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Endovascular treatment of cerebral venous sinus thrombosis and insights into intracranial coagulopathy

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Introduction:

Cerebral venous sinus thrombosis (CVST) is important to recognize as its presentation is variable and life-threatening^{1,2}. We describe a case of anticoagulation-refractory CVST and the use of endovascular therapy in treating and identifying coagulopathy differences between intracranial and peripheral blood samples.

Case report:

A 35-year-old G0P0 woman presented with 1-week of headaches and vision changes. Initial exam revealed papilledema but was otherwise unremarkable. Brain MRI/V demonstrated CVST without hemorrhage. Coagulation studies were normal with the exception of thrombocytosis ($600 \times 10^3/\text{uL}$). Hypercoagulability evaluation was sent and intravenous-heparin was started. Despite therapeutic anticoagulation levels, the patient became obtunded, had worsening edema on head CT (Fig-1A), and endovascular treatment was offered.

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Cerebral angiography demonstrated extensive CVST (Fig-1B) with minimal improvement after balloon angioplasty and suction thrombectomy prompting microcatheter-based continuous-tPA (0.5mg/h) through 2 separate microcatheters (superior sagittal and confluence sinus) and intravenous-heparin. Forty-hours of intracranial-tPA was required for radiographic resolution of CVST (Fig-1C). Intravenous-heparin was continued. One-hour after tPA cessation, intracranial blood (3mL) was collected from each microcatheter after wasting 1mL. Simultaneous peripheral antecubital venous samples were collected and all underwent coagulation testing using Rotational Thromboelastometry (ROTEM: Instrumentation Laboratory, MA). Both intracranial samples revealed ongoing fibrinolysis not seen peripherally (maximum-lysis 100% vs 0%). All samples revealed heparin anticoagulation-effect seen with prolonged intrinsic pathway (INTEM) coagulation-time (CT). However, faster INTEM-CTs were seen in both intracranial samples compared to the peripheral sample (345s vs 380s) (Fig-1D/E).

After microcatheter removal, the patient was extubated and had full recovery. Hypercoagulability evaluation later revealed JAK2 mutation consistent with essential thrombocytosis and the patient was transitioned to aspirin and apixiban treatment.

Discussion:

Endovascular treatments have been described for CVST³, however identifying coagulopathy differences between intracranial and peripheral blood using ROTEM was novel and may have provided insight for this patient's medical-treatment failure. Traditionally utilized plasma-based coagulation tests used for therapeutic heparin monitoring assess kinetics for initial fibrin formation through coagulation factors only. Unlike plasma-based tests, ROTEM is a whole-blood assessment of functional coagulation and assesses contribution of platelets, fibrinogen, coagulation factors and erythrocytes to the 3 phases of hemostasis: coagulation-time, clot-strength and fibrinolysis. The utility of whole blood viscoelastic hemostatic assays have been described in intracerebral hemorrhage⁴ and trauma⁵.

After tPA cessation, ROTEM identified continued intracranial fibrinolysis not seen peripherally potentially due to delayed drug wash-out while confirming that intracranial-tPA did not circulate systemically. ROTEM also revealed different coagulation kinetics between intracranial and peripheral samples. Faster INTEM-CTs were seen intracranially with these differences being larger than the test's reference range standard deviations⁶.

Though speculative, it is possible that our findings reflected lower intracranial anticoagulation levels compared to peripheral levels providing an explanation for anticoagulation-failure. Because traditional plasma-based testing to monitor anticoagulation levels (partial thromboplastin time) do not assess platelet contribution to coagulation, it is also plausible that our patients thrombocytosis prevented accurate anticoagulation level monitoring compared to ROTEM. Further investigation is warranted to evaluate if more tailored approaches are necessary to avoid under- and over-treating patients based on peripheral blood tests.

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Figure-1:

Medically refractory CVST

Abbreviations: CVST: cerebral venous sinus thrombosis; EXTEM: extrinsic-pathway;

INTEM: intrinsic-pathway; FIBTEM: fibrinogen-assay; CT: coagulation-time; MCF:

maximal-clot-firmness; ML: maximum-lysis

(A) CVST with edema but no hemorrhage on CT. (B) Angiography revealed extensive CVST with particular burden over superior sagittal and inferior sinus (red arrows) with radiographic resolution on CT-venogram after 40-hours of intracranial-microcatheter tPA infusion (C). Intracranial ROTEM sample 1-hour after tPA cessation revealed ongoing intracranial fibrinolysis (D: tapering amplitude on Y-axis; ML: 100%; EXTEM/INTEM-MCF: 57mm and 43mm respectively) not seen peripherally (E: ML0%; EXTEM/INTEM-MCF: 69mm and 65mm respectively). Faster intracranial intrinsic pathway activation coagulation-time was noted (D: arrow; INTEM-CT: 345s) compared to the peripheral sample (E: arrow; INTEM-CT: 380s) suggesting differences in anticoagulation between sites.