Continuous Tissue Plasminogen Activator Infusion Using a Minimally Invasive Irrigating Catheter for the Treatment of Intraparenchymal Hemorrhage Within the Basal Ganglia: Case Reports

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BACKGROUND AND IMPORTANCE: Intraparenchymal hemorrhage (IPH) is a debilitating and highly morbid type of stroke with limited effective treatment modalities. Minimally invasive evacuation with tissue plasminogen activator (rt-PA) has demonstrated promise for mortality/functional improvements with adequate clot volume reduction. In this study, we report 2 cases of continuous rt-PA infusion using a closed circuit, dual lumen catheter, and irrigation system (IRRAflow) for IPH treatment.

CLINICAL PRESENTATION: A 55-year-old man was admitted for acute onset left hemiparesis; he was found to have right basal ganglia IPH. He was treated with continuous rt-PA irrigation using the IRRAflow device, at a rate of 30 mL/h for 119 hours, with a total volume reduction of 87.8 mL and post-treatment volume of 1.2 mL. At 3-month follow-up, he exhibited a modified Rankin score of 4 and improved hemiparesis. A 39-year-old woman was admitted for acute onset left facial droop, left hemianopsia, and left hemiparesis; she was diagnosed with a right basal ganglia IPH. She was treated with drainage and continuous rt-PA irrigation at 30 mL/h for 24 hours, with a total hematoma volume reduction of 41 mL and with a final post-treatment volume of 9.1 mL. At 3-month follow-up, she exhibited a modified Rankin score of 3 with some improvement in left hemiparesis.

CONCLUSION: Continuous rt-PA infusion using a minimally invasive catheter with saline irrigation was feasible and resulted in successful volume reduction in 2 patients with IPH. This technique is similar to the Minimally Invasive Surgery Plus rt-PA for Intracerebral Hemorrhage Evacuation (MISTIE) approach but offers the potential advantages of less breaks in the sterile circuit, continuous intracranial pressure monitoring, and may provide more efficient clot lysis compared with intermittent bolusing.

KEY WORDS: IPH, rt-PA, Minimally invasive techniques, Case reports, Intracerebral hemorrhage

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Intraparenchymal hemorrhage (IPH) is associated with substantial morbidity/mortality and is the most debilitating type of stroke.[1] A recent trial examined the impact of thrombolytic irrigation using a minimally invasive catheter for the treatment of IPH, concluding no improvements in functional outcomes when compared with medical management, although there was a mortality benefit.[2] A secondary analysis demonstrated functional benefits if the target of <15 cc of residual hematoma was met.[3-5] Patients with <15 cc's had a higher likelihood of achieving a modified Rankin score of 0 to 3, although meeting this threshold was dependent on initial IPH size, the amount of alteplase given, and issues with catheter manipulation.[4,6] Multiple devices/approaches have been used for minimally invasive evacuation, including endoscopic evacuation, stereotactic puncture, and direct exoscopic port-based aspiration.[7-9] However, functional outcomes in patients who survive IPH remain low after surgical management; therefore, effective IPH treatments should be investigated.[1] We present our initial 2 cases of IPH successfully managed with continuous rt-PA infusion using a minimally invasive catheter, the

ABBREVIATIONS: HD, hospital day; **IPH,** intraparenchymal hemorrhage; **rt-PA,** recombinant tissue plasminogen activator.

IRRA flow device (IRRAS USA; Figure 1). This treatment provided significant reduction in IPH size and improvements in functional outcomes at follow-up visits.

CLINICAL PRESENTATION

A 55-year-old man with hypertension, alcohol, and tobacco-use disorder, admitted with dysarthria, left-sided facial droop, and hemiplegia. Computed tomography (CT) showed a right basal ganglia IPH of 89.2 mL. Figure 2 depicts IPH progression using CT. On hospital day (HD) 2, he required intubation because of decreased level of consciousness, and after informed consent, he underwent right parietal burr-hole craniotomy as he exhibited a Minimally Invasive Surgery Plus rt-PA for Intracerebral Hemorrhage Evacuation (MISTIE) type B clot.[6] The distal tip of the catheter resided in the anterior half of the clot, and intraoperative aspiration was attempted, but minimal clot was aspirated. After placement and confirmation by CT, a continuous solution of rt-PA comprising alteplase and normal saline at a concentration of 0.01 mg/mL (2 mg rt-PA; 200 cc normal saline), was begun irrigating 30 mL/h. This delivered 2.4 mg in 8 hours, which approximated the MISTIE trial approach of 2 mg rt-PA infused every 8 hours.[2] Daily CT scans were obtained throughout the treatment course. rt-PA irrigation was continued until fifth day of treatment (DT), when <15 cc IPH volume as set by the MISTIE trial was achieved.[2] He transitioned to saline irrigation alone at 20 mL/h for 24 h, as per MISTIE protocol to reduce the risk of rt-PA–related hemorrhage.[2] The catheter was removed sixth DT with a final post-treatment volume of 1.2 mL. He was discharged HD20, with mild dysarthria, improved left facial droop, and unchanged left upper extremity/left lower extremity (LUE/LLE) strength. At two-month follow-up, his m-RS score was 4, with significant improvements in LUE/LLE strength (3/5).

A 39-year-old woman with obstructive sleep apnea was admitted for left facial droop, hemianopsia, and decreased LUE/LLE strength (2/5). CT showed a right basal ganglia IPH of 50.2 mL. Figure 3 depicts IPH progression using CT. Because of her young age and large volume of hematoma with impending deterioration, earlier treatment was ensued. After discussion and informed consent, she underwent right frontal burr-hole HD2 as she exhibited a MISTIE type A IPH,[6] intraoperative aspiration removed 2 to 3 mL of blood. After catheter placement and confirmation by CT, a continuous rt-PA solution in the aforementioned concentration, irrigating at 30 mL/h, was begun. rt-PA infusion was discontinued third-DT, after reaching <15 cc and transitioned to saline for 24 h. The catheter was removed fourth-DT with a post-treatment volume of 9.1 mL. She was discharged HD10, with left hemianopsia, left facial weakness, and decreased LUE/LLE strength of 1/5. At 3-month follow-up, she was ambulatory using a wheelchair, with an mRS score of 3, improved facial, and LUE/LLE weakness. Institutional Review Board approval was covered under a prospective registry of patients being treated with the IRRAflow system (UNM-HRPO 21-051). These cases have been reported in line with the CARE checklist.[10]

DISCUSSION

Strengths and Limitations

The approach used delivered similar rt-PA volumes used in the MISTIE approach, but with several advantages. First, sterility was maintained once the circuit was connected, and our patients did not experience any secondary infections. The MISTIE trial reported a 1% brain bacterial infection rate[2]; however, a similar trial (CLEAR III), which used an external ventricular drain and alteplase, rates of ventriculitis reached 7%.[11] Second, continuous ICP monitoring prevents irrigation if the ICP is elevated. Finally, continuous rt-PA exposure to the clot may be more beneficial than 8-hour boluses as the target hematoma volume was reached in both

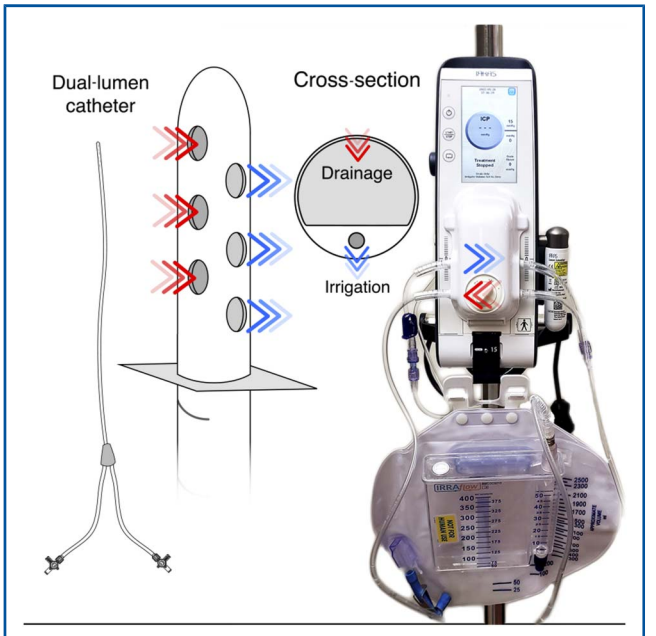

FIGURE 1. *The IRRAflow device (IRRAS USA). IRRAflow measures ICPs between infusions with ICP thresholds for irrigation and drainage set by the user. The irrigation and drainage system are self-contained; the user sets inputs for treat above as well as high/low intracranial pressure alarms, which limit irrigation. In addition, the siphoning effect is determined by an external bag like an external ventricular drain that can be adjusted. Irrigation amounts including volume and frequency can be adjusted, with ICP measurements performed between each irrigation cycle to prevent over-irrigation or over-drainage. In our cases, ICP values were found to be less relevant/accurate when compared with IVH cases and allowed for irrigation over a wider range of ICP values compared with standard IVH. ICP, intracranial pressure; IVH, intraventricular hemorrhage.*

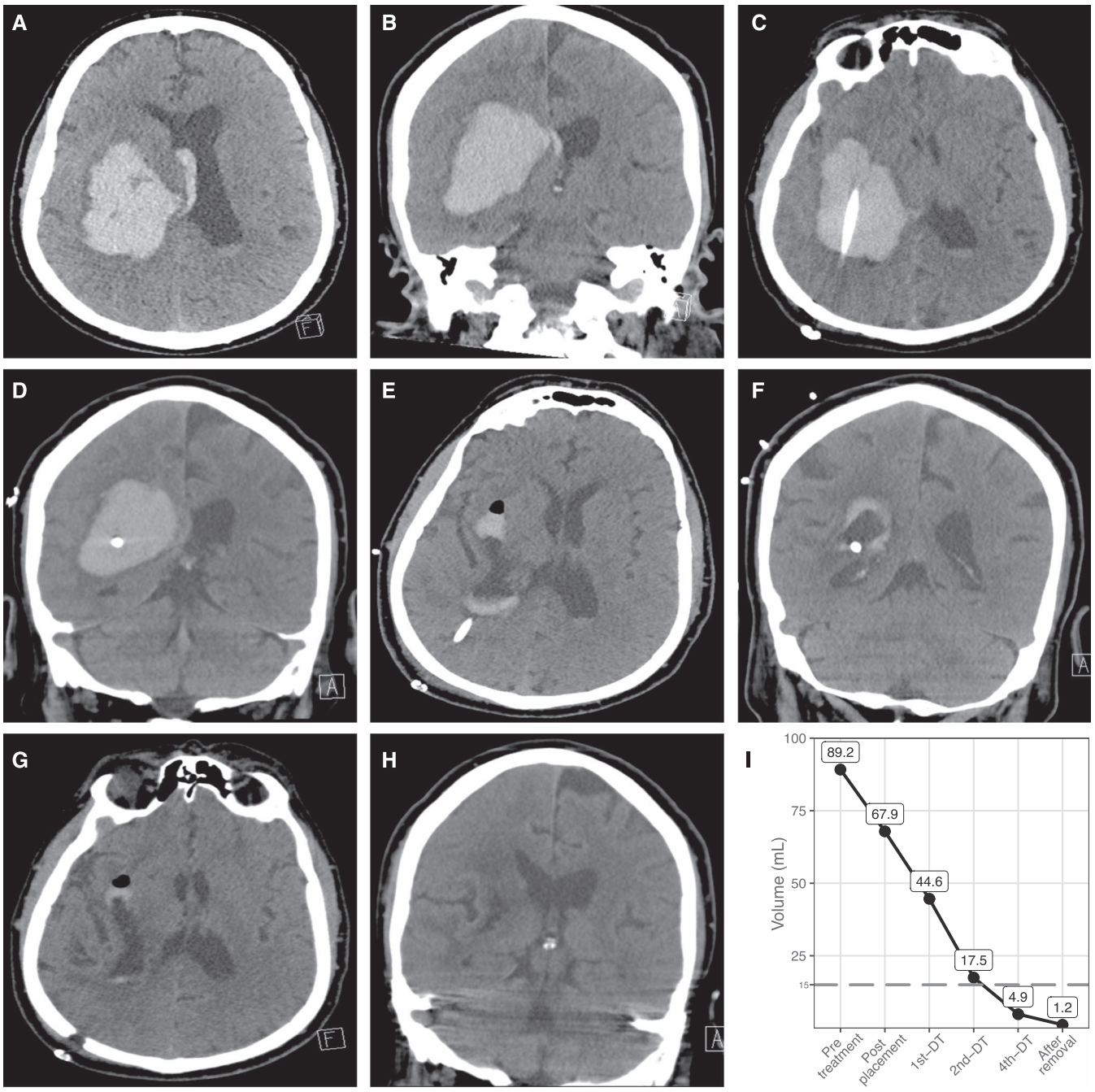

FIGURE 2. **A-I**, *Axial and coronal computed tomography scans represent IPH progression for Case 1.* **A** *and* **B**, *Pretreatment IPH measuring 89.2 mL (100%), with subsequent catheter placement on* **C** *and* **D**, *with a reduction in volume to 67.89 mL (76%).* **E** *and* **F**, *IPH on fourth-DT with a volume of 5 mL (5%).* **G** *and* **H**, *IPH after removal of the catheter at the end of treatment, measuring 1.2 mL (1.4%).* **I**, *Line plot shows the decrease in volume throughout the course of the intervention. Labels show volume at each time point, and the dotted line represents the 15 cc threshold used in the MISTIE trial as surgical target for hematoma volume. IPH, intraparenchymal hemorrhage.*

of our patients, with only 60% of patients achieving this goal in the MISTIE trial.[2] Similarly, both patients showed improved functional outcomes, with an mRS of 3 and mRS of 4, a value higher those seen in previous studies.[4] We saw significant reductions in IPH volume and improved outcomes, regardless of initial IPH size, age, or medical

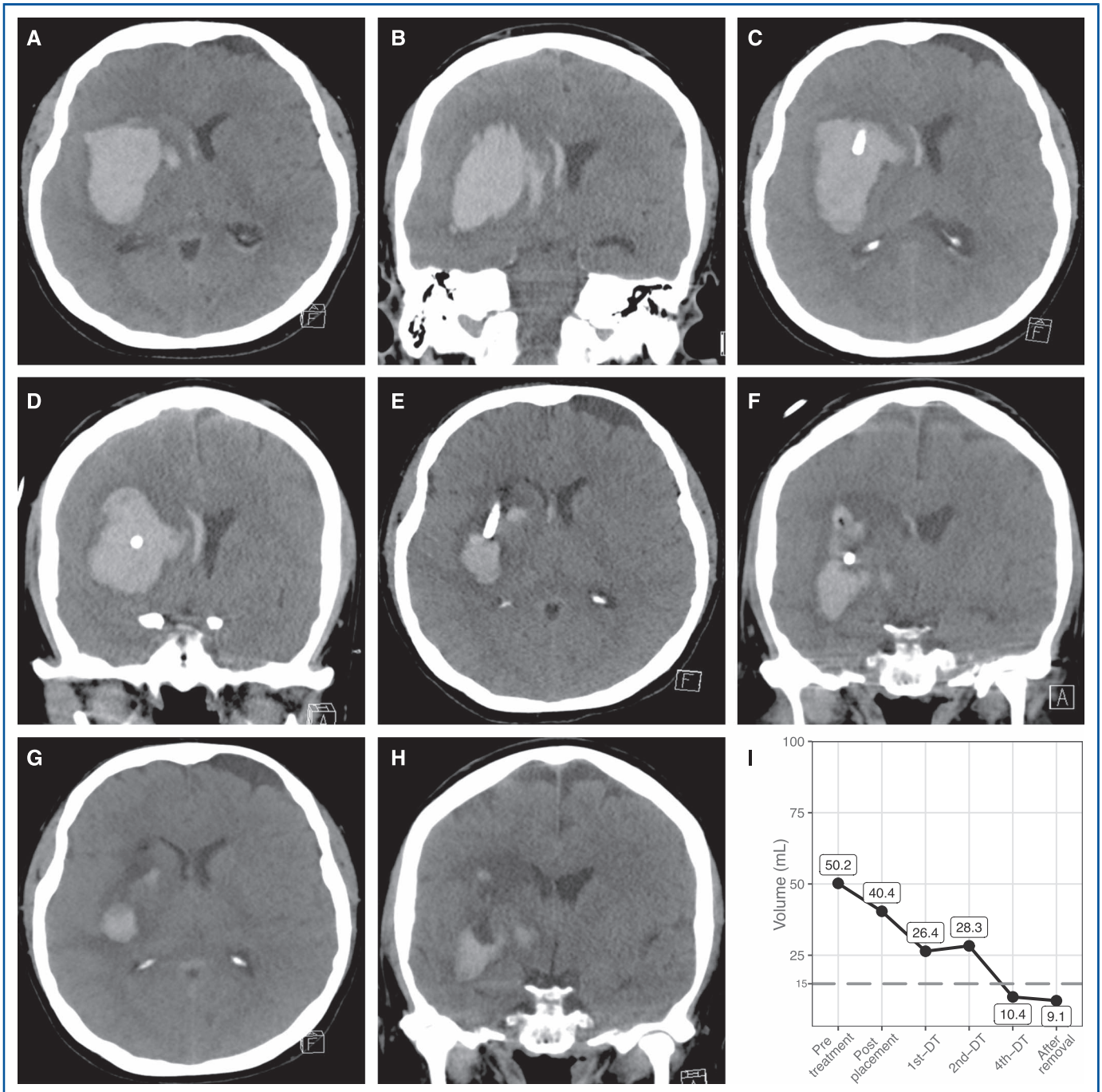

FIGURE 3. **A**-**I**, *Axial and coronal computed tomography scans represent IPH progression for Case 2.* **A** *and* **B**, *Pretreatment IPH measuring 50.2 mL (100%), with subsequent catheter placement on* **C** *and* **D**, *with a reduction in volume to 40.4 mL (81%).* **E** *and* **F**, *IPH on fourth-DT with a volume of 10 mL (21%).* **G** *and* **H**, *IPH after removal of catheter at the end of treatment, measuring 9.1 mL (18%).* **I**, *Line plot shows the decrease in volume throughout the course of the intervention. Labels show volume at each time point and the dotted line represents the 15 cc threshold used in the MISTIE trial as surgical target for hematoma volume. IPH, intraparenchymal hemorrhage.*

comorbidities, suggesting this treatment modality is feasible for all IPH cases. Limitations consist of a single-center study design with a small sample size. Larger series and comparisons are needed to establish the safety and efficacy of our approach. Despite these limitations, these cases present a promising refinement of the thrombolytic approach for IPH.

Relevant Medical Literature and Scientific Rationale

IPH is the most fatal type of stroke, but there is no consensus on when surgical intervention is indicated, with the mainstay of treatment being medical management.[2,12,13] In meta-analyses, minimally invasive approaches have shown potential benefits,[3-5] but this remains to be proven in randomized trials. Hanley et al[2] in a phase III randomized trial (MISTIE) observed a 6% to 8% mortality benefit with rt-PA bolusing; however, no improved functional outcomes were noted when compared with medical management. Patients with a <15 cc IPH size showed functional benefits, with catheter trajectory and placement significantly affecting whether this threshold was reached, arguing for the importance of accurate catheter placement in volume reduction.[4] Awad et al[4] showed <15 cc or >70% evacuation correlated with good functional outcomes, with the chance of having a good outcome increasing by 10% for each additional mL of hematoma removed. Similarly, studies have shown the IPH clot itself causes injury through the hematoma's direct compressive effects and secondary hemoglobin/coagulation product breakdown causing further inflammation and tissue deterioration, further supporting reductions in IPH volume.[14,15]

CONCLUSION

We achieved successful clot reduction in 2 cases of IPH using minimally invasive continuous thrombolytic irrigation. This approach may offer a refinement to the MISTIE approach with several theoretical advantages.

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