic investigations and therapy. However, cranial MRI was repeated (on a 1.5-T MRI device) thirdly (180 h after the first onset of symptoms) which showed diffusion restriction in the left medial medullary region (Figure 2). Taken together, the patient was diagnosed as stroke with false-negative initial DWIs. Hyporeflexia was attributed to the chronic effects of polyneuropathy associated with diabetes mellitus. The blood examinations showed normal hemogram (Hb: 13.0 g/dL, WBC: 8 000/mL), liver and kidney function tests, high-

density lipoprotein cholesterol of 50 mg/dL, low-density lipoprotein cholesterol of 170 mg/dL. Brain/neck tomography angiography showed widespread atherosclerotic plaques prominently in bilateral proximal internal carotid arteries (occurring 35%-40% stenosis). Other etiological investigations including echocardiography and 24-hour Holter monitoring were within normal ranges. The patient was discharged after aspirin and atorvastatin treatments with a neurological examination showing mild-moderate dysarthria and moderate right-sided paralysis (3/5).

3. Discussion

DWI is a cardinal tool for detecting acute brain ischemia and is recommended for the diagnosis of stroke according to national stroke guidelines[1]. However, it is also known that ischemic lesions in the acute phase of the stroke may not be detected by DWI. Chalela *et al.* reported that false-negative DWI results were found in 27% of patients with ischemic stroke using 1.5-T-MRI which was recorded within the first three hours of symptom onset[2]. They proposed some risk factors that may be associated with false-negative diffusion results such as lesion localization of brain stem, recording time of less than 3-hour interval from the symptom onset and NIHSS score less than 4[2]. Generally, false-negative DWI results have been associated with the short time interval from symptom onset to the recording time[2,3]. Shono *et al.* recommended repeated examination in all patients with negative DWI results whose MRI was recorded within the first two hours from symptom onset[3]. In accordance with this view, Oppenheim *et al.* did not report any false-negative DWI result during examination 24 h after the symptom onset[4]. However, there are also reports about patients with false-negative DWI results which were performed for a much longer time[5]. Chang *et al.* reported a case with acute onset ataxia with normal DWI recorded 72 h after clinical onset. DWI was performed again 14 d after, and eventually demonstrated acute ischemic lesion[6]. Makin *et al.* reported one third (76/264; 29%) of the patients did not show a lesion in DWI results 4 d (median) after stroke[7]. However, in this study the patient showed a focal neurological deficit as clinical manifestation and repeated DWI showing a diffusion restricted lesion (to reveal the neuroimaging sign of an ischemic stroke) was not performed in the follow-up. In my opinion, the inclusion criteria in this study might be effective in this high rates of patients with diffusion-negative strokes. Two DWIs performed on the 6th and 19th hour from the onset showed normal findings. However, the third DWI performed on the 180th hour after the onset showed diffusion restricted lesion in the left medial medullary region. It is worthy mentioned that severity of our patient was moderate (NIHSS score was 6). Mild stroke severity (low NIHSS score) is regarded as a risk factor for stroke patients with negative DWI[4,7].

Posterior circulation strokes have been considered to be associated

with negative DWI[4,7]. Edlow *et al.* found that rate of false-negative DWI scan result in the patients with posterior circulation ischemia was 5 times higher than the rate of patients with anterior circulation ischemia[8]. Our case had stroke in posterior circulation territory.

It has been reported that the degree of hypoperfusion below the threshold might not present a positive image in DWI[9]. It is known that neurological deficit is not always equivalent to an infarct. With cerebral blood flow at 15 to 20 mL/100 g per min, the development of cerebral infarction may take more than 2 h despite the existence of neurological deficit[7]. Considering that patients with posterior circulation stroke syndromes are more likely to show false-negative DWI results, high negativity rates of DWI may be related with some specific collateral features of posterior circulation due to differing perfusion dynamics of this region. In our case, some specific features of the collateral circulation, which individually vary, might be the critical factors causing negative DWI results.

On the other hand, 'stroke mimics' which is a crucial diagnostic challenge in the emergency department, could cause unnecessary and harmful treatment options[8]. Many patients with stroke-like symptoms do not have a stroke, termed as 'stroke mimics'. Recent studies showed that 3%-13% of patients were mistakenly diagnosed and treated as acute stroke[8]. In this case, with the negative results of two DWIs, the third DWI provided the final diagnosis of medullar ischemic stroke. Based on this case and related literature, the patients with suspected stroke should be evaluated repeatedly and sole MRI-based diagnosis should be avoided. Clinicians should pay more attention to stroke patients with negative DWI results, particularly with posterior circulation strokes, and should not hesitate to repeat DWI several times when the diagnostic status is unclear.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contribution

The sole author H.O. contributed substantially in the evaluation of the patient, conceptual and planing stages of the manuscript, writing and revising it critically and drafting it.

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