

Case Report

DWI Negative Large Artery Acute Ischemic Stroke: A Case Report with Review of Literature

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Abstract

MRI forms an important investigation tool in acute ischemic stroke. Diffusion weighted imaging is a very sensitive sequence to detect ischemia within few minutes. However in certain cases it can be negative especially in lacunar strokes, brainstem strokes and rarely in large artery strokes imaged very early into the onset of stroke. Other tools like MR Angiogram, Perfusion imaging may increase the sensitivity to detect stroke and initiate timely treatment which could prevent devastating consequences. Here authors describe a case of a 57 year old gentleman presenting with right sided weakness of 90 minutes duration with a moderate stroke severity. MRI Diffusion was negative. MR Angiogram didn't reveal any obvious intracranial occlusion. However MR Perfusion revealed an ischemic penumbra in left anterior cerebral artery territory. Patient didn't respond to iv thrombolysis and hence subjected to cerebral DSA which revealed thrombus and occlusion of left aca branch. Post mechanical thrombectomy with a stent retriever, he improved clinically and was functionally independent 2 weeks post discharge.

Keywords: Acute ischemic stroke; Diffusion weighted imaging; Magnetic resonance imaging; Perfusion Imaging

Abbreviations

MRI: Magnetic Resonance Imaging; CT: Computed Tomography; DWI: Diffusion Weighted Imaging; ADC: Apparent Diffusion Coefficient; FLAIR: Fluid Attenuated Inversion Recovery Sequence; PWI: Perfusion Weighted Imaging; DSA: Digital Subtraction Angiography; IV: Intravenous; AIS: Acute Ischemic Stroke; EVT: Endovascular Treatment

Introduction

Time is brain. Acute Ischemic Stroke (AIS) if untreated could be a debilitating and life threatening condition hence rapid diagnosis and treatment is necessary for optimizing the outcomes. Traditionally CT Brain has been used in emergency evaluation of patients with AIS to rule out intra-cranial bleed and selects patients for IV thrombolysis. Chalela et.al demonstrated Magnetic Resonance Imaging (MRI) to be more sensitive than CT in detecting acute ischemic stroke [1]. Recently there has been a significant increase in use of MRI in evaluation of patients with AIS [2]. At few centers MRI is used as primary screening tool to select patients eligible for thrombolysis or Endovascular Treatment (EVT). Particularly diffusion weighted magnetic resonance images compared to CT have better sensitivity, accuracy and interrater homogeneity [3]. Sensitivity of Diffusion Weighted Magnetic Resonance Images (DW-MRI) for detecting acute ischemic is stated to be 88-100% [4,5] and specificity 95-100% [4]. MRI-based thrombolysis is safer and potentially more efficacious than standard CT-based thrombolysis [6]. However, DW-MRI has its limitations and false negative DWI images in AIS have been described [7]. We report a case in which DWI-MRI was negative after 90 minutes of symptom onset and perfusion MRI images demonstrated early ischemia. Patient was aggressively treated and had a complete

clinical recovery.

Case Presentation

A 57-year-old man, right-handed, businessman by occupation presented to the emergency with sudden onset weakness in right side of body of 90 minutes duration with absolute inability to move right lower limb. There was no history of backpain, radicular pain, fall, seizure or syncope. He had diabetes mellitus and hypertension and was on regular medications. On clinical examination BP was 120/80mmhg, Pulse 82/min, regular. Cranial nerve examination was normal, right upper limb power was MRC (Medical Research Council) grade 3/5 and right leg power MRC grade 0/5 with hypoesthesia on right side. Stroke severity as per NIHSS (National Institutes of Health Stroke Scale) was 7.

MRI Brain stroke protocol done showed negative DWI (Figure 1: A and B) and Fluid attenuated images (FLAIR) (Figure 2A). MRA Angiogram didn't reveal any obvious extracranial or intracranial occlusion (Figure 2B). MR perfusion study done showed increased time to peak (Tmax) and Mean Transit Time (MTT) in para-sagittal left frontal lobe including paracentral lobule and peri-rolandic region suggestive of tissue at risk of ischemia (Figure 3 A and B). RAPID software showed significant diffusion and perfusion mismatch (Figure 3C). In view of significant deficit with ischemic penumbra despite normal diffusion, patient was considered eligible for IV Thrombolysis with alteplase and 0.9mg/kg tpa was administered. Patient failed to show improvement at the end of 1 hour. Emergent Digital subtraction angiography done showed left distal Anterior Cerebral Artery (ACA) thrombus, thrombotic occlusion of superior internal parietal branch origin and thrombus extending into bifurcation of internal parietal branch with hypoperfusion in parietal territory of ACA (Figure: 4 A

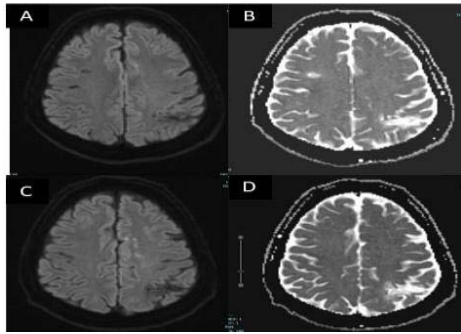


Figure 1: A and B DWI and ADC sequence showing no diffusion restriction. C and D follow up imaging showing punctate foci of diffusion restriction in left ACA territory.

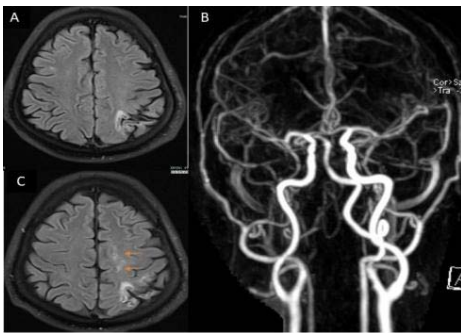


Figure 2: A: FLAIR image showing old gliosis in the left posterior parietal region, no acute infarct seen. B: Contrast angiogram circle of Willis showing no significant intracranial stenosis. C: Follow-up FLAIR image showing signal changes in the left ACA territory (arrows).

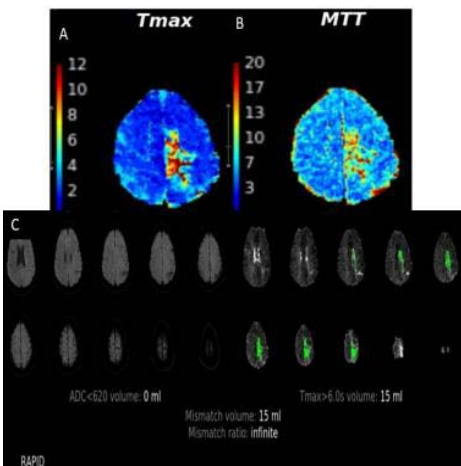


Figure 3: A and B: Perfusion maps showing prolonged T_{max} and MTT (Mean transit time). Figure 3C: RAPID software showing no diffusion restriction and ischemic penumbra of 15ml with a mismatch of 15ml.

and B). Mechanical thrombectomy was done with a 3x40 mm stent retriever following which blood flow to the branches of ACA artery was restored (Figure: 4 C and D). Post-procedure the weakness in right upper limb improved to normal immediately, however the weakness in right leg persisted for 24 hours. Post 24 hours the power in right leg improved to MRC grade 4/5 and he could walk with minimal

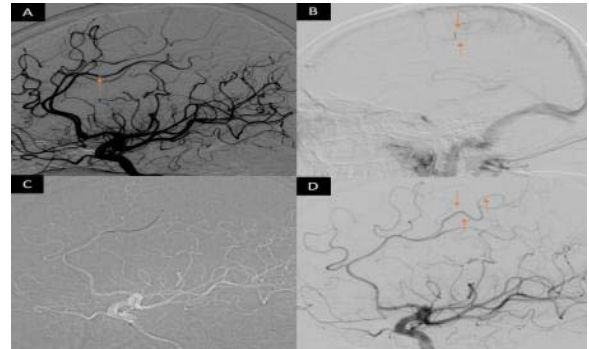


Figure 4: A: Lateral view of cerebral DSA showing a filling defect suggestive of a thrombus in the left ACA A2 segment (orange arrow). B: Delayed phases showing slow filling of the internal parietal branch of the left ACA (orange arrows). C: Roadmap showing a microwire in the occluded branch of the left ACA (arrows).

support. MRI brain repeated after 24 hours of the EVT showed few punctate acute infarcts in the left frontoparietal cortices (Figure 1: C and D) with FLAIR positivity (Figure: 2C). Patient had transient bladder involvement which improved. At discharge on day 5 patient modified Rankin scale was 1 and 0 on 2 weeks of follow-up. 2D ECHO and Holter analysis was negative for any cardiac cause and patient was kept on dual antiplatelets, statins and strict glycemia control.

Discussion

Imaging forms the backbone of stroke management. Multimodal MRI (DWI, ADC, SWI, FLAIR, MR Angio and perfusion) can provide useful information for accurate diagnosis of stroke, evaluation of the risks and benefits of thrombolysis, and prediction of outcomes [8]. Diffusion-weighted imaging is a highly sensitive tool for detecting acute ischemia. However, it may fail to demonstrate an acute stroke in about 20% of cases. Diffusion is the random Brownian motion of the molecules driven by thermal energy. In the human body, water is divided between intracellular and extracellular compartments. In an infarcted brain, there is failure of the sodium-potassium ATPase pump, resulting in a shift of water from the extracellular to the intracellular compartment, ultimately leading to cell edema and death. This is reflected as diffusion hyperintensity on MRI. Fundamentally, four ranges of regional Cerebral Blood Flow (CBF) values quantitatively define normal parenchyma (60–100 mL/100 g/min), oligemic tissue (22–60 mL/100 g/min), penumbra (10–22 mL/100 g/min), and infarction core (< 10 mL/100 g/min) [9]. At CBF levels such as 15 to 20 mL/100 g per minute, infarction may not develop for more than 2 hours [10]. As a result, if a perfusion defect does not cross a certain threshold level to cause cytotoxic edema, the DWI images may not show the classical hyperintense lesions seen in acute infarction, though clinical symptoms may be present due to ischemic penumbra. In our patient, this could explain the DWI negativity. Also, DW-MRI performed early may fail to demonstrate an acute infarct in anterior circulation.

Prevalence of DWI-negative AIS is 5.8% to 9.5% [7,11] (Oppenheim, Lian Zuo). DWI-negative AIS is now an increasingly recognized entity, and is mainly described for posterior circulation strokes [12]. However, only a few studies report DWI-negative MRI in anterior circulation stroke [13–16]. Wang et al [13] and Lefkowitz et al [14] reported 2 cases of false negativity involving lesions

located in the anterior circulation. They proposed that the degree of hypoperfusion in the early phase of ischemia remained below the threshold required to form an image with DWI as the reason for the false negativity, confirming with our finding. Meta-analysis by Edlow et al [12] concluded that causes of DWI negative strokes could be due to small volume of infarct especially in brainstem stroke and hyperacute stroke in which acute ischemia may be underestimated or missed. Bulut et al [17] studied DWI negative strokes and found equal number of cases involving anterior and posterior circulation. They stated the fact that false-negative DWI findings in acute stroke not only involve the posterior circulation and small lacunar or subcortical lesions but that they can also be observed in the anterior circulation and with large lesions.

DW-MRI negativity may have an impact on clinical decision-making process in centres using MRI as primary screening tool for diagnosis and to guide therapy in patient with acute stroke. The possibility of false negative DW-MRI in AIS should be kept in mind to avoid misdiagnosis or delay in treatment [7,12]. In our patient MR perfusion study aided in diagnosis of acute ischemia. It determines the ischemic penumbra which is a region of restricted blood supply in which the metabolism is preserved. This ischemic penumbra is vulnerable to progressing to infarcted dead tissue when the delayed perfusion exceeds a certain threshold. According to Lee et al [18], PWI (perfusion weighted imaging) abnormalities, and especially focal perfusion abnormalities, were independently associated with new acute lesions in follow-up DWI. If the hypoperfused state persists after recanalization, tissue damage in the ischemic penumbra seen as DWI-negative but PWI-positive lesion on MRI may evolve into irreversible cell death and damaged tissue, which will manifest as a DWI-positive lesion in the follow-up MRI. MR perfusion studies in addition to DWI MRI images increases sensitivity of diagnosis of AIS to 97.5% [5]. Also, MR perfusion studies aids in decision making for EVT through its DWI-perfusion mismatch indices and newer artificial intelligence softwares like RAPID which quantifies the ischemic penumbra helping in selecting patients for EVT and improve the outcomes in patients [19]. Patient had delayed recovery of right leg weakness after successful radiological treatment of ACA occlusion. This was opined to be due to neuronal stunning [20]. Neuronal stunning leading to delayed recovery can be seen as late as 3 months from the date of treatment.

In conclusion DWI MRI imaging is very sensitive but false negative results can be seen. Sensitivity of diffusion can be increased by Optimisation of diffusion sequence by increasing b value, repeating a corona diffusion, increasing spatial resolution and reducing geometric distortion. However that shouldn't delay the treatment as diagnosis of ischemic stroke should be balanced between clinical and radiological findings. MR perfusion can aid in diagnosing the proportion of DWI negative AIS facilitating faster treatment with reliably excluding stroke mimics.

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