



Thrombolysis in a stroke patient with Marfan syndrome

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DECLARATION In this patient with Marfan's syndrome and ischaemic stroke thrombolysis was associated with good outcome in spite of haemorrhagic transformation.

Competing interests

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Ethical approval

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Introduction

Marfan syndrome is an autosomal dominant inherited disorder of the connective tissue with pleiotropic manifestations in the classic triad of ocular, skeletal, and cardiovascular systems. Characteristic clinical features include a thin tall stature, pectus carinatum or excavatum, scoliosis, joint hypermobility, arachnodactyly, pes planus, a high arched palate, and ectopia lentis.¹ The syndrome has an incidence of around 1 in 9800.² Weakness of the blood vessels, especially the aorta, causes progressive dilatation of the aortic root leading to aortic regurgitation, dissection, or rupture, which is the most common life threatening feature of the Marfan syndrome.¹ Neurovascular complications of Marfan syndrome are rare, and mostly ischaemic in nature.³ An association between Marfan syndrome and intracranial aneurysms has been described in one autopsy series of 7 cases in 1997,¹ but was not confirmed in larger autopsy series of 25 Marfan cases.¹ Thrombolysis is now a standard treatment for acute ischaemic stroke. We found no report of thrombolytic treatment for acute ischaemic stroke in patients with Marfan syndrome in the literature.

Case report

A 57-year-old man with known Marfan syndrome was admitted to the emergency department with sudden onset of right arm and leg weakness and slurred speech 50 min before presentation. His

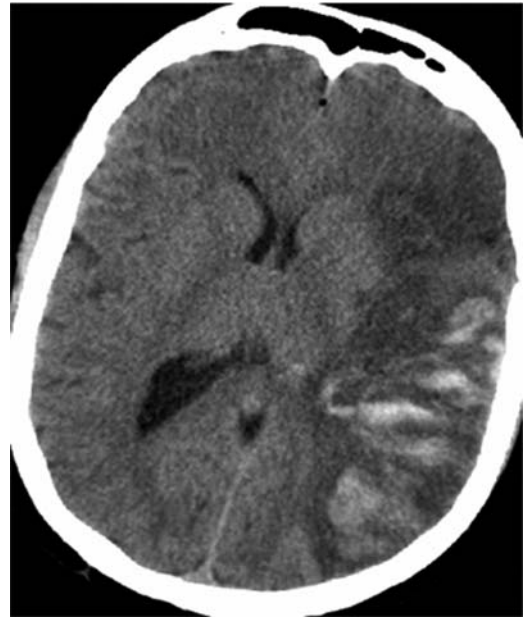
past medical history included a metallic aortic valve replacement 12 years ago, which was infected with MRSA and so this was replaced with tissue valve a month later. Other history included mild congestive heart failure (New York Heart Association class II) and a transient ischemic attack 2 years ago. Echocardiography (ECHO) 1 year prior to this admission had shown an ejection fraction of 41% but stable prosthetic valves. He was fit and independent in activities of daily living. His medications on admission were frusemide, bisoprolol, amlodipine, losartan, spironolactone, and fluoxetine. He was no longer taking aspirin and dipyridamole at the time of admission.

On examination, he had a partial left anterior circulation syndrome with right hemiparesis (Medical Research Council grade power of 3/5 in the arm and 4/5 in the leg), a right upper motor neuron facial palsy, expressive dysphasia, and right sided visual neglect. His National Institute of Health Stroke Scale (NIHSS) score was 12. His blood pressure was low at 100/80 mm Hg. Apart from the thoracotomy scar, and the tall features of Marfan syndrome his physical examination was normal. Routine blood tests, electrocardiogram and chest X-ray were normal. A computed tomogram (CT) of the head, performed 2 h after symptom onset, did not show evidence of infarction or haemorrhage (Figure 1). Intravenous thrombolysis with alteplase at a dose of 0.9 mg/kg bodyweight was started 2 hours and 30 min after the onset of symptoms. There were no immediate complications, and he remained haemodynamically stable. Twenty hours later he became drowsy. His NIHSS score worsened to 18 with more pronounced right hemiparesis. A repeat CT head scan (Figure 2) showed an established left

Figure 1
CT head scan before thrombolysis showing no evidence of established infarct or haemorrhage



Figure 2
CT head scan 20 hours post thrombolysis showing left middle cerebral artery territory infarct with haemorrhagic transformation within the infarcted area



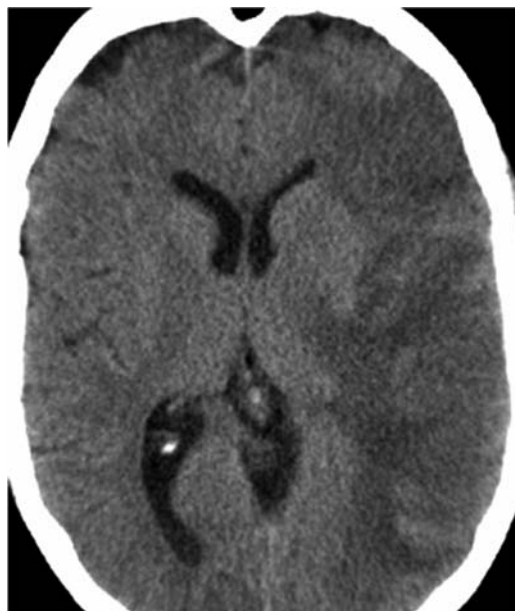
middle cerebral artery territory infarct with haemorrhagic transformation within the infarcted area. There was also swelling of the ipsilateral left cerebral hemisphere with mild midline shift towards right. Over the next few days, the patient gradually improved with continued physiotherapy. At 9 days, he was able to transfer independently from bed to chair. His NIHSS score was 7 with word finding problems, partial right hemianopia, right visual neglect and a mild right hemiparesis. A Repeat CT head scan at 2 weeks showed an established infarct and complete resolution of haemorrhagic transformation (Figure 3). At this stage he was commenced on aspirin. He was discharged home after 3 weeks when he was mobilizing independently, though he had mild right upper limb weakness, dysphasia and cognitive impairment. At three months he was able to communicate and physically independent, but he was unable to return to his usual hobbies and work because his memory had deteriorated, he could not coordinate his right hand, and had word finding

problems. He underwent further investigations to discover the aetiology of the stroke. Carotid Doppler did not show any evidence of significant carotid stenosis. ECHO cardiography showed a normal aortic root and a normally functioning prosthetic aortic valve though the ejection fraction was low at 41%. There was no evidence of aortic dissection.

Discussion

To our knowledge, this is the first report of a patient with Marfan syndrome treated with thrombolysis for acute ischaemic stroke. In our patient, thrombolysis was complicated by haemorrhage into the infarcted brain. This resulted in transient deterioration of his neurological status, but overall recovery was good, considering the extent of the infarction. There was no evidence of an underlying vascular malformation, and the pattern of the haemorrhage suggested widespread haemorrhagic transformation rather than a bleed

Figure 3
CT head scan at 2 weeks showing established left middle cerebral artery territory infarct as previously demonstrated. The haemorrhagic transformation is longer visible



from an abnormal vessel. It is therefore unlikely that his haemorrhage was due to Marfan-related connective tissue disease. It is highly likely that this patient's stroke could be cardioembolic because of poor left ventricular function and prosthetic valves. This is a risk factor for haemorrhagic complications. While it is important to report this finding, it would not be appropriate to withhold thrombolysis from patients with Marfan syndrome in future on the basis of our report. It is also important to rule out the possibility of aortic dissection in Marfan patients before thrombolysis.

Although the pathophysiology of the disease would make a predisposition to intracranial aneurysms likely, there is no convincing evidence for this from published reports. The incidence of intracranial aneurysms in Marfan syndrome in the two reported autopsy series is 2/7 in one⁴ and 1 small out of 25 in the other.⁵ Taking the

two studies together, there were two asymptomatic haemorrhages (age 32 and age 30) and one symptomatic fatal subarachnoid haemorrhage (age 20) in 32 reported cases. This is not sufficient information to judge whether there is a significant difference from the population rate of 1.3%.⁶

As in the patient reported here, cerebral ischaemic events are the most common neurovascular complications of Marfan syndrome. In a retrospective case series of 513 patients with Marfan Syndrome, 3.5% had cerebrovascular events, 83% of these were ischaemic (11 transient ischaemic attacks, 2 cerebral infarcts, 2 spinal cord infarctions) and 16% (3 patients) haemorrhagic (2 subdural haematomas, and 1 spinal subarachnoid haemorrhage). The mean age of affected patients in this series was 39.6 years, considerably lower than the average for strokes in the general population. A high risk source of cardiac embolism was identified in 77% (prosthetic cardiac valves, atrial fibrillation).³

Current evidence suggests that Marfan patients are at risk of cerebral ischaemic events at a young age. The patient we report here, developed a haemorrhagic complication after thrombolysis, which did not affect his recovery. More reports on thrombolysis outcome in Marfan patients are required to assess its safety in this patient group.

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