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Case report

Recurrent thrombolysis of a stuttering lacunar infarction captured on serial MRIs

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ABSTRACT

Lacunar strokes account for about a fourth of all ischemic strokes. Pontine infarcts often present with stuttering symptoms, referred to as pontine warning syndrome (PWS). Patients presenting with fluctuating symptoms can appear to have rapidly improving symptoms and thus often go untreated despite the risk of recurrent deficits. MRI carries a higher sensitivity in detecting posterior circulation strokes compared to computed topagraphy, but does not always indicate irreversible injury. Here we present the first description of a stuttering lacune, captured radiographically on serial magnetic resonance imaging (MRI), that was initially averted with the administration of intravenous (IV) tissue plasminogen activator (tPA), only to return a month later and progress on imaging despite re-administration of tPA. During the first admission, our patient had spontaneous resolution of symptoms with complete reversal on restricted diffusion soon after IV tPA administration. On the second admission, the stuttering symptoms returned as did the same pontine lesion. Although his stuttering lesions lasted for several days, and the pontine lesion did ultimately progress to partial infarction on MRI, he was discharged home without neurologic deficits. Our case suggests that tPA may be of benefit in patients with lacunar pontine strokes even if symptoms rapidly improve or resolve.

1. Introduction

A 77-year-old man with a history of hypertension, hyperlipidemia, coronary artery disease, and a recent coronary artery bypass graft (CABG) presented with acute onset left side weakness, slurred speech, and dizziness (NIHSS = 8) 66 min after last seen normal. Consideration for thrombolysis with brain magnetic resonance imaging (MRI) showed restricted diffusion and decreased perfusion in the right medial pons (Figs. 1 and 2A). Intravenous (IV) tissue plasminogen activator (tPA) was administered 110 min after symptom onset. Within 30 min of initiating thrombolysis, his NIHSS decreased to 2. MRI obtained 24 h after thrombolysis showed no evidence of restricted diffusion or decreased perfusion (Fig. 2B) and the patient was asymptomatic (NIHSS = 0). His stroke evaluation was unremarkable, including an echocardiogram and intracranial and extracranial vessel imaging. The stroke etiology was thought to be due to small vessel disease. Aspirin (81 mg), clopidogrel, and a statin prescribed after his recent CABG were continued for secondary stroke prevention. The patient was discharged home without any neurologic deficits. Thirty days later, the patient presented again with left sided weakness, dysarthria, and dizziness. MRI acquired 59 min after symptom onset showed re-appearance of the previously seen right pontine diffusion and perfusion lesions (Fig. 2C). After completion of the MRI, his symptoms completely resolved. Approximately 45 min later, the symptoms re-occurred, and the patient was treated with IV tPA. During tPA infusion, his symptoms improved. MRI obtained shortly after IV tPA infusion revealed resolution of the restricted diffusion and persistence of the perfusion lesion (Fig. 2C and D). During the hospital stay, the patient had 3 episodes of clinical worsening lasting between 30 min to several hours. His blood pressure during both the initial and second admission ranged from a systolic of 130–160's and a diastolic of 80–100's. There was no correlation between the re-occurrence of symptoms and the patient's blood pressure. However, he did seem to respond to intravenous fluid bolus with normal saline.

The patient was discharged home without neurologic deficits. An MRI at discharge showed hyperintensity on diffusion imaging with a

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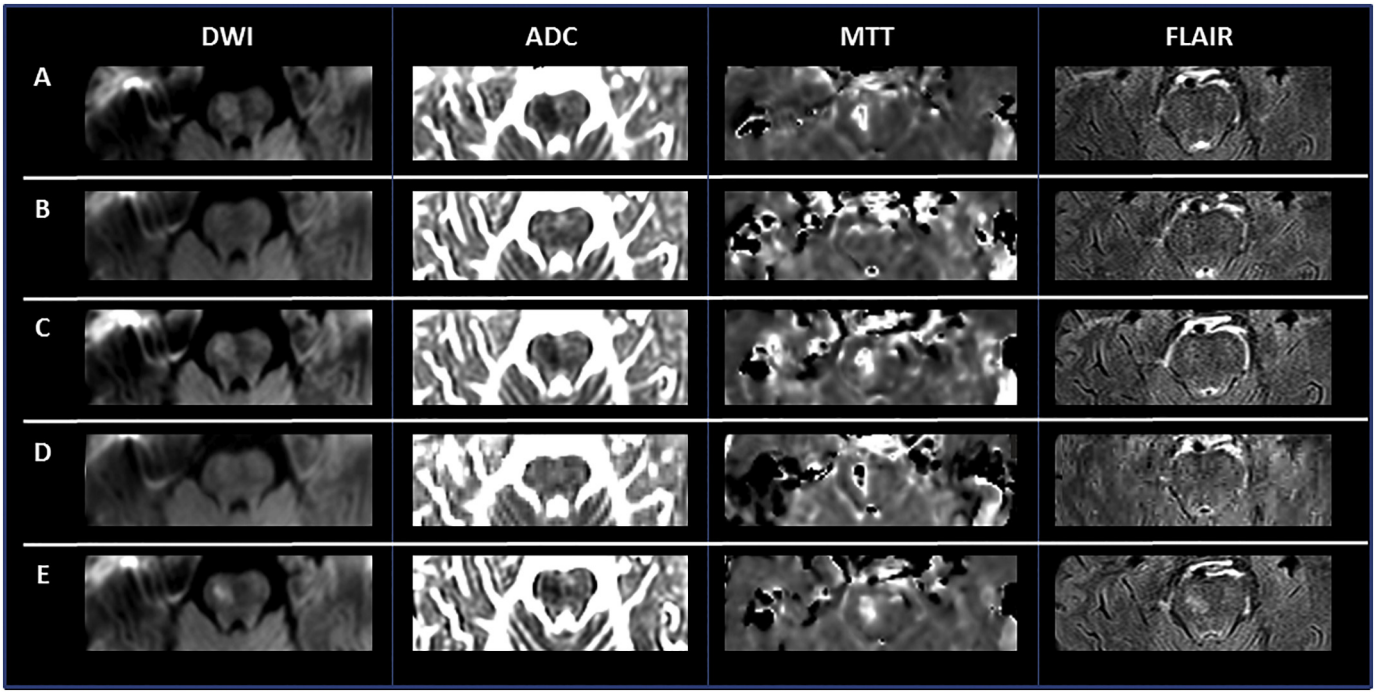

Fig. 1. This visual timeline depicts the patient's clinical course with corresponding representative MR diffusion sequences.

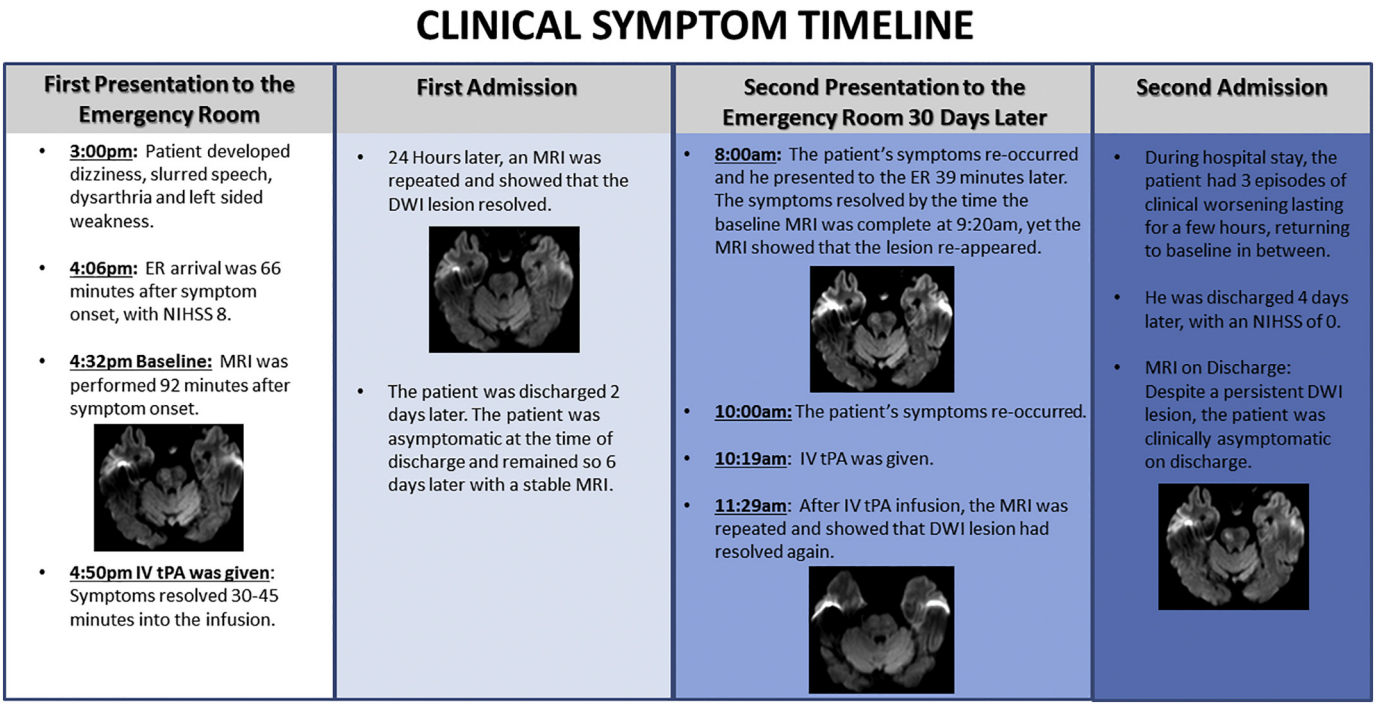

Fig. 2. The right pontine infarct and perfusion lesion (A) resolved 24 h after thrombolysis (B), and re-occurred 30 days later (C). The diffusion lesion resolved approximately 1 h after thrombolysis was given, but the perfusion deficit persisted (D). By the time of discharge, the patient was still clinically asymptomatic despite having a persistent perfusion deficit for 4 days and a diffusion lesion evident on the FLAIR.

corresponding FLAIR lesion and persistent perfusion deficit. A week after discharge, the patient reported no further re-occurrence of his symptoms.

2. Background

Lacunar strokes account for about a fourth of all ischemic strokes. Fisher first demonstrated that lacunar infarcts can be the result of a single perforating artery occlusion [1]. Compared to non-lacunar strokes, lacunar strokes occur in younger patients with lower admit National Institutes of Health Stroke Scale (NIHSS) resulting in lower 90-day modified Rankin scale (mRS) and mortality rates [2–4]. Incidence of lacunar pontine lacunar infarcts is unknown, but approximately 15% of acute vertebrobasilar infarcts are pontine, commonly caused by lipohyalinosis of the paramedian basilar arteries [5].

Pontine infarcts often present with stuttering symptoms that resolve

and return over time, referred to as pontine warning syndrome (PWS) [5–7]. The clinical presentation of pontine lacunar syndromes can be variable despite corresponding to the same anatomical location [7]. MRI carries a higher sensitivity in detecting posterior circulation strokes compared to CT, but the presence of hyperintensity on diffusion weighted imaging (DWI) or hypointensity on apparent diffusion coefficient (ADC) does not always indicate irreversible injury [7,8]. In our case, reversibility of the restricted diffusion occurred with resolution of the perfusion deficit.

Patients presenting with fluctuating symptoms can appear to have rapidly improving symptoms and thus often go untreated despite the risk of recurrent deficits. There is limited literature on benefits of treating pontine infarcts, but one large cohort study found IV tPA to be beneficial for lower discharge mRS in lacunar stroke [9]. Moreover, another study found that in patients deemed “too good to treat,” those who went untreated, were more likely to have poor outcome than those that were treated with IV tPA. [10].

Repeated treatment with IV tPA for recurrent stroke is rare. However, a small study of 19 patients with repeated IV tPA administration for recurrent stroke within 3 months did not report any symptomatic intracranial hemorrhages [11].

3. Discussion

Here we present the first description of a stuttering lacune, captured on MRI, that was initially averted with the administration of IV tPA, only to return a month later and progress on imaging despite re-administration of tPA. The early time course of this case is very similar to a previous case we reported [8]; for both patients, there was complete reversal of the clinical and radiographic appearance of a lacunar stroke within hours. However, the previous patient (first case) was not treated during either admission while the current patient (second case) received IV tPA at both time points. Although both patients had a return of the diffusion lesion, the first case recurred within days while the second case’ recurrence was avoided for a month. With MR imaging, it was possible to capture the stuttering nature of lacunar strokes along its natural history, and contrast this with the clinical symptoms in the presence of acute IV tPA administration. This draws attention to the underlying pathophysiology of lacunar stroke.

Lacunar syndromes result from small vessel disease. Basilar artery branch disease represents a common mechanism of isolated pontine stroke. The underlying pathophysiology of this type of pontine lacunar infarction can occur secondary to micro-embolization from an atheromatous plaque in the ostium of a pontine penetrator, direct disease of the occluded vessel due to lipohyalinosis, a non-thrombotic occlusive disease, or from thrombosis of the vessel [1,12]. It is also possible that some combination of these pathologies was present in our patient. Despite a thorough investigation, we did not find evidence of significant vertebrobasilar disease, so we believe the pathology of the stroke is likely small vessel disease or a combination of lipohylanlinosis and micro-embolization.

As described previously, pontine warning syndrome occurs when a patient has recurrent stereotyped episodes of posterior circulation associated neurological symptoms such as motor or sensory dysfunction, dysarthria or ophthalmoplegia that herald basilar artery branch stroke causing permanent deficits [13]. This also resembles capsular warning syndrome described in the anterior circulation where angiopathy of a single penetrating vessel such as lenticulostriate branches are implicated [14].

Another intriguing aspect of this case is the lack of deficits on hospital discharge, despite fluctuating clinical symptoms during his second admission and imaging evidence of infarction in the pons. During the first admission, our patient had spontaneous resolution of symptoms with complete reversal on restricted diffusion soon after IV tPA administration. He did not present again till a month later with recurrent symptoms. The second time he had a stuttering course but ultimately complete neurological recovery despite sustaining partial infarction in the pons on diffusion imaging with corresponding FLAIR and persistent perfusion deficit, as noted on post treatment images. One possible mechanism for his clinical outcome is ischemic tolerance [15]. Ischemic preconditioning has been shown to protect against cerebral ischemia in animal models and has gained interest as a possible neuroprotective mechanism in humans. Furthermore, tPA has been shown to have neuroregenerative effects such as protection of cerebral cortical neurons from oxygen and glucose deprivation induced cell death, which may have contributed to our patient's complete clinical recovery [16].

Multiple studies have shown a beneficial effect of treating lacunar stroke with tPA [17,18]. However, the benefit of thrombolysis in mild stroke and lacunar stroke is debated. A large registry reported that 61% of tPA eligible patients were not offered tPA due to mild or rapidly improving symptoms, but these patients had worse clinical outcomes than patients given tPA on case-matched analysis [10]. In a large Canadian case-cohort study, lacunar stroke patients that received thrombolysis were more likely to be discharged home and independent [9]. A recent study that closed early do to not meeting the enrollment target was the Study of the Efficacy and Safety of Alteplase in Participants with Mild Stroke (PRISMS) [19]. No difference was found between aspirin and thrombolysis in the PRISMS clinical trial, but unlike our case, MRI was not required for patient selection.

4. Concluding remarks

This case, captured on serial MRI, highlights a dynamic clinical outcome of a stuttering pontine stroke in the setting of repeated treatment with IV thrombolysis. It suggests that tPA should be considered in patients with lacunar pontine strokes even if they are rapidly improving or clinically resolved.

Author contributions

IAN and ANS collected data, drafted, edited and equally contributed to the manuscript. KC contributed to draft and editing of the manuscript. EE contributed to draft of the manuscript. DR contributed to the editing of manuscript. JKL and RL critically revised the manuscript. All authors made contributions to conception and interpretation of the case presentation.

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Disclosures

The authors report no disclosures.

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