CASE REPORT

Intraventricular thrombolysis after endovascular treatment of a ruptured arteriovenous malformation

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SUMMARY

Intraventricular haemorrhage (IVH) secondary to arteriovenous malformation (AVM) rupture carries significant morbidity and mortality. External ventricular drainage of IVH is frequently complicated by thrombus formation within the ventricular catheter and therefore often unsuccessful at treating hydrocephalus in this setting. Intraventricular administration of recombinant tissue-type plasminogen activator (rtPA) has proved successful in the treatment of spontaneous panventricular haemorrhage. However, usage of rtPA is contraindicated in the setting of a ruptured AVM or aneurysm in which the bleeding source has not been secured. There are only a few reports of intraventricular thrombolysis in the treatment of IVH from AVM rupture. We present the case of successful application of rtPA to treat IVH after endovascularly securing the haemorrhage site of the AVM. Intraventricular thrombolysis remains an option for the treatment of IVH in the setting of AVM rupture and should be considered on a case-by-case basis.

BACKGROUND

Intraventricular haemorrhage (IVH) can occur spontaneously or in the setting of a ruptured cerebral aneurysm or arteriovenous malformation (AVM). IVH leads to worse patient outcomes secondary to obstructive hydrocephalus and increased intracranial pressure (ICP). The mortality associated with IVH is proportional to the amount of blood and number of ventricles involved. When all ventricles are casted, the mortality ranges from 50% to 100%.^{1 2}

IVH is commonly associated with ruptured periventricular AVMs and was seen in as many as 16% of cases in one series.¹ The treatment of IVH involves placement of an external ventricular drain (EVD) to clear the ventricles, re-establish cerebrospinal fluid (CSF) flow and prevent the development of increased ICP. Intraventricular administration of thrombolytic agents such as recombinant tissue-type plasminogen activator (rtPA) has shown early success in clearing the ventricular system faster and preventing thrombus formation and occlusion of the ventricular catheter in cases of spontaneous IVH in the Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVH) trial. CLEAR-IVH was a phase II trial which provided evidence that intraventricular catheter delivered rtPA cleared IVH and reduced the 30-day mortality rate in patients with IVH with third or fourth ventricle obstruction. A meta-analysis demonstrated that usage of intraventricular

thrombolytics decreased mortality from IVH from 53% to 16% compared with ventricular drainage alone.³ To date, the CLEAR trial has excluded IVH secondary to ruptured cerebral aneurysms and AVMs.

The use of intraventricular thrombolytics is contraindicated in the setting of a ruptured cerebral aneurysm or AVM as the risks of re-rupture outweigh the benefits of the thrombolytic therapy.⁴ Despite these risks, a few case reports have shown the successful application of intraventricular thrombolytics in the setting of a ruptured AVM either before or after securing the haemorrhage site of the AVM.^{1 2 5–7} We present our experience with intraventricular administration of rtPA for the treatment of IVH in the setting of a ruptured AVM and review the existing literature of cases on this subject.

CASE PRESENTATION

A middle-aged patient with a known diagnosis of an intracerebral AVM was found unresponsive at work. The patient arrived at our hospital intubated with a Glasgow Coma Scale score of 4T with decerebrate posturing.

INVESTIGATIONS

Head CT demonstrated a left temporal haematoma and scattered calcifications with panventricular IVH and obstructive hydrocephalus (figure 1). A right frontal EVD was emergently placed. CT angiography revealed a left temporal AVM centered adjacently to the left temporal horn. On digital subtraction angiography (DSA), a Spetzler–Martin grade II AVM was identified with a nidus measuring 3 cm with three main arterial posterior cerebral artery feeders. There was a 1.4 cm intranidal venous varix (figure 2), presumed to be the source of the haemorrhage.

TREATMENT

Microcatheter Onyx (ev3, Covidien Vascular Therapies, Irvine, California, USA) embolization was performed using a Scepter XC balloon catheter (Microvention-Terumo, Tustin, California, USA). Post-embolization DSA showed successful embolization of the majority of the AVM nidus with a small residual in the superior aspect of the AVM. There was complete obliteration of the high-risk venous varix (figures 3 and 4).

OUTCOME AND FOLLOW-UP

During the patient's hospitalization there were periods of increased ICP secondary to ventricular

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Figure 1 (A, B) Axial non-contrast CT head showing a left temporal hematoma and scattered calcifications with intraventricular extension. Pan-ventricular hemorrhage and hydrocephalus is noted. (C, D) Axial and coronal reconstructions of a CT angiogram showing a serpentine collection of vessels in the left temporal lobe consistent with a 3.0 cm Spetzler–Martin grade II arteriovenous malformation.

Figure 2 Digital subtraction angiography of (A) left internal carotid artery injection and (B, C) left vertebral artery injection demonstrating filling of a 3.0 cm arteriovenous malformation from branches of the left posterior cerebral artery. A 1.4 cm intranidal venous varix was present. (D) Early venous drainage is seen into the vein of Labbe and Trolard.

Figure 3 Digital subtraction angiography. (A) Lateral and (B) anteroposterior select microcatheter injections via three pedicle branches of the posterior cerebral artery prior to Onyx embolization of the arteriovenous malformation (AVM). (C, D) Post-embolization angiography of the left vertebral artery showing decreased contrast opacification and reduction in size of the AVM nidus.

catheter obstruction. Because the presumed site of haemorrhage (the venous varix) was secured, rtPA was initiated through the right frontal EVD on hospital day 5; 1 mg rtPA was given through the EVD twice a day with serial head CTs to evaluate for IVH clearance from the third and fourth ventricles. During each treatment session 3 cm³ of cerebrospinal fluid was aspirated followed by administration of 1 mg rtPA diluted in 2 cm³ saline. An additional 1 cm³ saline was then pushed through the EVD to clear the dead space of the catheter. The EVD remained clamped for 1 h unless increased ICP was encountered. The patient slowly regained consciousness as the IVH cleared.

Follow-up head CTs showed decreased ventriculomegaly and IVH in all ventricles with clearance of the third and lateral ventricles ([figure 5](#)). The patient tolerated the EVD clamp and was discharged to a rehabilitation facility after a tracheostomy and gastrostomy. At 3 months after discharge the patient had a very mild expressive aphasia and mild right hemiparesis.

DISCUSSION

The presence of IVH contributes significantly to morbidity and mortality. In fact, mortality with the presence of any IVH is up to 50%.⁸ This high mortality rate is proportional to the amount

Figure 4 (A, B) Post-embolization digital subtraction angiography demonstrating the Onyx cast.

Figure 5 Serial follow-up CTs following administration of intraventricular recombinant tissue-type plasminogen activator (rtPA) at hospital day 5 (A, B), day 8 (C, D), and day 13 (E, F) showing clearance of intraventricular hemorrhage, reduction in size of the ventricles, and re-establishment of cerebrospinal fluid flow through the lateral and third ventricles.

of ventricular haemorrhage and increases when the third and fourth ventricles are involved.^{1 9} Tuhim *et al*⁹ studied the prognostic significance of IVH extension in 129 patients with supratentorial intracerebral haemorrhage (ICH), 47 of whom had IVH; 20 of the 47 patients with IVH (43%) died. They found that primary IVH was more benign than ICH with IVH extension and the volume of ICH contributed significantly to the outcome.⁹

Intraventricular thrombolysis has been successfully administered and shown to decrease mortality from 30% to 10% and improve patient outcome.³ Some indications for intraventricular administration of rtPA for the treatment of IVH are panventricular haemorrhage or ventricular haemorrhage in the fourth ventricle with obstructive hydrocephalus. The phase II CLEAR-IVH trial showed that patients treated with a combination of EVD and rtPA had significantly lower ICPs, shorter duration of EVD use, and fewer ventricular catheter obstructions than patients treated with EVD alone. Additionally, complications such as increased haemorrhage or ventriculitis were rare in the trial.

The CLEAR-IVH trial only evaluated patients with spontaneous IVH and excluded IVH secondary to ruptured intracranial aneurysms and AVMs. There exists a theoretical risk of re-bleeding from the unsecured aneurysm or AVM when rtPA is given. A periventricular AVM has a theoretically higher risk of re-rupture, especially when the source of bleeding—whether it is the AVM nidus, an intranidal aneurysm, a flow-related aneurysm, or a venous varix—is located adjacent to the ventricle and is directly exposed to the rtPA. There are a limited number of case reports documenting re-haemorrhages when rtPA is administered prior to securing the aneurysm or AVM.^{4 10}

Three important factors should be considered prior to initiation of intraventricular rtPA in the setting of a ruptured AVM. First, we believe that every effort should be made to secure the bleeding site before administering rtPA. In our case we achieved complete obliteration of the venous varix which was the high-risk feature and presumed source of haemorrhage prior to

initiation of rtPA. However, there are a handful of case reports that have successfully applied rtPA before securing the bleeding source without re-haemorrhage of the AVM.^{2 4-6 8 10} In these cases, the AVMs were located in the right temporal lobe adjacent to the temporal horn, left lateral ventricle, left thalamus, and left frontotemporal lobe. We felt that it was safer to first secure what we felt was the rupture site—the venous varix—in our patient and then administer rtPA. Only one other case has reported rtPA being started after a parasagittal ruptured AVM was endovascularly secured.⁷ No re-haemorrhage was seen in that case.

Second, the location of the AVM and its distance from the ventricles should be considered. AVMs that are located further from the ventricles intuitively would have a reduced chance of re-bleeding compared with periventricular AVMs because the AVM nidus is not in direct contact with the ventricles. This comes from the risk that rtPA will come into direct contact with a periventricular AVM, lyse the protective thrombus or haematoma surrounding the rupture site.¹ In all but one of the reported cases the AVM was in the immediate periventricular location and in close contact with the injected rtPA.¹ Despite their location, no re-bleed was encountered.

Third, the appropriate dose, frequency, and duration of rtPA have not been established. In the phase II CLEAR-IVH trial, patients with spontaneous IVH received 3 mg/3 mL of rtPA every 12 h.¹⁰ In the reports on rtPA use in ruptured AVMs, rtPA doses ranged from 2 to 5 mg every 12 h.^{1 2 5 7} There were no differences in the rate of re-haemorrhage across the different doses.⁵ Given the variations in dosing, we believe that the minimum effective dose of rtPA should be administered in the setting of a recently ruptured AVM where re-rupture is a concern. In our case, 1 mg of rtPA twice daily was effective. To determine the endpoint of intraventricular rtPA, serial neurological examinations and head CTs should be used to follow the progress and determine the endpoint of rtPA therapy. In our patient, once rtPA was initiated, we followed the patient's clinical examination, daily ventricular outputs and evaluated head CTs, focusing especially on clearance of the third and fourth ventricles.

Another circumstance where rtPA may be helpful in IVH from a ruptured AVM is an obstructed ventricular catheter in the setting of hydrocephalus. External ventricular drainage can relieve obstructive hydrocephalus and elevated ICP associated with IVH; however, the ventricular catheter frequently obstructs and fails to divert CSF, leading to ICP elevation and potential brain herniation. In one study reviewing 48 spontaneous supratentorial haemorrhages with IVH extension the authors found that, although the presence of hydrocephalus was associated with a poor outcome, ventricular drainage did not help eight of nine patients.¹¹ Thus, it may be reasonable to attempt rtPA to recanalise an obstructed ventricular catheter for treatment of life-threatening hydrocephalus from IVH, even in the setting of a ruptured periventricular AVM.

Learning points

- ▶ Intraventricular administration of tissue plasminogen activator should be considered on a case-to-case basis.
- ▶ The bleeding site of an arteriovenous malformation should be secured as soon as possible to reduce the risk of re-haemorrhage from intraventricular recombinant tissue-type plasminogen activator.
- ▶ Intraventricular haemorrhage should be followed with serial head CTs focusing on clearance of the third and fourth ventricles.

Competing interests None declared.

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