CASE REPORT

Thrombolysis for stroke in pregnancy at 39 weeks gestation with a subsequent normal delivery

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Accepted 27 July 2015

SUMMARY

Stroke during pregnancy is fortunately a rare event, however, it can have severe consequences, with 9.5% of all maternal deaths being related to stroke. The most common presentation is an ischaemic stroke. There has been much debate as to the correct treatment for such cases' and whether thrombolysis can be used safely in pregnancy. Our case describes a 28-year-old woman with a previous normal vaginal delivery presenting in her third trimester with a sudden onset of dense left hemiparesis. She was successfully treated with alteplase, an intravenous recombinant tissue-type plasminogen activator, and made a full recovery after normal delivery of a healthy infant. This case report highlights one of the first documented successful outcomes from thrombolysis for this condition in the UK and may help inform future management of these women.

BACKGROUND

There has been much debate as to the correct treatment for ischaemic stroke in pregnancy and whether thrombolysis can be used safely.[1] As pregnancy has been a solid contraindication of all clinical trials of intravenous recombinant tissue-type plasminogen activator (IV rt-PA), there are no relevant guidelines for the use of thrombolysis in pregnancy. Although IV rt-PA does not cross the placenta, the theoretical risk of uterine or fetal haemorrhage has precluded this,[2] which prevents clinicians from considering thrombolysis as a possible treatment option.

CASE PRESENTATION

A 28-year-old woman at 39 weeks gestation into her second pregnancy was seen in the emergency department of her local general district hospital within 30 min of developing an acute onset of left-sided hemiparesis, which had been preceded by a headache of 2 days duration and was witnessed by her husband. Neurological examination revealed a left-sided hemiparesis, left-sided facial weakness and tongue deviation, and impaired sensation of the left side, which was more pronounced in the upper limb. The patient had no preceding risk factors and no medical history, her blood pressure was normal at 132/61 mm Hg with no history of preeclampsia, her fasting glucose was 3.9 mmol/L and ECG was normal. On admission, her National Institutes of Health Stroke scale (NIHSS) was 11, indicating a moderate stroke. CT showed no intracranial bleeding, excluding a haemorrhagic stroke. She continued to deteriorate and therefore an urgent decision with regard to treatment was needed.

TREATMENT

The complex decision to thrombolyse this patient was made following discussions between the emergency department, and medical and obstetric consultants, with consent from the patient. Thrombolysis with alteplase was initiated in the emergency department within 2 h of onset, and subsequently continued in the air ambulance on transfer to a tertiary unit with access to multidisciplinary stroke facilities. A post-thrombolysis MRI made the diagnosis of a lacunar-type stroke (LACS) involving the right middle cerebral artery. Twenty-four hours post-thrombolysis, the patient's NIHSS score had improved to 6 and she was transferred back to her initial district general hospital. On return to the district general hospital post-thrombolysis she was commenced on aspirin 75 mg once a day.

To allow for initiation of further treatments, it was decided to induce labour; the stroke team advised this to be carried out 48 h post-thrombolysis to minimise the effect of the alteplase on obstetric interventions. Assessment for induction of labour revealed the patient to have a Bishops score that was compatible with artificial rupture of membranes (ARM). The patient was reviewed by senior obstetricians and a high-risk intrapartum management plan was implemented; this included the avoidance of pushing in the second stage, to prevent the creation of excessive intracranial pressure, and an active third stage to reduce the risk of postpartum haemorrhage. Labour progressed well with a Neville Barnes forceps delivery to prevent pushing in the second stage; the patient was subsequently taken to theatre for a manual removal of placenta, as the placenta had not delivered and had a 2 L PPH.

OUTCOME AND FOLLOW-UP

The patient had on-going postnatal care that was individualised to her requirements, and included the initiation of clopidogrel and prophylactic tinzaparin, a low-molecular-weight heparin (LMWH). Close liaison with the stroke rehabilitation team ensured appropriate continuation of care in the form of physiotherapy and rehabilitation. When reviewed 8 months later, the patient had almost made a complete recovery.

Further investigations carried out postnatally revealed a normal thrombophilia screen (negative antinuclear antibodies and antineutrophil cytoplasmic antibodies, antithrombin 3–136, protein S), both carotid and bilateral leg Dopplers were normal, and a patent foramen ovale was not

To cite: Ritchie J, Lokman M, Panikkar J. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2015-209563

demonstrated with transthoracic echocardiogram. The patient's cholesterol levels were found to be raised (total cholesterol 6.9 mmol/L, low-density lipoprotein cholesterol 3.4 mmol/L, triglyceride 3.7 mmol/L). After discussion, it was decided that these raised levels were unlikely to have contributed to the patient's risk of stroke. Therefore, she had no known risk factors for stroke other than pregnancy.

DISCUSSION

The pregnant population is at higher risk of stroke, compared to the non-pregnant population of a similar age, with the greatest incidence during the third trimester, perinatal and postnatal. The incidence of stroke in pregnancy varies widely in the literature and has reportedly been as high as 34/100 000 deliveries,[3] compared to the non-pregnant population of the same age group, where the incidence is 11/100 000 women.[4] Additionally, there are also recent data suggesting that the incidence of stroke in pregnancy is increasing.[5]

Between 1979 and 2008, in the UK, there were 347 maternal deaths due to stroke, which results in an incidence of fatal stroke of 1.61/100 000 maternities.[6] Stroke in pregnancy has a case fatality rate of 20%.[1] Factors that can increase the risk of stroke in pregnancy include a history of migraine,[1] gestational diabetes,[1] preeclampsia and hypertension,[1 5 7] smoking,[5 7] arterial disease and hyperlipidaemia. Age over 35 years[3] is an additional risk factor, which has been reported as increasing the risk twofold.[5] In the UK Obstetric Surveillance System (UKOSS) study, 33% of women were aged 35 years or older. The risk of antenatal stroke is higher in the third trimester.[3] This is partly due to the increased hypercoagulability state in the third trimester, and increased incidence of preeclampsia and gestational hypertension. Pregnancy in general is associated with an increased risk of thromboembolism due to the normal haemostatic changes that occur in pregnancy, which increase hypercoagulability; these include increases in the clotting factors, a decrease in protein S levels, a fall in the activity of activated protein C and inhibition of fibrinolysis.[8]

Strokes are categorised into two subsets: ischaemic and haemorrhagic. Most strokes occurring in pregnancy tend to be ischaemic,[9] however, both types of stroke in pregnancy are associated with high morbidity and mortality. In the general population, acute ischaemic strokes can be treated by thrombolysis in the form of IV rt-PA. This therapy has been shown to dramatically improve stroke symptoms and improve outcomes, although it must be administered within 4.5 h of the onset of symptoms.[10] Another method of administering rt-PA is intra-arterially (IA rt-PA). Thrombolysis is an effective, approved therapy for revascularisation in ischaemic stroke, myocardial infarction, pulmonary embolism and thrombosis of cardiac valve prosthesis. However, there is very limited evidence on the use of thrombolysis in pregnancy for any of these indications.

Pregnancy has been a solid contraindication of all clinical trials of IV rt-PA. Although IV rt-PA does not cross the placenta, the theoretical risk of uterine or fetal haemorrhage has precluded this.[2] Hence, there are no guidelines for IV rt-PA in this context.[11] Despite this, there have been a small number of case reports documenting successful use, in pregnant women, for conditions other than stroke, most with no adverse effects. The risks of IV rt-PA to the mother include uterine haemorrhage or haematoma and intracranial haemorrhage. The risks to the fetus are still largely unknown; animal studies have shown no teratogenic effects and as IV rt-PA does not cross the placenta, it presents a low possibility of fetal haemorrhage, however, there may be the risk of preterm labour and placenta abruption.[12] The UK UKCOSS has reported that, of 12 women with ischaemic arterial stroke, none underwent thrombolysis. A Japanese paper from 2013 looked at all the 16 reported cases of acute revascularisation therapy for stroke during pregnancy,[13] none of those cases had occurred in the UK and only four cases were in the third trimester. Maternal and fetal outcomes were good in the four cases where treatment was administered in the third trimester. Nine patients underwent IV rt-PA, and seven of those nine patients had a good outcome, one had a uterine haemorrhage at 12/40 and had a medical abortion, and one had a haemorrhagic infarction at 6/40 and died due to complications from angioplasty. Only one other case of the use of thrombolysis for stroke in the UK exists, which was published in March 2014 in the *Journal of Neurology*;[14] this was a patient in her third trimester who was successfully treated and went on to have an elective caesarean section.

Our patient also received aspirin and then tinzaparin (LMWH). LMWH has been shown to be a safe and effective treatment in pregnancy.[15]

Ischaemic stroke in pregnancy is associated with a small risk of recurrence in future pregnancies; this is increased if the patient has a clear cause for her initial stroke. The overall risk of recurrence is 1% within 1 year and 2.3% within 5 years.[16]

Learning points

We have reported the second case of thrombolysis for stroke in pregnancy in the UK, and the first to have a subsequent normal delivery.

- This case had a good maternal and fetal outcome and demonstrates that intravenous recombinant tissue-type plasminogen activator can be used in pregnancy.
- While it is important to recognise that the use of thrombolysis should be considered cautiously and be determined by the severity of the symptoms, and, in addition, that the risks and benefits must be weighed up on an individual basis, it should no longer be viewed as an absolute contraindication.
- Therefore, stroke in pregnancy should be dealt with quickly and efficiently to allow transfer, if needed, to a tertiary centre that can administer thrombolysis.

Acknowledgements The author acknowledged Dr Andrew O'Neill.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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