

## CASE REPORT

# Simultaneous treatment of ischaemic bowel and ischaemic stroke with intravenous thrombolysis therapy

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## SUMMARY

Novel treatment of simultaneous mesenteric and cerebral ischaemia with systemic thrombolysis. A 75-year-old man presented to the acute stroke team with aphasia, right-sided weakness and distressed with a pain he was unable to localise. He was treated with intravenous thrombolysis with tissue plasminogen activator for a left middle cerebral artery stroke. Decompensation on the ward during thrombolysis with worsening abdominal distension and pain, hypotension and tachycardia prompted a CT angiogram scan, which displayed proximal inferior mesenteric artery occlusion. Thrombolysis treatment resulted in excellent improvement of both his dysphasia and weakness from the left cerebral ischaemic stroke and reperfusion of the ischaemic bowel, without surgical intervention.

## BACKGROUND

In recent years, intravenous thrombolysis has become the mainstay of treatment of acute ischaemic cerebrovascular events with extremely successful results. National guidance clearly documents the timely use of thrombolysis as a cornerstone of ischaemic stroke management. Thrombolysis is also regularly used for the treatment of myocardial and pulmonary ischaemia. However, the use of systemic thrombolysis in many other types of ischaemic events remains highly controversial.

Here, we describe an interesting case of the successful treatment of simultaneous cerebral and mesenteric embolic ischaemia with systemic thrombolysis. Mesenteric ischaemia is the loss of blood supply to all or part of the intestines which if left untreated can lead to life-threatening bowel necrosis and the need for invasive surgery. Despite guidance on the use of local endovascular thrombolysis for mesenteric thrombosis, the use of systemic thrombolysis is poorly documented. With knowledge of the possible devastating adverse effects of thrombolysis treatment, this is an area of medicine that would benefit from further research in order to assess the realities of providing systemic thrombolysis as a routine treatment for mesenteric ischaemia.

## CASE PRESENTATION

A 75-year-old Caucasian right-handed man was seen as an acute stroke call with sudden onset severe expressive dysphasia, and mild right-sided facial weakness. Although generally well and independent

with all his activities of daily living, he had multiple comorbidities including previous right middle cerebral artery (MCA) stroke with a right carotid endarterectomy 5 years prior, hypertension, hypercholesterolaemia, lower limb peripheral vascular disease requiring stent insertion, ischaemic heart disease, tissue aortic valve replacement for severe aortic stenosis, a permanent pacemaker and paroxysmal atrial fibrillation (AF). He was also recently diagnosed with localised small cell lung cancer undergoing radiotherapy and chemotherapy with curative intent. Prior to admission, he had otherwise been well with no preceding infective illness. He was compliant with his medications (clopidogrel, ramipril, felodipine, ezetimibe and tiotropium bromide inhaler) but was not on any anticoagulation for paroxysmal AF.

On admission, he was tachycardic, hypotensive and visibly in pain. Neurological examination revealed severe expressive dysphasia with a right-sided upper motor neuron facial weakness. Cardiovascular, respiratory and abdominal examinations revealed no obvious cause of his distress and no obvious source of infection. CT of his head confirmed no acute intracerebral haemorrhage and he was thrombolysed following a period of resuscitation at 4 hours after symptom onset. During the alteplase infusion, he clinically deteriorated, with worsening agitation, hypotension and new abdominal distension. Thrombolysis treatment was therefore halted after having had 75% of the total alteplase dosage.

## INVESTIGATIONS

Serial electrocardiograms (ECG) displayed no ischaemic or dynamic change but showed AF with a rapid ventricular response and incomplete left bundle branch block. Laboratory results on admission displayed a severe neutrophilia of  $39.6 \times 10^9/L$ , haemoglobin 113 g/L, platelets  $214 \times 10^9/L$ , C reactive protein of 4.8 mg/L and stage I acute kidney injury (creatinine 113  $\mu\text{mol/L}$ ). Troponin-T levels were 24 ng/L initially with no significant rise at 12 hours. Initial CT head displayed no evidence of acute infarct or intracerebral haemorrhage and CT angiogram showed no significant stenosis or thrombus of the carotid or vertebral arteries.

Shortly after his deterioration during thrombolysis, he was found to have a raised lactate of 3.7 mmol/L on an arterial blood gas. CT thorax



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and abdominal angiogram confirmed no aortic dissection and no pulmonary embolus but did identify occlusion of proximal 1.5 cm of the inferior mesenteric artery (IMA) with concurrent thickening of the sigmoid colon (see figure 1).

### DIFFERENTIAL DIAGNOSIS

This patient presented clinically with a left MCA stroke syndrome. His pain was difficult to localise due to aphasia, however, the initial concerns given the tachycardia and hypotension were regarding concurrent sepsis, acute coronary syndrome or aortic dissection. Following identification of acute ischaemic bowel secondary to IMA occlusion on CT, we hypothesised that he had suffered multiple emboli simultaneously to his left MCA and IMA. The most likely differential was multiple emboli secondary to AF. Other differentials we considered were: multiple emboli due to bacterial endocarditis, venous thromboemboli (VTE) with intracardiac shunt (eg, patent foramen ovale (PFO), atrial septal defect) or presentation of a prothrombotic state/thrombophilia.

### TREATMENT

Initial treatment included analgesia, intravenous fluids and empirical antibiotics for presumed sepsis. As his dominant presentation was with a left MCA syndrome, he underwent intravenous thrombolysis with alteplase at 4 hours post-symptom onset just within the thrombolysis window, as no clear contraindication had been identified.

After identification of acute mesenteric ischaemia, the patient was reviewed urgently by the surgical team, who felt immediate surgical intervention was contraindicated due to high bleeding risk following thrombolysis treatment, but that repeat review 12 hours post-thrombolysis would be required for potential resection of the ischaemic bowel. However, by the following morning, the patient's clinical picture had dramatically

improved. He was no longer in abdominal pain and was passing loose stools. He also had rapid improvement of his speech and was able to speak in short sentences. His tachycardia had resolved and repeat blood gases showed an improvement of his lactate to 1.0 mmol/L. On repeat review by the surgical team, he was deemed to no longer require surgical intervention due to likely partial revascularisation of the colon due to thrombolysis. He was started on a split dose low-molecular-weight heparin (LMWH) as medical management of his mesenteric ischaemia.

Repeat CT head at 24 hours post-thrombolysis showed no interval change and no haemorrhagic transformation of his ischaemic stroke; he was unable to undergo MRI due to his pacemaker. Transthoracic echocardiogram later in the admission displayed a mildly dilated left ventricle, akinetic basal inferoseptum, well-seated tissue aortic valve with no obvious intracardiac thrombus or PFO.

### OUTCOME AND FOLLOW-UP

This patient was initially treated in the hyperacute stroke unit. He was subsequently repatriated to his local hospital for ongoing rehabilitation and was continued on therapeutic dose LMWH as anticoagulation for his paroxysmal AF. He is no longer dysphasic and the only remaining neurological deficit is mild right hand dyspraxia, and his diarrhoea has settled. Ongoing cardiology, haematology and stroke review are awaited to determine the cause of his multiple emboli and to decide his anticoagulation plan.

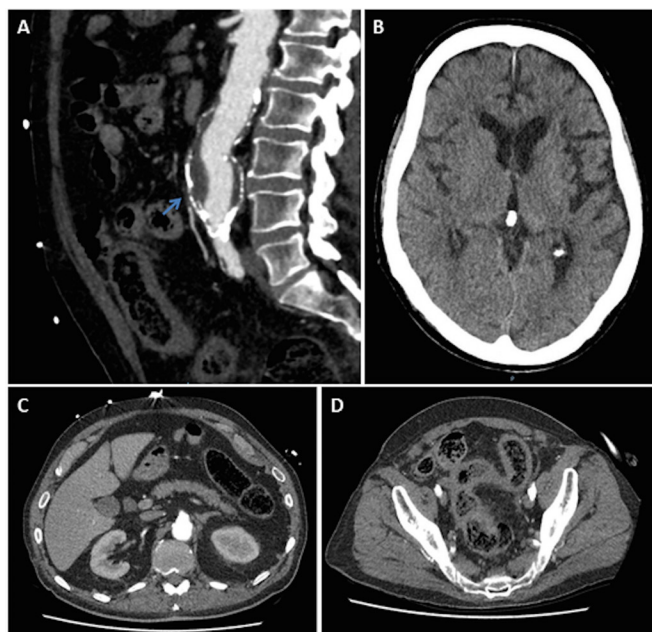
### DISCUSSION

Our case demonstrates multiple emboli to the IMA and left MCA causing two simultaneous clinical syndromes which both improved with systemic intravenous thrombolysis therapy. The embolic source in our case remains unclear; however, given the presence of non-anticoagulated AF, excluding a cardiac thrombus with more extensive cardiac investigations would be important.

Multiple simultaneous arterial embolic occlusions are uncommon. In most cases, a right-to-left intracardiac shunt, such as a PFO, in conjunction with VTE, or left-sided cardiac thrombi is identified. Many cases of paradoxical emboli to the arterial system in the context of a PFO have been reported.<sup>1</sup> However, our patient did not demonstrate the clinical features of acute or chronic VTE. He has not yet undergone a bubble echo to exclude a PFO. Several case reports demonstrate simultaneous embolic arterial occlusions without evidence of right-to-left intracardiac shunting<sup>2-4</sup>; in two cases,<sup>2,4</sup> left atrial pathology was found, in one case the cause was unknown.<sup>3</sup>

We hypothesise that, in our case, the systemic intravenous alteplase not only served to recanalise the left MCA but also helped restore blood flow within the IMA. To our knowledge, this is the first case of treatment of dual embolic arterial occlusions with systemic intravenous thrombolysis.

Systemic thrombolysis is currently indicated for acute ischaemic stroke,<sup>5</sup> acute myocardial infarction<sup>6</sup> and pulmonary embolus,<sup>7</sup> within certain criteria and if there are no contraindications. The role of systemic intravenous thrombolytic therapy in mesenteric ischaemia is poorly understood. Current World Society of Emergency Surgery guidelines include the use of local endovascular thrombolysis to revascularise partial mesenteric arterial occlusions<sup>8</sup> but do not include a role for systemic thrombolysis. Although successful treatment of mesenteric venous thrombosis has been demonstrated in case reports,<sup>9</sup> no trials of systemic thrombolysis in mesenteric arterial occlusions have been conducted.



**Figure 1** CT images. (A) Sagittal view of CT abdomen showing occlusion of proximal 1.5 cm of IMA (see arrow). (B) CT head showing no acute abnormality. (C) No features of ischaemic colitis of ascending/transverse colon, due to supply by superior mesenteric artery. (D) Diffuse sigmoid thickening in keeping with ischaemic colitis of IMA territory. IMA, inferior mesenteric artery.

The effect of systemic intravenous thrombolysis as a treatment for multiple embolic pathologies has not been well studied. Although we report the beneficial outcome of both embolic phenomenon post-thrombolysis in our case, other reports have demonstrated potential harm when thrombolysis is given in the presence of an embolic source, for example, an intracardiac thrombus,<sup>10</sup> due to destabilisation of the thrombus and generation of further emboli.

In conclusion, our case demonstrates an uncommon scenario of dual embolic pathologies simultaneously benefitting from systemic intravenous thrombolysis. Although thrombolysis is a well-established treatment of acute ischaemic stroke, the role of systemic thrombolysis in patients with acute embolic mesenteric ischaemia requires further clarification.

### Learning points

- ▶ Patients presenting with multiple embolic arterial occlusions require investigations to exclude cardiac causes (intracardiac thrombus, bacterial endocarditis and atrial myxoma).
- ▶ Patients with clinical features or risk factors for recent venous thromboemboli in the context of acute arterial occlusions should be investigated for intracardiac shunt (eg, patent foramen ovale, atrial septal defect and patent ductus arteriosus).
- ▶ The role of systemic intravenous thrombolysis in multiple embolic phenomena and mesenteric ischaemia is unclear.

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