

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Materials

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Methods

HIMEA protocol and interpretation

Platelets from healthy blood donors (blood group O) were incubated with patient serum and saline buffer, as well as heparin at high (UFH 96 IU/mL) and low (UFH 0.96 IU/mL) concentrations, respectively, for testing by the heparin-induced multiple electrode aggregometry (HIMEA) on the Multiplate analyzer (Dynabyte Medical, Germany). In each HIMEA setup, platelets from the same donor were also tested with normal pooled plasma (negative control) and with plasma from a patient with established HIT diagnosis (positive control).

The area under the curve (AUC) measures impedance versus time.

In regular HIT-testing, a positive heparin-dependent platelet aggregation result requires low activation ($AUC < 28$ U) in saline control channel, a sigmoid curve with $AUC \geq 28$ U at low dose heparin, and high dose heparin resulting in an AUC reduction with $>50\%$ of the low dose heparin.

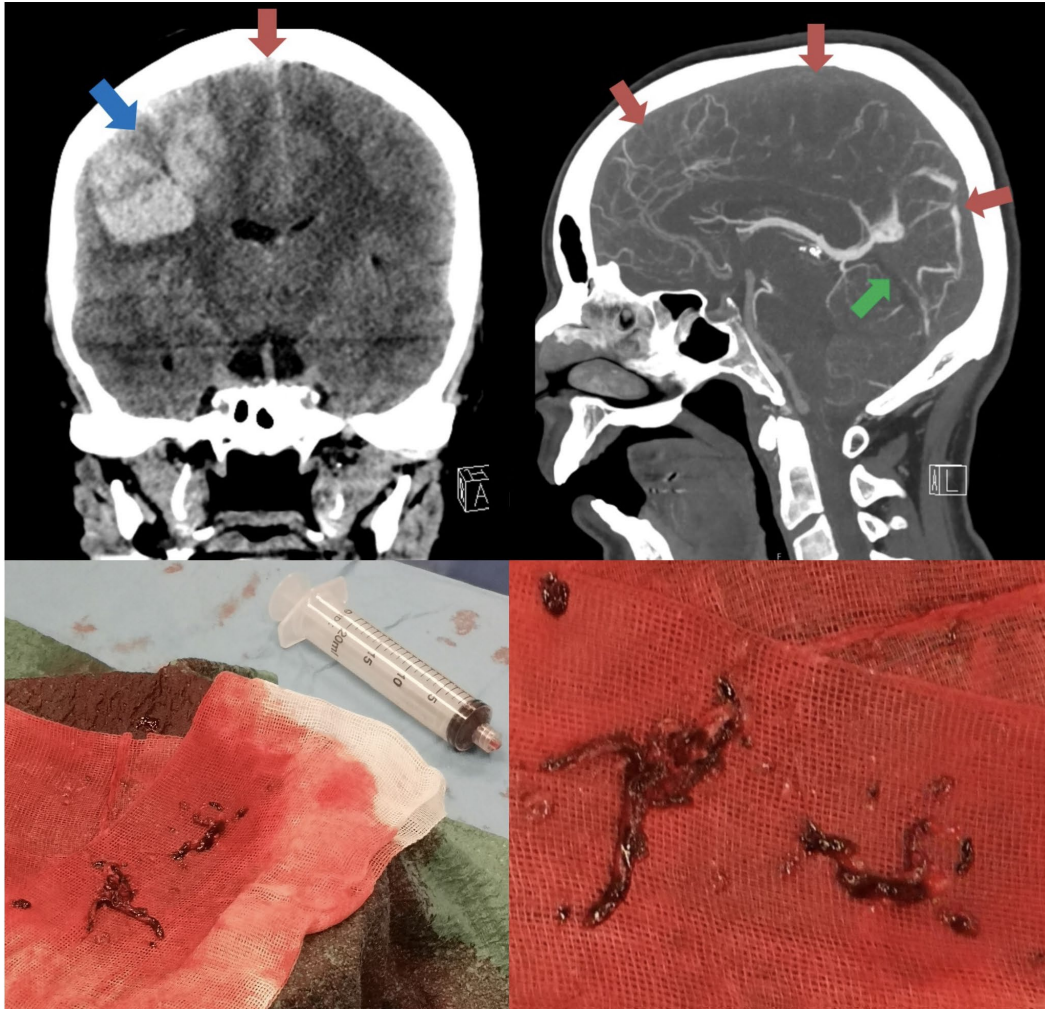


Figure S1. Brain CT scans with angiography and thrombus retrieved during venous thrombectomy in case 5.

A: Coronal CT demonstrating venous infarction with dominant hemorrhagic component (blue arrow). Area with high attenuation indicates thrombus in superior sagittal sinus (red arrow).

B: Sagittal CT venography: Completely lack of contrast in superior sagittal sinus (red arrows) and straight sinus (green arrow) as a result of massive cerebral venous sinus thrombosis.

C and D: Thrombus retrieved from superior sagittal sinus with mechanical endovascular venous thrombectomy. Although considered as experimental, endovascular treatment with mechanical thrombectomy can be a potential strategy to obtain recanalization in patients

with cerebral venous thrombosis who deteriorate clinically despite medical therapy 1. In Case 5 cerebral venous thrombosis was seen in all the major sinuses, including superior sagittal, straight, right transverse, left transverse and left sigmoid, on computer tomographic venography. Cortical vein thrombosis was also evident in draining veins to superior sagittal sinus from the area with hematoma in the right hemisphere. As the patient clinical situation deteriorated rapidly, endovascular treatment with thrombectomy was decided as an attempt to improve cerebral venous outflow and lessen intracranial pressure. The patient was brought to the angiosuite where digital subtraction angiography after contrast injection from carotid and vertebral arteries, showed extremely delayed venous outflow and closed sinuses corresponding to findings on CTV. The thrombectomy was performed with access from the groin, via the left internal jugular vein, through the left jugular foramen. Alternating the use of stent retriever and direct aspiration on distal access catheter, complete recanalization was achieved with the exception of some cortical thrombosis and minor of thrombus remnants in the straight sinus.

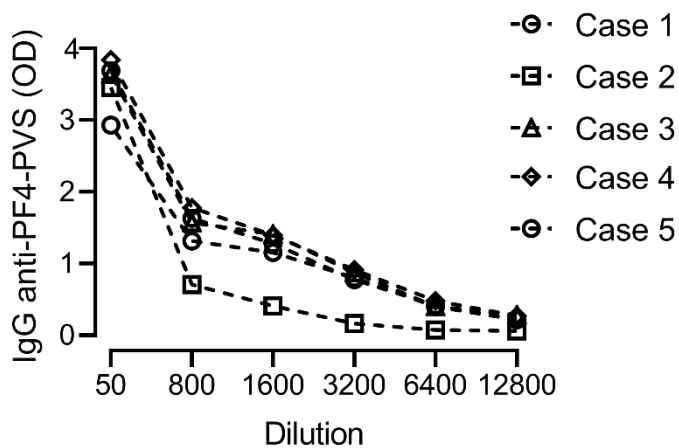


Figure S2: Serial dilution of patient sera in IgG anti-PF4/polyanion ELISA.

Serial dilution of patient sera was analyzed with LIFECODES PF4 IgG ELISA assay (Immucor, Waukesha, WI) according to manufacturer's instructions.

Serum samples (Case 1-5) were diluted as per protocol (1:50) and thereafter diluted 1/16 and further in two fold serial dilutions (i.e. 800, 1600, 3200, 6400, 12800) as indicated on the X axis. See also Figure 2.

References

1. Andersen TH, Hansen K, Truelsen T, Cronqvist M, Stavngaard T, Cortsen ME, Holtmannspötter M, Højgaard JLS, Stensballe J, Welling KL, Gutte H. Endovascular treatment for cerebral venous sinus thrombosis - a single center study. *Br J Neurosurg.* 2020 Jul 10:1-7. doi: 10.1080/02688697.2020.1786498. Epub ahead of print. PMID: 32648493.]