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Subdural Catheter Injection of Tissue Plasminogen Activator for Residual Hematoma Post Drainage of Acute-On-Chronic Subdural Hematoma: A Novel Case Report of Two Patients

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Title: Subdural Catheter Injection of Tissue Plasminogen Activator for Residual Hematoma Post Drainage of Acute-On-Chronic Subdural Hematoma: A Novel Case Report of Two Patients

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Keywords: Acute Subdural Hematoma; Chronic Subdural Hematoma; Catheter Injection; Recombinant Tissue Plasminogen Activator; tPA; Thrombolytic Therapy

Short Title: Subdural tPA for Residual SDH Post-Drainage

## Abstract

Background: Residual hematoma following operative management of acute subdural hematoma contributes to reoperation and is cited as a reason for deferment of less invasive drainage strategies. Although local antithrombolytic therapy has been studied in intracerebral hemorrhage and chronic subdural hematoma, to date there are no reports of recombinant tissue plasminogen activator for residual hematoma post drainage for acute subdural hematoma.

Clinical Presentation: Two patients presented with altered mental status secondary to acute-on-chronic subdural hematomas and underwent emergent craniotomies. The first, a 78-year-old man, had poor subdural drain output and deteriorated with seizures and evidence of a new acute subdural hematoma formation. Recombinant tissue plasminogen activator was injected through the subdural catheter on postoperative day three. The second patient, a 64-year old male, received recombinant tissue plasminogen activator postoperatively. Subsequently, both experienced good subdural drainage, clinical and radiological improvement and successful discharge to a skilled nursing facility.

Conclusions: Subdural thrombolytic therapy has can improve hematoma evacuation. A potential implication of this is facilitation of minimally invasive options such as twist-drill craniotomy, previously deferred due to inadequate evacuation. However, there is a paucity of evidence and more research is needed to substantiate the safety and efficacy, refine this technique and guide patient selection.

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22 needed to substantiate the safety and efficacy, refine this technique and guide patient selection.

## 23 Background

24 The relevance of acute subdural hematoma (aSDH), with a mortality rate of 52-57% and comprising up  
25 to 30% of severe head injuries, is ever increasing due to an ageing population that remains active with  
26 increasing comorbidities and anticoagulant use.<sup>11,14,18,19</sup> Despite aggressive management, reoperation rates  
27 remain high principally due to recurrence or residual hematoma.<sup>4,6</sup>

28 The use of subdural injection of thrombolytic agents in chronic SDH (cSDH) has been reported to  
29 successfully improve drainage in patients after inadequate evacuation of hematoma.<sup>3,7,8</sup> However, this has  
30 only been reported in one study in the context of aSDH in which three patients underwent subdural  
31 urokinase injection following inadequate intraoperative evacuation of hematoma.<sup>12</sup>

32 In this paper, we report the first use of subdural recombinant tissue plasminogen activator (tPA) in two  
33 patients with acute-on-chronic SDH (acSDH).

## 34 Case Descriptions

### 35 Case 1

36 A 78-year-old male presented with altered mental status, GCS 4-8, before being sedated and intubated.  
37 On arrival, examination was E1 M1 VT and INR was 2.2 secondary to rivaroxaban. CT showed acSDH of  
38 2.5cm maximal thickness and 1.4cm of midline shift with mass effect. The patient was administered 2070  
39 units of prothrombin complex concentrate and emergently taken to the operating room for right-sided  
40 craniotomy for subdural hematoma evacuation. The dura was tense and upon durotomy, there was  
41 effusion of motor-oil colored subdural clot under pressure, with acute blood evacuated circumferentially  
42 in the subdural space. A subdural drain was placed and the dura was tacked to the bone, reapproximated  
43 and covered with DuraGen. Postoperatively, INR was 1.2 and the patient was started on Keppra.

44 Immediately postoperative CT showed improvement of mass effect and midline shift but with residual  
45 hematoma of maximal thickness of 1.2cm and 0.8cm midline shift. On postoperative day one, the patient  
46 was following commands, E4 M6 VT, subdural catheter drained 4mL. On postoperative days two to  
47 three, the patient experienced seizures and the examination deteriorated at E1 M1 VT, the subdural  
48 catheter drained 6-21mL and CT showed residual hematoma, now with an expanding acute components.  
49 The patient received 0.5mg of tPA through the subdural catheter to promote breakdown of the residual

50 acute subdural. On postoperative day four, the patient's examination improved to E2 M5 VT, subdural  
51 drainage increased to 237mL and CT showed interval evacuation of much of the residual subdural with  
52 maximal thickness 0.5cm and midline shift of 0.1cm. Examination improved to E4 M6 VT and drain  
53 output was 74mL, 142mL and 53mL on postoperative days six to eight before removal on day eight,  
54 extubation on day nine and subcutaneous heparin restarted on day ten, when the patient was discharged in  
55 stable condition to a skilled nursing facility.

## 56 **Case 2**

57 A 64-year-old male presented with altered mental status secondary to a ground-level fall, GCS 13 but  
58 deteriorated and was sedated and intubated. On arrival, examination was E1 M1 VT with 5mm sluggish  
59 pupils. CT showed acute bilateral SDH of 1.9cm on the right and 1.5cm on the left, 1.4cm of mass effect  
60 but no midline shift. The patient was emergently taken to the operating room for bilateral craniotomies.  
61 The dura was tense and the operation proceeded as the first case.

62 Immediately postoperatively the next morning, the patient was following commands, E4 M6 VT. CT  
63 showed improvement of mass effect and midline shift but with residual hematoma of maximal thickness  
64 of 1.2cm on the left and 0.8cm on the right. Due to the large amount of residual hematoma and high  
65 possibility of drain blockage, the decision was made to administer 0.5mg of tPA through bilateral  
66 subdural catheters. On postoperative day two, examination was stable, subdural drainage was 143mL on  
67 the right and 103mL on the left and CT showed continued decrease of subdural hematomas bilaterally, 0.2  
68 on the right and 0.4cm on the left. On postoperative day three, subdural drainage was 34mL on the right  
69 and 50mL on the left and both were removed. The patient was discharged on postoperative day seven to a  
70 skilled nursing facility in stable condition with plan to start subcutaneous heparin on postoperative day  
71 14.

## 72 **Discussion**

73 Although the indications for operative intervention in aSDH are well defined, there is poor consensus on  
74 the optimal management. With little evidence supporting one procedure over another, operative strategy  
75 depends on individual patient factors along with surgeon preference.<sup>1</sup> One important operative  
76 consideration is extent of hematoma evacuation, with residual hematoma leading to cSDH or requiring  
77 reoperation. Reoperation rates of 9.1% after SDH evacuation and 27.9% after aSDH evacuation have

78 been reported with recurrent or residual hematoma comprising the largest proportion of these, at 38% of  
79 reoperations.<sup>4,6</sup> On the other hand, avoidance of residual hematoma must be balanced with other  
80 considerations, including risk from surgery in the context of patient age, comorbidities and antithrombotic  
81 or anticoagulant use. Illustrating this point, a meta-analysis of decompressive craniectomy versus  
82 craniotomy for aSDH demonstrated lower rates of residual hematoma but higher morbidity and mortality  
83 after decompressive craniectomy.<sup>17</sup> This has especially important implications for elderly and/or  
84 comorbid patients, whose candidacy for more invasive strategies may be less appropriate. While twist-  
85 drill craniotomy is often used for cSDH, its use in aSDH has only been reported by one group due to  
86 difficulties in draining an acute clot through a closed drainage system.

87 Huang and colleagues reported outcomes after twist-drill craniotomy for aSDH in a case series of seven  
88 patients (age range 65-81) in which a large craniotomy was deferred due to age, comorbidities or family  
89 refusal.<sup>12</sup> Four patients showed 79-90% hematoma evacuation on postoperative CT, requiring 1-2 days of  
90 drainage. In the remaining three patients, less than 20mL of hematoma was intraoperatively evacuated,  
91 and as per protocol, 5,000-10,000 IU of urokinase in 2mL of saline was injected through a subdural  
92 catheter, clamped for 2-4 hours. These patients subsequently showed a 70-91% hematoma evacuation on  
93 CT and required 2-5 days of drainage. Favorable outcomes with no cases of rehemorrhage or ipsilateral  
94 cSDH were reported at six months. This study provided a successful and intriguing first example of both  
95 twist-drill craniotomy and subdural injection of urokinase to treat aSDH less invasively, thereby limiting  
96 the elevated operative risk of larger craniotomies or craniectomies. Further, minimally-invasive  
97 stereotactic craniotomy in conjunction with thrombolytics have been used for operative clot evacuation in  
98 intracerebral hemorrhage (ICH), with the (Minimally Invasive Surgery Plus Alteplase for Intracerebral  
99 Hemorrhage Evacuation) MISTIE trials substantiating the safety and efficacy for the procedure.<sup>10,15,16</sup>

100 In contrast to urokinase used in the three patients treated by Huang and colleagues, tPA was used in our  
101 patient.<sup>10</sup> tPA offers a theoretical advantage of higher specificity to fibrin compared to urokinase and  
102 some in vitro studies have shown faster rates of thrombolysis compared to urokinase.<sup>2,9</sup> In clinical studies  
103 however, both agents show similar fibrinogenolysis, outcomes and complications, including a  
104 retrospective comparison of tPA versus urokinase for thrombolytic evacuation of spontaneous ICH.<sup>5,13</sup>

105 In our first patient, tPA was administered on postoperative day three. Our decision was not based on  
106 predefined measurements at a single timepoint, rather a dynamic, multifactorial decision based on the

107 patients deteriorating examination, poor subdural drain output and evidence of both residual and acute  
108 component of hematoma on CT imaging. In contrast, tPA was administered to the second patient  
109 immediately postoperatively, the decision based on the large residual on postoperative CT, similar to  
110 Huang and colleagues, who administered thrombolytic therapy immediately postoperatively based on  
111 intraoperative evacuation volume.<sup>10</sup> It was felt that subdural thrombolytic therapy would reduce the risk  
112 of subdural drain blockage from the clot.

113 The advantage of subdural thrombolytic therapy to increase hematoma evacuation following operative  
114 aSDH is minimization of the residual hematoma, which may reduce reoperation rates.<sup>4</sup> This has important  
115 implications for operative strategy: surgeons who may have performed a more invasive procedure for  
116 maximal clot evacuation may opt for a less invasive procedure with the option for thrombolytic therapy to  
117 increase drainage postoperatively with associated lower operative risk.<sup>17</sup> Further, improved hematoma  
118 drainage from thrombolytic therapy may facilitate the consideration of procedures previously deferred  
119 due to inadequate drainage, such as twist-drill craniotomy.<sup>12</sup> Thus, aSDH patients unsuitable for larger  
120 procedures such as craniotomy or decompressive craniectomy, due to comorbidities, medications or  
121 refusal, may benefit from less invasive procedures such as twist-drill craniotomy in combination with  
122 thrombolytic therapy. Local thrombolytics therapy to facilitate less invasive operative strategies has also  
123 been demonstrated in intracranial hemorrhage and to a lesser extent cSDH and is in keeping with a  
124 universal trend of minimally invasive surgery to reduce operative morbidity and mortality.<sup>3,7,8</sup>

125 As the only two patients treated with subdural tPA and among only five treated between with any  
126 subdural antithrombotic therapy for SDH with an acute component, the safety and efficacy of this  
127 technique remains to be proven. Moreover, the impact of a variety of factors is unknown, including  
128 patient factors, dose and timing of injection. Certainly, more research is needed to study outcomes, refine  
129 this technique and guide patient selection.

## 130 Conclusions

131 We report the first two cases of subdural injection of tPA following drainage of acSDH, with subsequent  
132 clinical and radiological improvement and favorable outcome. Subdural thrombolytic therapy has  
133 implications for improving hematoma evacuation and may facilitate the use of minimally invasive options  
134 such as twist-drill craniotomy.



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## 190 Figure Legends

### 191 **Figure 1.** Serial noncontrast CT head imaging of case 1

192 a – preoperative, showing acute-on-chronic SDH of 2.5cm maximal thickness and 1.4cm of  
193 midline shift with mass effect.

194 b – immediately postoperative, pre-tPA, showing improvement of mass effect and midline shift  
195 but with residual hematoma of maximal thickness of 1.2cm and 0.8cm midline shift.

196 c – postoperative day two, pre-tPA, showing residual hematoma, now with expanding acute  
197 components.

198 d – postoperative day six, post-tPA, showing

### 199 **Figure 2.** Serial noncontrast CT head imaging of case 2

200 a – preoperative, showing acute-on-chronic bilateral SDH of 1.9cm on the right and 1.5cm on the  
201 left, 1.4cm of mass effect but no midline shift.

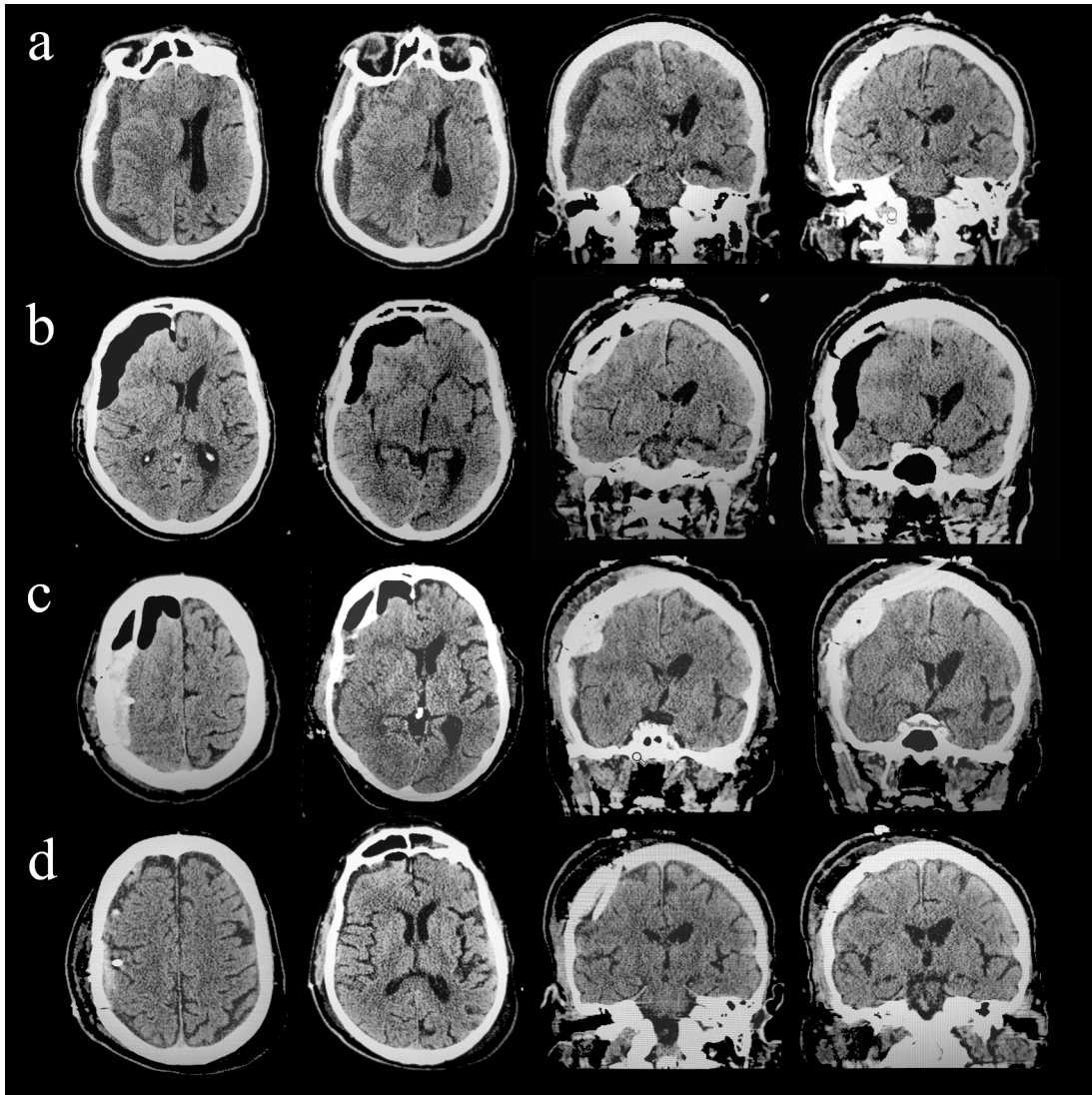
202 b – immediately postoperative, pre-tPA, showing improvement of mass effect and midline shift  
203 but with residual hematoma of maximal thickness of 1.2cm on the left and 0.8cm on the right.

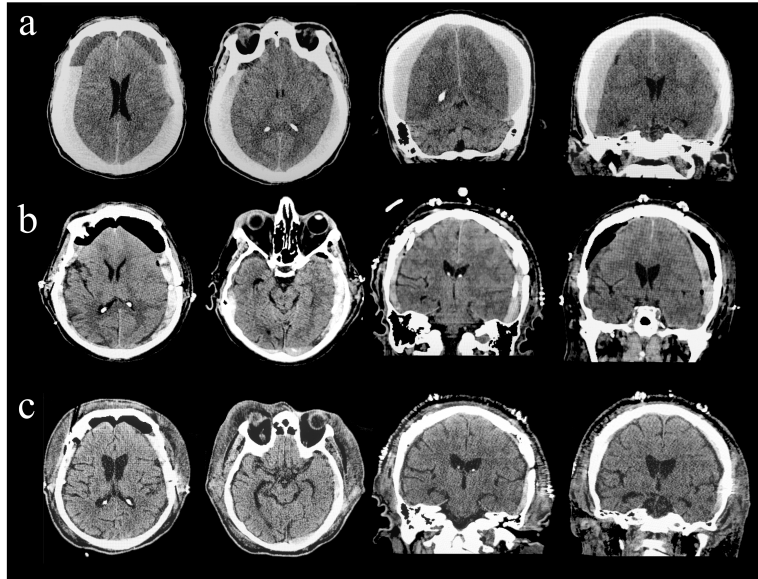
204 c – postoperative day two, post-tPA, showing continued decrease of subdural hematomas  
205 bilaterally, 0.2 on the right and 0.4cm on the left.

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207

208





aSDH acute subdural hematoma

acSDH: acute-on-chronic subdural hematoma

cSDH: chronic subdural hematoma

GCS: Glasgow coma scale

INR: international normalized ratio

tPA: tissue plasminogen activator

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