Case Report

Endovascular Treatment of Cerebral Venous Sinus Thrombosis and Insights into Intracranial Coagulopathy

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Cerebral venous sinus thrombosis (CVST) requires anticoagulation to promote vessel recanalization. Current anticoagulation paradigms utilize plasma tests from peripheral venous/arterial samples for therapeutic monitoring. We describe a medically-refractory case of CVST in a 35-year-old woman later found to have JAK2 mutation and essential thrombocytosis. Despite therapeutic anticoagulation levels, worsening cerebral edema and progression to coma prompted endovascular treatment. Failed endovascular thrombectomy attempts led to placement of 2 separate indwelling microcatheters for continuous infusion of tissue plasminogen activator (tPA). Forty-hours of continuous-tPA in addition to systemic intravenous-heparin led to complete radiographic and clinical resolution of CVST. Whole blood coagulation testing using Rotational Thromboelastometry (ROTEM) from simultaneous samples taken intracranially (via cerebral microcatheters) and peripherally (via antecubital vein) all revealed prolonged intrinsic pathway activation clotting times consistent with heparin anticoagulation use. However, both intracranial ROTEM samples identified faster clotting times compared to the peripheral sample suggesting lower anticoagulation levels intracranially. Our findings were speculative and hypothesis generating as to whether this explained medical treatment failure. If there are coagulopathy differences at local sites of injury not adequately captured by peripheral blood draws, further investigation is required to identify better approaches to avoid under-treatment of similar cases.

Key Words: Cerebral venous sinus thrombosis—anticoagulation—intracranial coagulopathy—rotational thromboelastometry

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.

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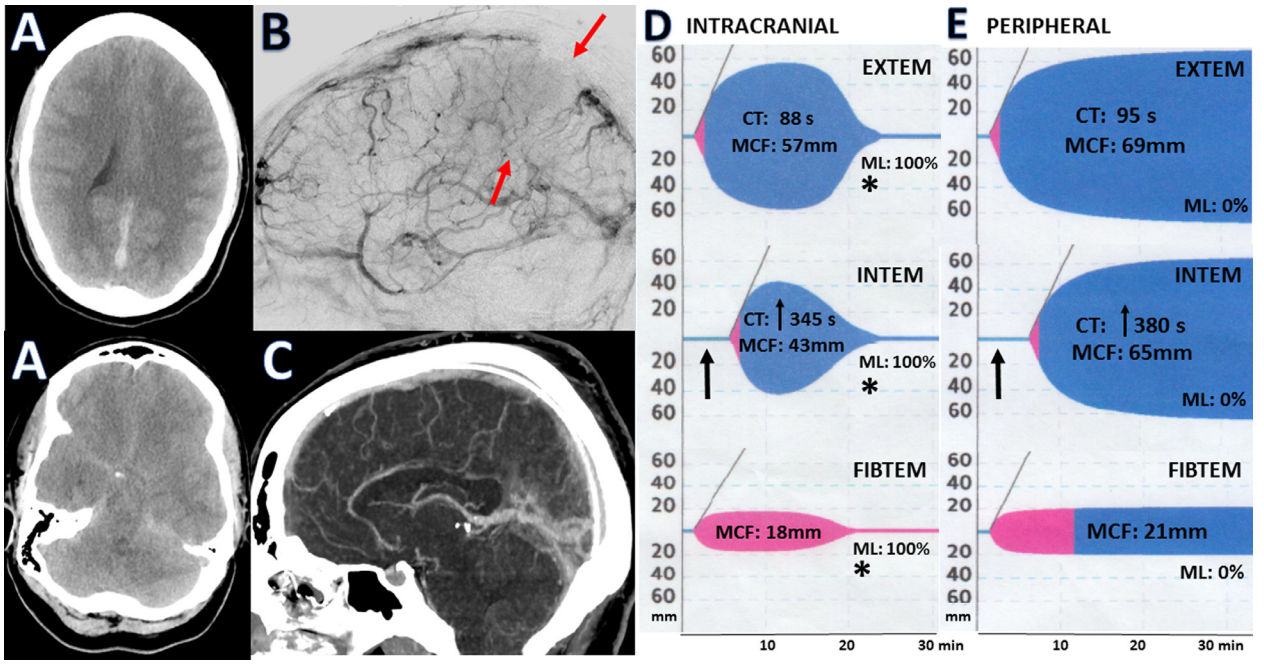

Figure 1. *Medically refractory CVST. (A) CVST with edema but no hemorrhage on CT. (B) Angiography revealed extensive CVST with particular burden over superior sagittal and inferior sinus (red arrows) with radiographic resolution on CT-venogram after 40 hours of intracranial-microcatheter tPA infusion (C). Intracranial ROTEM sample 1 hour after tPA cessation revealed ongoing intracranial fibrinolysis (D: tapering amplitude on Y axis; ML: 100%; EXTEM/INTEM-MCF: 57 mm and 43 mm, respectively) not seen peripherally (E: ML0%; EXTEM/INTEM-MCF: 69 mm and 65 mm, 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. Color version of figure is available online.*

Abbreviations: CT, coagulation-time; CVST, cerebral venous sinus thrombosis; EXTEM, extrinsic-pathway; FIBTEM, fibrinogen-assay; INTEM, intrinsic-pathway; MCF, maximal-clot-firmness; ML, maximum-lysis.

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 magnetic resonance imaging/venography demonstrated CVST without hemorrhage. Coagulation studies were normal with the exception of thrombocytosis (600×10^3/uL). Hypercoagulability evaluation was sent and intravenous-heparin was started. Despite therapeutic anticoagulation levels, the patient became obtunded, had worsening edema on head computed tomography (Fig 1, A), and endovascular treatment was offered.

Cerebral angiography demonstrated extensive CVST (Fig 1, B) with minimal improvement after balloon angioplasty and suction thrombectomy prompting microcatheter-based continuous-tPA (0.5 mg/h) through 2 separate microcatheters (superior sagittal and confluence sinus) and intravenous-heparin. Forty hours of intracranial-tPA were required for radiographic resolution of CVST (Fig 1, C). Intravenous-heparin was continued. One hour after tPA cessation, intracranial blood (3 mL) was collected from each microcatheter after wasting 1 mL. 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% versus 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 versus 380s; Fig 1, D,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 apixaban treatment.

Discussion

Endovascular treatments have been described for CVST[3]; 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 has been described in intracerebral hemorrhage[4] and trauma.[5]

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 deviations.[6]

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) does 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.

Authors' Contributions

Roh: Acquisition of data, analysis and interpretation, draft of the manuscript, critical revision of the manuscript for important intellectual content. David Roh, MD takes full responsibility for the data, the analyses and interpretation. This author has full access to all of the data and this author has the right to publish any and all data separate and apart from any sponsor. Carroll: Acquisition of data, analysis and interpretation, draft of the manuscript, critical revision of the manuscript for important intellectual content. Melmed: Acquisition of data, critical revision of the manuscript for important intellectual content. Elkind: Critical revision of the manuscript for important intellectual content. Eisenberger: Critical revision of the manuscript for important intellectual content. Francis: Critical revision of the manuscript for important intellectual content. Park: Analysis and interpretation, critical revision of the manuscript for important intellectual content. Agarwal: Analysis and interpretation, critical revision of the manuscript for important intellectual content. Claassen: Analysis and interpretation, critical revision of the manuscript for important intellectual content. Meyers: Acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content.

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