CASE REPORT

An uncommon complication of acute stroke thrombolysis

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mallan1@doctors.org.uk**SUMMARY**

Thrombolysis with tissue plasminogen activator is a well-established treatment for acute ischaemic stroke. We report a case of an 87-year-old woman who developed an acute ischaemic limb, on the background of stroke thrombolysis, and underwent an embolectomy. A rare but serious complication, there are few reports of similar thromboembolic events, particularly in patients with known atrial fibrillation as presented in this case. Early recognition of this rare complication may prevent long-term, and at times fatal, complications.

BACKGROUND

Recombinant tissue plasminogen activator (rt-PA) is a serine protease, which acts to convert plasminogen to plasmin, and thus plays a role in the degradation of fibrin clots. Rt-PA is a well-established treatment for acute ischaemic stroke.

The majority of common complications following thrombolytic therapy focus around haemorrhagic incidents.¹ However, complications can also arise due to the paradoxical occurrence of a thromboembolic event. Fragmentation of a thrombus following systemic thrombolysis with rt-PA, and distal migration of the emboli can lead to subsequent arterial occlusion. A limited number of papers have reported these secondary events following stroke thrombolysis.² Some of these reports are associated with a pre-existing cardiac thrombus and atrial fibrillation (AF). We report a case of a patient who, following thrombolysis, developed an acute ischaemic limb.

CASE PRESENTATION

An 87-year-old woman presented with a right facial droop, dysarthria and aphasia. NIH stroke scale score (NIHSS) was calculated as 8. A diagnosis of partial anterior circulatory stroke was made and the patient was started on 45 mg of rt-PA (Alteplase) within 140 min of the onset of symptoms. At 1 h post-thrombolysis the NIHSS was 8 and at 17 h post-thrombolysis the score dropped to 3. The facial weakness had resolved, with only a mild dysphasia and dysarthria.

However, the following morning the patient began to report an acutely painful left foot. On assessment by a doctor at 19 h post-thrombolysis, the foot was cold with no palpable pulses from the femoral distally in the left leg. There was no mottling, paresthesia or paralysis. The right foot was warm with palpable pulses distally. A provisional diagnosis of acute limb ischaemia secondary to emboli was made.

The patient had previously been on warfarin for AF. This had been discontinued due to a history of

haematemesis, and the patient was being administered digoxin alone. Hypertension was being managed with ramipril and amlodipine.

INVESTIGATIONS

A CT scan of the brain, carried out at admission, showed no focal infarction or haemorrhage and an ECG confirmed that the patient was in AF. The echocardiogram report showed an ejection fraction of 55–60%, mild biatrial dilation (left atrial area=22.8 cm²) and a dilated aortic root.

Doppler examination confirmed the lack of pulses of the left leg and the patient underwent a CT angiogram (CTA). The results showed two areas of complete occlusion, one in the left external iliac artery (figure 1A) and the second in the distal superficial femoral artery. Both of these vessels were of normal calibre, with no surrounding collaterals, thus suggesting that this was an acute occlusion. The images also showed the presence of a prominent intramural thrombus in the distal aorta (figure 1B). The results suggested an acute arterial occlusion.

Of note, Doppler examination of the internal and common carotid arteries showed no stenosis.

TREATMENT

The patient was started on intravenous heparin, 28 h post-thrombolysis, following a CT scan of the head to rule out an intracerebral bleed. The patient subsequently underwent a left-sided embolectomy, where a significant clot was removed from the left femoral and iliac arteries.

OUTCOME AND FOLLOW-UP

Reperfusion of the left leg was unsuccessful and the patient continued to report a severe pain. A femoral–femoral crossover bypass was not performed, as the calibre of the crural vessels were poor. An amputation was recommended for pain relief and to prevent gangrene which had begun to develop. However, the patient did not wish this, and died due to overwhelming sepsis secondary to gangrenous necrosis of the left leg.

DISCUSSION

The patient suffered from an ischaemic stroke, most likely of embolic origin, and was thrombolysed. Subsequently, she developed an acute ischaemic limb. The timing of thrombolysis and the onset of the ischaemic limb would suggest that fragmentation of a thrombus and subsequent peripheral embolisation could have been induced by the administration of rt-PA. It could be suggested that the peripheral embolisation occurred as an

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Figure 1 (A) CT angiogram (CTA) showing a prominent intramural thrombus in distal aorta. (B) CTA showing patent right external iliac artery with contrast (green arrow) and occluded left external iliac artery (red arrow) with no contrast passing through. Note that both vessels are of normal calibre with no surrounding collaterals.

independent event of the thrombolysis and due to AF alone, as indeed was the case in the initial cerebral embolisation causing the stroke. Given the more extended period between the onset of the stroke and the ischaemic limb, it seems less likely that this is the case.

In comparison with intracerebral haemorrhage, which has been found to occur in 6.4% of patients with stroke thrombolysis,¹ there are limited reports of peripheral arterial occlusion following thrombolysis. A case was reported of an acute ischaemic limb secondary to an emboli, less than 1 h from the onset of thrombolysis.³ A similar case with ischaemic limb occurring 4 days post-thrombolysis, along with a newly associated cerebral infarct, was also reported.² It is worth noting that, in the two cases, fragmentation of a thrombus and peripheral embolisation were believed to be the mechanism causing the pathology. In both of these cases the patients were in AF and in the former case a transoesophageal echocardiogram (TOE) revealed the presence of an intracardiac thrombus.

Of the few reports of embolisation following thrombolysis for stroke, be it a myocardial infarction, a new stroke or peripheral embolisation, many implicate the underlying aetiology to be fragmentation of an intracardiac thrombus, which had formed secondary to AF.² One study found that of the six patients who developed recurrent ischaemic stroke after intravenous rt-PA, two of them developed recurrent strokes 3 days post-thrombolysis and five had an AF.⁴ However, no TOEs were reported in this paper and therefore an intracardiac thrombus prior to thrombolysis was not confirmed.

No reports thus far have associated peripheral embolisation with fragmentation of an aortic thrombus. In this particular case, the echocardiogram showed only a mildly dilated atrium and aortic root, thus raising the question of the origin of the initial thrombus. What is likely is that the source of the emboli was from the abdominal aortic thrombus seen on the CTA, which fragmented post-thrombolysis, and that the original infarct causing the stroke was embolic from a fibrillating heart. Other possibilities could include peripheral embolisation from an intracardiac thrombus, which fragmented completely during thrombolysis and was hence not seen on a following echocardiogram.

Given that the aforementioned references only speculate an intracardiac thrombus as a cause for peripheral embolisation post-thrombolysis, the aetiology remains unclear. Accordingly, further studies need to be carried out to determine the risk of acute embolic events post-thrombolysis in association with AF and to determine the possible underlying mechanisms.

In contrast, there are numerous papers which report acute embolic stroke following thrombolysis for myocardial infarction associated with an intracardiac thrombus. It has now become a recognised, if somewhat uncommon, complication.⁵ This has been addressed with the concomitant infusion of intravenous heparin during thrombolysis. Unfortunately, due to the risk of intracerebral haemorrhage, intravenous heparin is not recommended in stroke thrombolysis.

It should be noted that, this patient, who was previously on warfarin but had stopped taking it, had a CHA₂ DS₂ VASc score of 4, classifying her as a moderate-to-high risk of stroke in association with AF (4% per year).⁶ This case emphasises the need for appropriate anticoagulation in the population of patients with AF and appropriate risk factors.

There are no current measures that can be carried out to prevent a peripheral embolisation that would delay the administration of rt-PA. The presence of AF alone would not warrant the use of TOE to exclude an intracardiac thrombus or indeed investigations to exclude a thrombus from elsewhere.² The rationale underlying this is that the use of TOE would delay the onset of thrombolysis. Instead, due to the infrequency of these thromboembolic events, administration of rt-PA should take precedence. Management should, therefore, focus around early recognition and prompt invasive treatment such as an embolectomy. Accordingly, centres undertaking stroke thrombolysis should be aware of these embolic complications and have resources available to manage the consequences.

Learning points

- ▶ Thrombolysis with recombinant tissue plasminogen activator has significant potential side effects which patients should be counselled on prior to administration. These include haemorrhagic incidents and thromboembolic events.
- ▶ Acute limb ischaemia secondary to embolisation is a rare but serious complication of acute stroke thrombolysis. At present, there are a few investigations, which can be carried out prior to administration of thrombolysis, to prevent thromboembolic events.
- ▶ Management currently centres around early recognition and early treatment of events, such as an embolectomy.
- ▶ The case highlights the critical need for anticoagulation in a patient with known atrial fibrillation and associated risk factors (CHA₂ DS₂ VASc score) in prevention of strokes.

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