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## **Emergency splenectomy in immune thrombocytopenia presenting with intracranial hemorrhage**

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**Short title:** Emergency Splenectomy for ITP-associated intracranial hemorrhage

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### **Author contributions**

MAP designed the study and drafted the manuscript. NPA and NK contributed surgical and neurosurgical data. VM supervised the project. All authors contributed to data interpretation and approved the final manuscript.

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De-identified data are available from the corresponding author upon request.

**Conflicts of interest**

The authors declare no competing interests.

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## **Emergency Splenectomy in Immune Thrombocytopenia Presenting with Intracranial Hemorrhage**

### **To the Editor,**

Immune thrombocytopenia (ITP) is an autoimmune condition characterized by isolated thrombocytopenia with no clinically apparent cause. (1) Intracranial hemorrhage (ICH) represents its most catastrophic complication, occurring in approximately 1% of patients (1.8% of adults and 0.4% of children) and carrying a reported mortality of 24–40%. (2–5) Risk factors associated with a higher mortality include intraparenchymal location of hemorrhage, platelet count  $\leq 10 \times 10^9/L$  at ICH, prior bleeding grade, and a low GCS at admission. (6) A rapid rise in platelet count is critical in this setting. While high-dose corticosteroids, intravenous immunoglobulin (IVIG) and platelet transfusions constitute standard management, responses may be delayed or inadequate in patients with evolving neurological compromise. Furthermore, IVIG is an expensive therapy with only a transient effect and is often inaccessible to many patients in low- and middle-income countries (LMICs). Splenectomy is a cost-effective alternative that provides durable remission in chronic ITP by removing the primary site of platelet destruction and autoantibody production. (7) Recent guidelines provide provisional support for an urgent splenectomy made on a case by case basis in patients with a critical bleed, when other interventions have failed to sufficiently improve platelet count. This provisional guidance comes from very limited data. (8). In a previous retrospective analysis of 254 patients with chronic or persistent ITP who underwent splenectomy from our center, response was seen in 90 % patients (CR in 74.4%), with 70 % in remission at a median of 54.3 months (range 1-290). (9) However, the data supporting the role of emergency splenectomy as a salvage intervention in ITP-associated ICH is insufficient.

We retrospectively analyzed patients with ITP who presented with radiologically confirmed ICH and underwent emergency splenectomy at our center between January 2008 and July 2025. Clinical characteristics, radiological features, perioperative management, hematologic responses, and long-term outcomes were evaluated. Overall survival (OS) and event-free survival (EFS) were estimated using the Kaplan–Meier method. Statistical analyses were performed with SPSS. The study was approved by the Institutional Review Board of Christian Medical College, Vellore

Patients were classified as having acute, persistent, or chronic ITP using standard definitions. (10) Complete response (CR) was defined as platelet count  $\geq 100 \times 10^9/L$  without clinically significant bleeding, while response (R) was defined as platelet count

$\geq 30 \times 10^9/L$  with at least a two-fold increase from baseline and no clinically significant bleeding. Relapse was defined as loss of CR or R after one month of sustained response. Patients aged  $\leq 18$  years were considered children. ICH was confirmed by non-contrast CT brain imaging. All patients were evaluated by neurosurgery prior to splenectomy, and when required, neurosurgical procedures were performed simultaneously with or immediately after splenectomy.

During the study period, a total of 172 patients underwent splenectomy for ITP. Of these, 27 (15.6%) patients (25 adults and 2 children aged 7 and 14) presented with intracranial hemorrhage (ICH) and underwent an emergency splenectomy. Median age was 37 years (7–57), with 21 (77.8%) females. 15 (55.5%) patients had chronic ITP, 10 (37.1%) had acute ITP and 2 (7.4%) persistent ITP. Median platelet count at presentation was  $7,000 \times 10^9/L$  (range 1,000–26,000  $\times 10^9/L$ ).

The median duration from symptom onset to admission was 2 (1–14) days. Headache was the most common presentation seen in 20 patients (74.1%), followed by altered sensorium in 7 (25.9%) and focal neurological deficits in 6 (22.2%). The median number of lines of therapy prior to admission with ICH was 2 (range 1–4). Nine patients (33.3%) had documented co-morbidities, including diabetes mellitus in 5 (18.5%; one steroid-induced), hypertension in 2 (7.4%), and hypothyroidism in 4 (14.8%). Neuroimaging demonstrated intraparenchymal bleeds in 15 patients (55.5%), subdural hemorrhage in 10 (37.1%), and subarachnoid hemorrhage in 2 (7.4%) (Figure 1). Radiological findings showed a midline shift in 12 (44.4%), hydrocephalus in 9 (33.3%), and infratentorial bleeds in 5 (18.5%). At admission, 20 patients (74.1%) had a GCS of 13–15, while 3 (11.1%) presented with a poor score of 3–8.

All patients received high-dose dexamethasone and platelet transfusions, while IVIG was administered in only four patients (14.8%), largely because of financial constraints. All 27 patients underwent emergency splenectomy, which was open in 20 (74.1%), laparoscopic in 6 (22.2%), and converted from laparoscopic to open in 1 because of splenic hilar bleeding. Accessory spleens were identified and removed in 3 patients (11.1%). Combined neurosurgical procedures (2 craniotomies and 4 burr hole evacuations) were performed in 6 patients (22.2%).

Two (7.4%) patients who underwent open splenectomy developed early postoperative pneumonia, which settled with antibiotics, chest physiotherapy and incentive spirometry.

None of the patients had significant post-operative bleeding from the surgical site. The median duration of hospitalization was 10 days (range 2–25)

Four patients died due to the progression of ICH. Among the remaining 23 evaluable patients, 18 (78%) achieved complete response (platelet  $\geq 100 \times 10^9/L$  without bleeding), with a median time to platelet recovery of 3 days (range 1–30). Overall, 7 patients had expired during the study period. (Supplementary Table 1) Overall mortality attributable to ICH was 14.8%. One patient died seven days after splenectomy due to diffuse alveolar hemorrhage, despite treatment with TPO agonists. Two patients in remission subsequently died of pneumonia, one at 41 days post-splenectomy and the other 7 years after the splenectomy. At a median follow-up of 34 months, 17 patients remain alive in sustained remission. The 3-year OS and EFS were 77.8% and 61.8%, respectively (Figure 2 and Supplementary Figure 1).

A moderate or severe GCS score ( $\leq 12$ ;  $n=7$ ) at presentation was significantly associated with poorer survival compared to mild GCS score (3-year OS 42.9% vs. 90%;  $p=0.001$ ). (Figure 1). Presence of midline shift ( $n=12$ ) also predicted worse survival (58.3% vs. 93.3%;  $p=0.012$ ). The anatomical location of hemorrhage did not significantly influence outcomes. Relapse occurred in 6 (22.2%) at a median of 4.1 months. All relapsed patients responded to subsequent second-line therapies.

The median age of our cohort (37 years) and female predominance are consistent with the typical epidemiology of ITP. (11) More than half of our patients had chronic ITP, which is in keeping with registry data suggesting that ICH is more frequent in chronic versus newly diagnosed cases. (2,5) The hematologic response rate observed in this emergency setting (75%) is comparable to elective splenectomy outcomes in chronic ITP (70–90%). (9,10) The overall mortality attributable to ICH in this series was 14.8%, which appears lower than the 24 to 40% reported in earlier registry and retrospective data. (3,4,6) This should be interpreted cautiously because patients selected for surgery may have represented a subgroup with relatively favorable neurological status and better outcomes, but the improved outcomes could also be due to rapid time to splenectomy with neurosurgical intervention in all patients for whom it was deemed necessary. All patients who died due to ICH had poor sensorium or focal neurological deficits at presentation, supporting earlier findings that baseline GCS strongly predicts outcome. (6) Of the six patients who underwent simultaneous neurosurgical procedures, 4 survived, implying that lifesaving neurosurgical interventions should not be deferred, provided that neurological prognosis is good.

Relapse after splenectomy was observed in 22.2% of patients, with a median time to relapse of 4.1 months, consistent with other series where relapse generally occurs in the first 24 months.<sup>(12)</sup> These figures are slightly higher than relapse rates in elective splenectomy series (10–15%), possibly reflecting the aggressive disease biology in patients presenting with life-threatening bleeding. Nonetheless, all relapsed patients in our cohort responded to second-line therapies, highlighting that splenectomy does not impact subsequent responsiveness to medical treatment.

Although IVIG combined with corticosteroids remains the standard first-line treatment for ITP-associated intracranial hemorrhage, only four patients in our cohort received IVIG, primarily because of financial constraints and limited availability rather than a preference for splenectomy. In our setting, the cost of IVIG exceeds that of splenectomy by more than two-fold, and the platelet response achieved with IVIG is often transient, whereas splenectomy may provide a more sustained response thereby being a more cost-effective treatment approach. However potential short- and long-term risks of splenectomy, including perioperative bleeding, thromboembolic complications, overwhelming post-splenectomy sepsis and pulmonary hypertension, should be balanced against its life-saving benefit in patients with ITP-associated intracranial hemorrhage. <sup>(13)</sup>

This study has limitations inherent to its retrospective design and modest sample size. There is an inherent bias, as sicker patients may have been excluded from surgical intervention. Our cohort included a mix of acute, persistent, and chronic ITP, which may influence long-term outcomes differently. Data on quality of life and neurological prognosis is not available. Nevertheless, the strengths lie in the comprehensive long-term follow-up, standardized perioperative protocols, and integration of hematology, surgery, and neurosurgical teams.

In conclusion, emergency splenectomy can be considered a life-saving salvage option in patients with ITP presenting with ICH. Splenectomy is safe and provides rapid hematological recovery in most patients and contributes to durable long-term remission in a substantial proportion of them. A splenectomy remains a cost-effective and practical therapeutic strategy for patients with ITP and presenting with an ICH.

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**Table 1.** Baseline clinical characteristics, radiological features, management, and outcomes of patients undergoing splenectomy for immune thrombocytopenia with intracranial hemorrhage.

|                                                | <b>Total n=, n (%)/ Median (Range)/<br/>Mean <math>\pm</math> SD</b> |
|------------------------------------------------|----------------------------------------------------------------------|
| Median Age (years)                             | 37 (7-57)                                                            |
| Female Sex                                     | 21(77.8%)                                                            |
| Duration of Symptoms prior to admission (days) | 2 (1-10)                                                             |
| Type of ITP                                    |                                                                      |
| Acute                                          | 10 (37.1%)                                                           |
| Persistent                                     | 2 (7.4%)                                                             |
| Chronic                                        | 15 (55.5%)                                                           |
| Duration from admission to splenectomy(days)   | 2 (1-14)                                                             |
| No of prior lines of therapy                   | 2 (1-4)                                                              |
| IVIg prior to splenectomy                      | 4 (14.8%)                                                            |
| TPO Agonists                                   | 3 (11.1%)                                                            |
| Hemoglobin (g/dl)                              | 9.1(4.5-14)                                                          |
| Platelet count (x 10 <sup>9</sup> /L)          | 7000(1000- 26,000)                                                   |
| Glasgow Coma Scale at admission                |                                                                      |
| 13-15 (Mild)                                   | 20 (74.1%)                                                           |
| 9-12 (Moderate)                                | 4 (14.8%)                                                            |
| 3-8 (Severe)                                   | 3 (11.1%)                                                            |
| Location of Bleed                              |                                                                      |
| Intraparenchymal                               | 15 (55.5%)                                                           |
| SAH                                            | 2 (7.4%)                                                             |
| SDH                                            | 10 (37.1%)                                                           |
| Midline Shift                                  | 12(44.4%)                                                            |
| Hydrocephalus                                  | 9 (33.3%)                                                            |
| Posterior fossa hemorrhage                     | 5 (18.5%)                                                            |
| Type of Splenectomy                            |                                                                      |
| Open                                           | 20 (74.1%)                                                           |
| Laparoscopic                                   | 6 (22.2%)                                                            |
| Laparoscopic converted to Open                 | 1 (3.7%)                                                             |
| Neurosurgical procedure                        | 6 (22.2%)                                                            |
| Burr Hole                                      | 4 (14.8%)                                                            |

|                                            |               |
|--------------------------------------------|---------------|
| Craniotomy                                 | 2 (7.4%)      |
| Mortality due to ICH                       | 4 (14.8%)     |
| Complete Response to splenectomy<br>(n=24) | 18 (75%)      |
| Duration of admission (days)               | 10 (2-25)     |
| Mortality due to Infection                 | 2 (7.4%)      |
| Relapse                                    | 6 (22.2%)     |
| Time to relapse (months)                   | 4.1(1.4–51.9) |

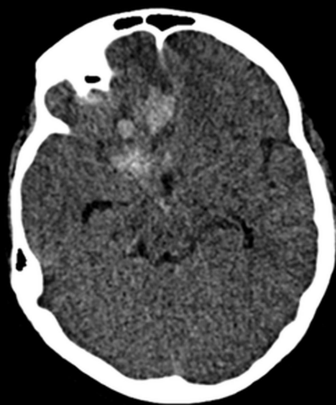
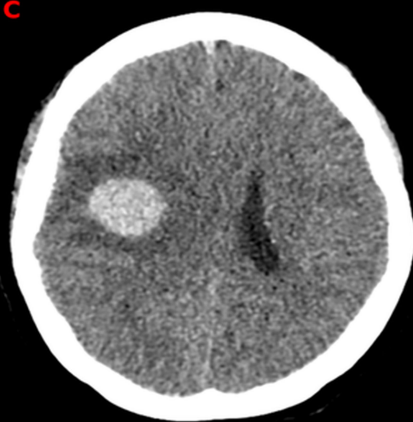
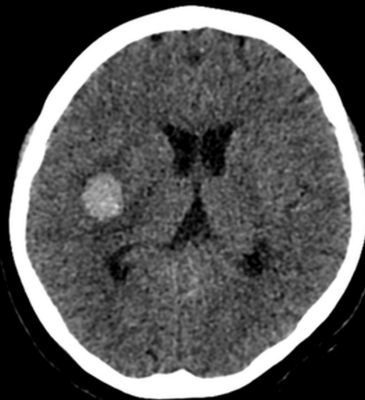
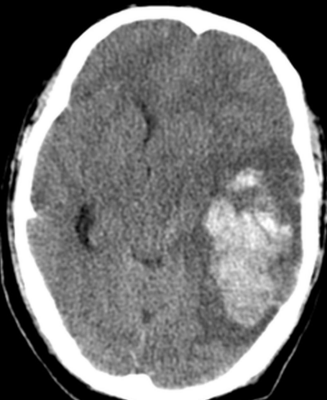
ITP = immune thrombocytopenia; IVIG = intravenous immunoglobulin; TPO agonists = thrombopoietin receptor agonists; Hb = hemoglobin; ICH = intracranial hemorrhage; SAH = subarachnoid hemorrhage; SDH = subdural hemorrhage; GCS = Glasgow Coma Scale;

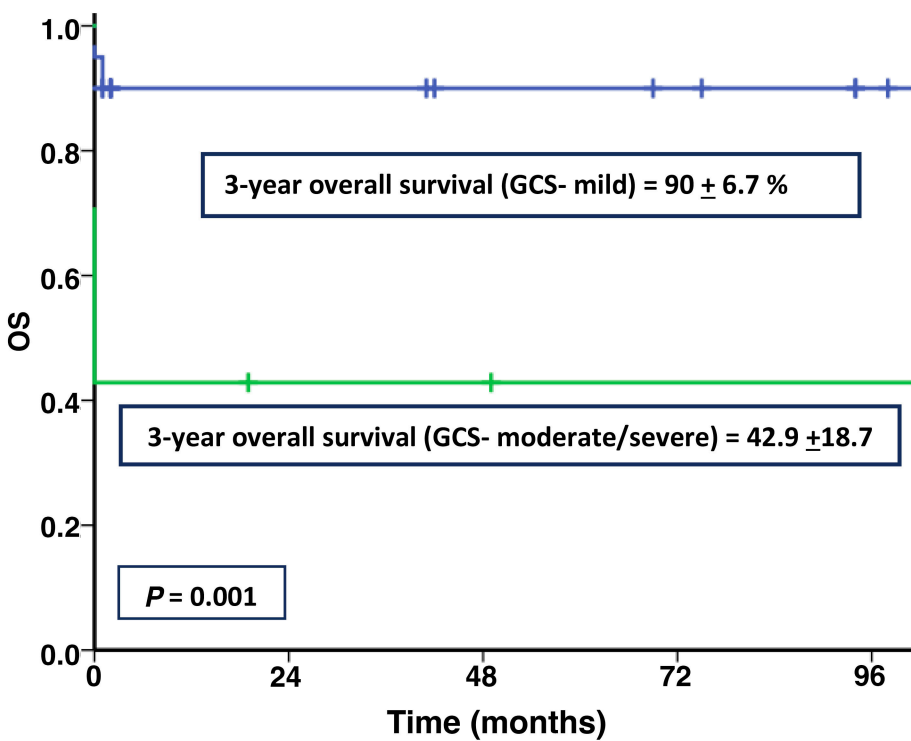
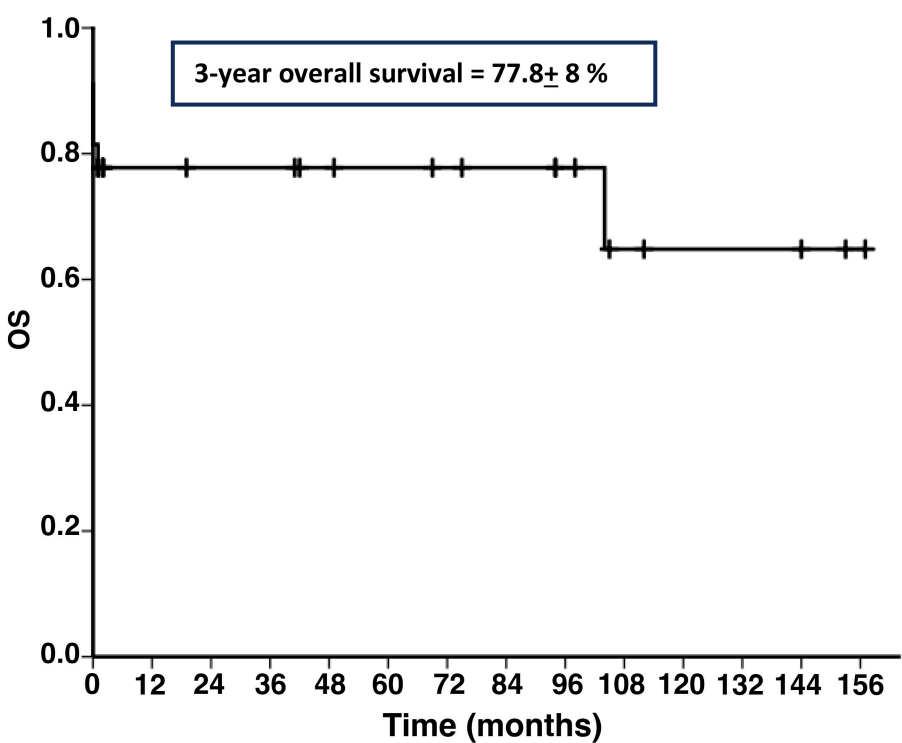
Response to splenectomy defined as achievement of platelet count  $\geq 30 \times 10^9/L$  with at least a two-fold increase from baseline and absence of bleeding; Mortality due to ICH and infection refer to deaths directly attributable to these causes during the index admission or follow-up.

**Figure 1. Representative non-contrast CT brain images showing the spectrum of hemorrhage patterns in ITP-associated intracerebral hemorrhage.**

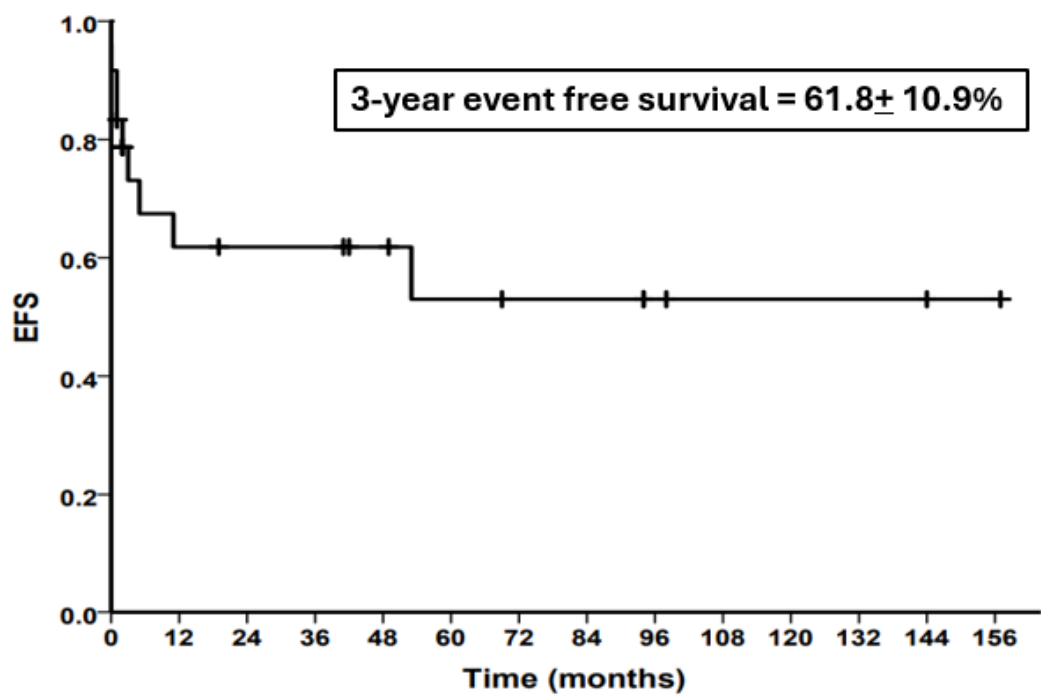
(A) Acute left cerebellar intraparenchymal hemorrhage with fourth ventricular effacement, without tonsillar herniation, in a 30-year-old woman; managed with open splenectomy and right salpingo-oophorectomy in view a tubo-ovarian mass with torsion; survived. (B) Acute right basifrontal intraparenchymal hemorrhage with mild mass effect and 3 mm midline shift in a 14-year-old boy; managed with open splenectomy; survived. (C) Multifocal right frontal and parietal intraparenchymal hemorrhages with edema and midline shift in a 45-year-old woman; managed with laparoscopic splenectomy; survived. (D) Multiple cerebral and cerebellar intraparenchymal hemorrhages with hydrocephalus and tonsillar herniation in a 25-year-old woman; underwent suboccipital craniectomy, C1 laminectomy, hematoma evacuation, and open splenectomy; expired on postoperative day 1. (E) Large left temporo-parieto-frontal intraparenchymal hematoma with significant mass effect and herniation in a 40-year-old man; underwent open splenectomy; expired on postoperative day 1. (F) Right temporoparietal intraparenchymal hematoma in a 33-year-old man treated with craniotomy and hematoma evacuation along with an open splenectomy; survived.

**Figure 2. Kaplan–Meier estimates of overall survival (OS) for the entire cohort and stratified by Glasgow Coma Scale (GCS) at diagnosis.**

**A****B****C****D****E****F**



**Supplementary Figure 1.** Kaplan–Meier estimate of event-free survival (EFS) for the study cohort. Event-free survival (EFS) was defined as the time from diagnosis to the occurrence of any of the following events: failure to achieve response, relapse after an initial response or death from any cause. Patients who did not experience an event were censored at the time of last follow-up



**Supplementary Table 1:** Clinical characteristics and radiological findings of patients who expired during the study period

|    | Age | Sex | Type of ITP | Admission to splenectomy (days) | Characteristics of bleed                                          | GCS on admission | Midline shift | Response to splenectomy | Cause of death                                               |
|----|-----|-----|-------------|---------------------------------|-------------------------------------------------------------------|------------------|---------------|-------------------------|--------------------------------------------------------------|
| 1. | 30  | F   | Acute       | 1                               | Acute intraparenchymal hemorrhage                                 | 11               | Yes           | NA                      | Expired on post op day 2 due to CNS Bleed                    |
| 2. | 50  | F   | Chronic     | 4                               | Acute on chronic SDH, right frontal intra parenchymal Haemorrhage | 15               | Yes           | Yes                     | Expired on post op day 41 due to an interstitial pneumonia   |
| 3. | 22  | F   | Chronic     | 1                               | Acute intraparenchymal hemorrhage with SAH                        | 12               | Yes           | NA                      | Expired post op day 1 due to CNS Bleed                       |
| 4. | 54  | F   | Chronic     |                                 | Acute SDH                                                         | 8                | Yes           | Yes                     | Expired 8 years post op due to Listeria Sepsis and Pneumonia |
| 5. | 42  | F   | Chronic     | 5                               | Acute intraparenchymal hemorrhage with SAH                        | 15               | No            | NA                      | Expired on post op day 8 due to DAH                          |
| 6. | 34  | F   | Acute       | 1                               | Acute intraparenchymal hemorrhage                                 | 12               | Yes           | Yes                     | Expired post op day 1 due to CNS Bleed                       |
| 7. | 25  | M   | Acute       | 1                               | Acute intraparenchymal hemorrhage                                 | 8                | No            | NA                      | Expired post op day 1 due to CNS Bleed                       |

Abbreviations: ITP – immune thrombocytopenia; GCS – Glasgow Coma Scale; SDH – subdural hematoma; SAH – subarachnoid hemorrhage; CNS – central nervous system; NA – not applicable.