Hemorrhagic stroke complicated by cerebral venous sinus thrombosis with idarucizumab

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We present a case of a 76-year-old man with an acute hypertensive left basal ganglia and thalamic hemorrhage with intraventricular extension whilst on dabigatran 150 mg twice per day for an unprovoked lower limb deep vein thrombosis (DVT) 2 years ago. The dabigatran level was 523 ng/mL and he received 5 g of idarucizumab. The level dropped to <40 ng/mL on repeat blood sample.

Clinically, he had dense hemiparesis on the right upper and lower limb, speech disturbance, and right homonymous hemianopia; however, his Glasgow Coma Scale score (GCS) was 13. Subsequent CT scans of the brain on day 1 and 4 showed stable appearance of hemorrhage.

Further CT scans on day 8 and 18 were performed due to fluctuating level of consciousness (LOC), and they showed similar stable intraparenchymal hemorrhage with surrounding vasogenic edema; there was no radiologic evidence of obstructive hydrocephalus and no other abnormalities were reported. The patient was later found to have recurrent aspiration pneumonia; therefore it was thought that the fluctuating LOC was secondary to a combination of chest infection and from the thalamic hemorrhage.

Due to progressive worsening of the patient's LOC, MRI scan of the brain and a subsequent CT venogram were performed on day 34, and they showed extensive venous sinus thrombosis involving superior sagittal, right sigmoid, and transverse sinuses, extending inferiorly into the proximal internal jugular vein (figures 1 and 2). A left upper limb Doppler ultrasound performed on the same day over a tender IV cannulation site revealed acute thrombus involving cephalic and basilic veins extending into median cubital vein.

Therapeutic heparin infusion was commenced; 4 days later, the patient had considerable drop in hemoglobin secondary to melaena. Gastroscopy revealed severe esophagitis. Heparin infusion was recommenced postgastroscopy and was later switched to enoxaparin. Doppler ultrasound was performed 10 days later due to edematous right lower limb and revealed DVT involving the superficial femoral vein, popliteal vein, and posterior tibial veins. A previous Doppler study performed early in his admission, prior to the commencement of anticoagulation, was normal. Enoxaparin was eventually bridged to warfarin for long-term anticoagulation.

Although there has been no meaningful functional recovery almost 3 months after the intracranial hemorrhage, and the patient is now looking into nursing home placement, he is awake, alert, and able to have some level of communication with his family members.

PRACTICAL IMPLICATIONS

Idarucizumab can lead to acute thrombosis in a patient with an underlying procoagulant state.

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Figure 1 MRI brain shows intraparenchymal hemorrhage and cerebral venous sinus thrombosis

Discussion

Idarucizumab, being the first approved direct oral anticoagulant (DOAC) reversal agent, is increasingly being used to reverse dabigatran in the acute setting. The potent and rapid reversal of anticoagulation could put patients at risk of acute thrombosis. The concurrent intracranial bleed and cerebral venous sinus thrombosis highlights the challenge of anticoagulation in this case study.

In our case, the management of cerebral venous sinus thrombosis with anticoagulation was complicated by acute gastrointestinal bleeding. The patient also developed in-hospital left arm and right lower limb venous thrombosis, which were possibly related to an underlying procoagulant state. A thrombophilia screen was not performed in the setting of anticoagulation. There was no history at any point to suggest an underlying malignancy and there was no known family history of hypercoagulable state. There was no record of thrombophilia screen being performed at the time of initial diagnosis of DVT 2 years ago.

Idarucizumab has been shown to have no procoagulant activity in animal studies and human volunteers.^{1,2} The REVERSE-AD study of 503 patients on dabigatran reported rates of thrombotic events postidarucizumab as similar to the rates after major procedures or hospitalization for uncontrolled bleeding.³ However, in patients with underlying thrombophilia in addition to hospitalization factors, rate of thromboses may be higher. While thrombotic events were reported in the REVERSE-AD study, we are not aware of any previous reports of cerebral venous sinus thrombosis postidarucizumab.

As newer DOAC reversal agents become available, neurologists should be aware of the potential risk of cerebral venous sinus thrombosis, especially when recovery is not occurring as expected, or clinical deterioration occurs.

Author contributions

C.S. Phua: drafting/revising manuscript, acquisition of information. A. Bonura: acquisition and interpretation of data,

Figure 2 CT brain and CT venogram show intraparenchymal hemorrhage and cerebral venous sinus thrombosis

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