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CASE REPORT

Hyperacute ischemic stroke without lesions on diffusion-weighted imaging in a patient treated with rtPA thrombolysis

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Key Clinical Message

We report a comatose patient with severe neurological deficits who was without spontaneous language or movement. He had a good response to recombinant tissue plasminogen activator (rtPA) thrombolysis even though there were no detectable lesions on diffusion-weighted imaging (DWI). DWI is very sensitive for diagnosing hyperacute ischemic stroke, and rtPA thrombolysis is the best treatment. However, rtPA thrombolysis in ischemic stroke patients without lesions on DWI has rarely been reported.

Keywords

Diffusion-weighted imaging, hyperacute ischemic stroke, recombinant tissue plasminogen activator, thrombolysis.

Introduction

Diffusion-weighted imaging (DWI) has a high diagnostic accuracy for identifying ischemic stroke, even in a very early stage, and recombinant tissue plasminogen activator (rtPA) thrombolysis is so far the most efficient treatment for acute ischemic stroke within the 4.5-h window from symptom onset [1]. In most reported series, more than 95% of acute ischemic lesions could be detected on DWI. Results from Tatlisumak et al.'s study also indicated that DWI was better than computed tomography (CT) for identifying patients with acute focal neurological deficits [2]. Only a few false-negative DWI results were reported in acute ischemic stroke, and the majority of patients only had minor symptoms (NIHSS score <4) [3–6]. Cases of hyperacute moderate to severe ischemic stroke without detectable lesions on DWI have rarely been reported. The efficacy and safety of rtPA thrombolysis for these patients remains unclear. We report a patient with severe neurological deficits without detectable lesions on DWI who received thrombolytic therapy.

Case Description

A 70-year-old male patient was transferred to our emergency department at 4:00 PM. Less than an hour earlier that day at 3:15 PM he felt tired and went to bed after he carried a water tank. At 3:20 PM he was found with pallor skin and no response to any stimulus. He also had a paroxysmal tic in both upper extremities. He did not spit out foam, have urinary or fecal incontinence, or tongue biting. He had a medical history of hypertension, diabetes, and dyslipidemia for 10 years. He did not take medicine regularly. He only took antihypertensive and oral antidiabetic drugs occasionally and the dosage was unknown. Other relevant history included smoking 20 cigarettes per day for 50 years.

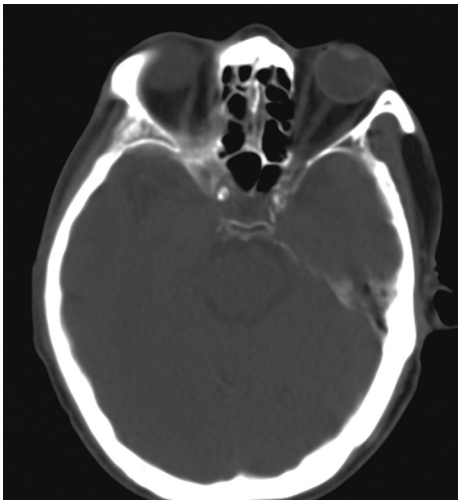

Figure 1. No hemorrhage or infarction on CT, axial.

On admission, his blood pressure was 182/93 mmHg, blood glucose 4.5 mmol/L, and heart rate 80 bpm and regular. Neurologically he was comatose without spontaneous language or movement. The diameters of his both pupils were not equal, the right was 4 mm and the left 2 mm. All extremities moved in response to pain stimulation. The Babinski sign on both sides was positive. His NIHSS score was 21. CT (Fig. 1) was performed immediately and showed no hemorrhage or infarction. After a CT scan at 4:40 PM, the mental state of the patient somewhat improved. He could speak, but both lower extremities remained weak, and both Babinski signs remained positive. To exclude other possible causes such as epilepsy, magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were performed immediately. We found only minor leukoaraiosis on T2 MRI and no lesions on DWI, but the basilar artery could not be visualized on MRA (Fig. 2A and B). MRI and MRA were completed at 5:25 PM, at which time the patient again became comatose. Intravenous rtPA therapy was started at 5:35 PM with the patient having an NIHSS score of 21. The neurological deficits were dramatically improved with the patient having an NIHSS score of 0 during rtPA infusion therapy. The following day after thrombolytic therapy, DWI and MRA were performed again. DWI showed no lesion (Fig. 3A) and the basilar artery could be visualized though stenosis remained (Fig. 3B).

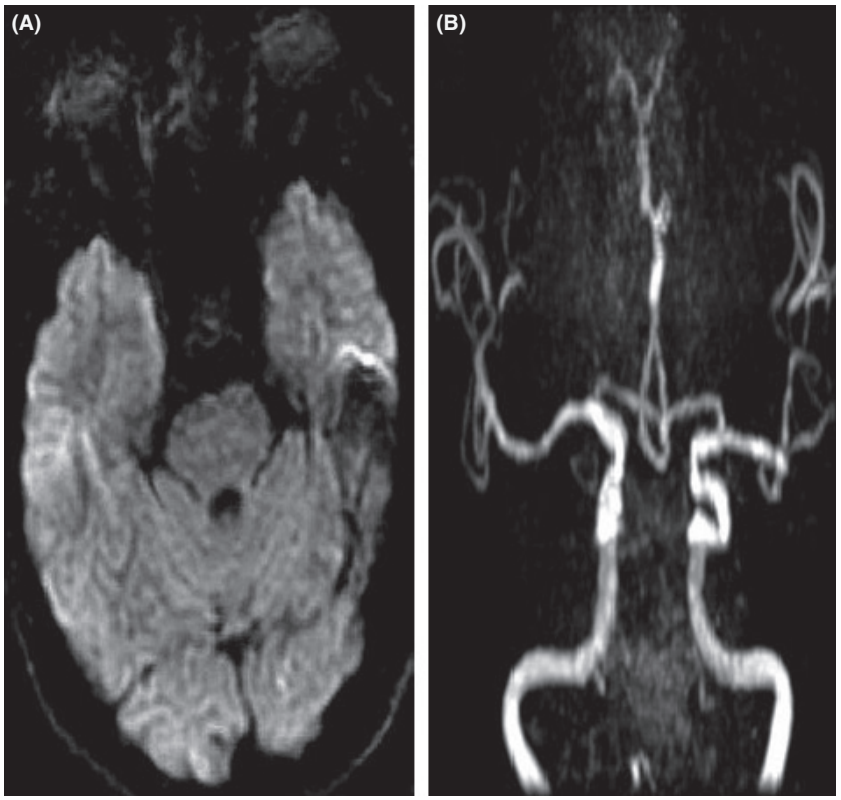

Figure 2. (A) No lesions on DWI before thrombolysis, DWI, axial. (B) The basilar artery was disappeared on MRA before thrombolysis, MRA, coronal.

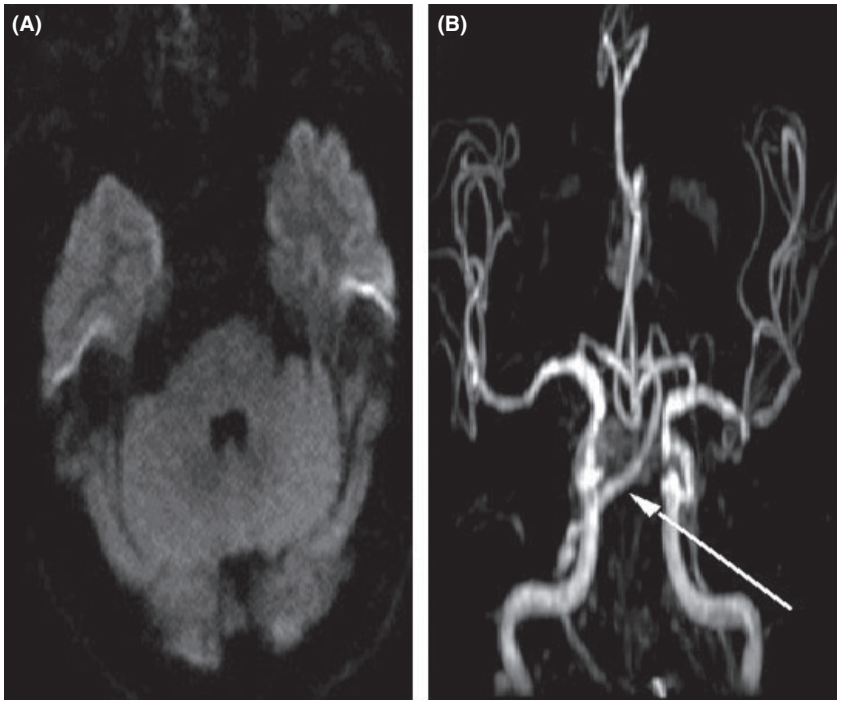

Figure 3. (A) No lesions on DWI after thrombolysis, DWI, axial. (B) The basilar artery presented with moderate stenosis on MRA after thrombolysis (the arrow), MRA, coronal.

Discussion

DWI is the most sensitive imaging modality for acute stroke because of its ability to depict an ischemic lesion early. Nevertheless, there is increasing evidence of false-negative DWI results on examinations to detect acute ischemic stroke [7]. Ishikawa et al. [8] reported three acute stroke patients with false-negative DWI results, and explained that a possible reason for this may be that the time from symptom onset to DWI was short, and, therefore, cellular edema might not yet have occurred, even in the presence of a major arterial lesion, or possibly the development of collateral circulation can obscure abnormalities on DWI. Dirnagl et al. [9] reported that severe leukoaraiosis can increase ischemic tolerance through long-standing ischemic preconditioning, hindering the development of cytotoxic edema, which might cause false-negative DWI results. In our case, false-negative results on DWI before thrombolysis are best explained by the very short time from symptom onset and brainstem location, and those after thrombolysis are best explained by prompt reperfusion. The occurrence of large, reversed lesions on DWI in the middle cerebral artery territory was reported by Ezaki et al. [10]. In their case report, the lesion on initial DWI was almost completely resolved, and MRA showed complete recanalization of the occluded artery with diminished clinical symptoms. Sakamoto et al. [11] in their case report showed that DWI abnormalities were completely resolved and reversibility of both diffusion and perfusion MRI abnormalities was observed after successful thrombolytic therapy.

Previous reports demonstrated that false-negative DWI results were not unique to ischemia, but also occured in various pathological conditions, such as seizures, spreading depression, excitotoxic cerebral injuries, and hypoglycemia [12, 13]. In our patient, the above pathological conditions were ruled out. The absence of lesions on DWI and thrombolysis within a short time might be the reasons for our patient's good clinical outcome. At present, the only specific approved therapy for acute ischemic stroke is intravenous rtPA given within 4.5 h.

Symptomatic intracranial hemorrhage (SICH) is the most serious complication of thrombolytic therapy, and the incidence of SICH is closely related to the time window and infarction area. In patients eligible for intravenous rtPA, the benefit of therapy is time-dependent, and treatment should be initiated as quickly as possible [14]. Arnold et al. [15] reported that basilar artery occlusion patients with less extensive tissue damage on DWI had a better clinical outcome following interarterial thrombolysis. Others [16] have reported that a smaller pretreatment DWI lesion volume was found to be associated with a favorable outcome after treatment with intravenous rtPA. Seitz's group [17] indicated that patients with recanalization had smaller

initial lesions on DWI than those without recanalization. Schellinger and Kohrmann proposed that patients with a small DWI lesion and artery occlusion on MRA were the optimum target group for recanalization/reperfusion approaches and benefitted from reperfusion [18].

In conclusion, hyperacute cerebral infarctions are likely to have false-negative results on DWI but there are considerable neurological deficits. Thrombolysis with intravenous rt-PA was safe and effective in our case.

Conflict of Interest

None declared.

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