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Intracranial Hemorrhage as Initial Presentation of Cerebral Venous Sinus Thrombosis

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Abstract

Intracranial Hemorrhage (ICH) as initial presentation is an uncommon complication of Cerebral Venous-Sinus Thrombosis (CVT). Clinical and neuro-imaging studies of 4 cases of ICH due cerebral venous-sinus thrombosis seen at the William Osler Health System in Toronto will be presented. Discussion of the immediate and long-term management of these interesting cases will be reviewed with emphasis on the appropriate neuro-imaging studies. Literature review of Direct Oral Anticoagulants (DOAC) in the long-term management of these challenging cases will be discussed.

Introduction

The following are four cases of Cerebral Venous-Sinus Thrombosis (CVT) who present initially as Intracranial Hemorrhage (ICH). Clinical details, including immediate and long term management and neuro-imaging studies are presented.

Results

Case 1

A 43 years old R-handed house wife, South-Asian decent, who was admitted to hospital on 06-10-2014 with sudden headache and right hemiparesis. Her past health shows no prior hypertension or stroke. She is not on any hormone replacement therapy, non-smoker and non-drinker. Married with 1 daughter. Examination shows BP=122/80, P=70 regular, GCS=15, with right homonymous hemianopsia, right hemiparesis: arm=leg 1/5, extensor R. Plantar response.

She was started on IV Heparin after her unenhanced CT showed acute left parietal intracerebral hemorrhage and her MRV showed extensive sagittal sinus thrombosis extending into the left transverse sinus (Figures 1,2). Follow-up CT brain in 24 h showed no increase in ICH. Hypercoagulable work-up was negative. She remained stable on therapeutic doses of Warfarin until 2 weeks later when CT showed expanding left Subdural Hematoma (SDH). She had successful drainage of her left SDH. In 11-2014, she was discharged home on Warfarin. Follow-up MRV 6 months later showed complete resolution of her sagittal sinus thrombosis (Figure 3) and she remained on low dose aspirin for 2 years. When seen 5 years since onset, she had very little neurological deficit on no medications.

Case 2

August 2016, 45 years old R-handed IT worker of Chinese decent presented with sudden confusion followed by generalized seizure. Past health includes remote history of migraines, but on no medication, non-smoker and non-drinker. Ten days prior was involved in a rear-end motor

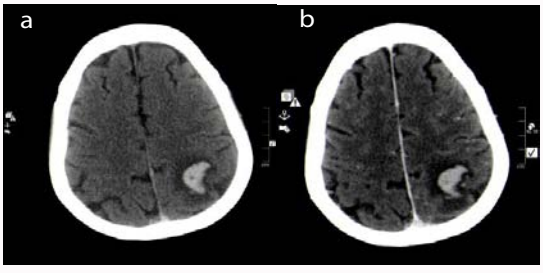

Figure 1: (a) Non-enhanced CT head demonstrates a left parietal lobe hemorrhage and hyperdense Superior Sagittal Sinus (SSS). (b) On the post-contrast CT head, empty sella sign is difficult to appreciate as the clot in the SSS is hyperdense.

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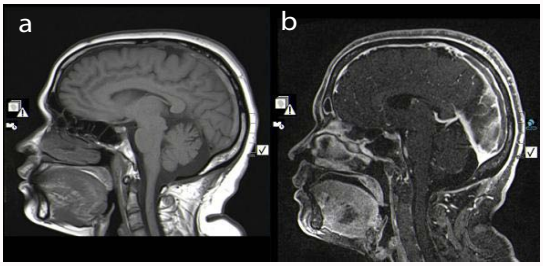

Figure 2: (a) Sagittal T1 demonstrates hyperintense SSS in keeping with acute thrombus. (b) Post-contrast sagittal enhanced MRV Vibe demonstrates a large filling defect in the SSS in keeping with the venous thrombus.

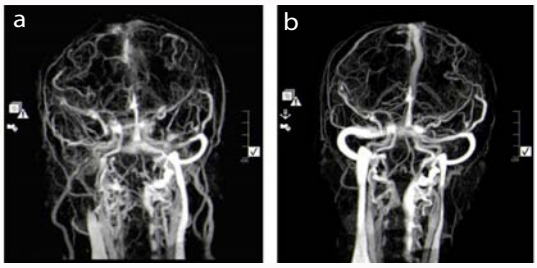

Figure 3: (a) 3D Maximum intensity projection demonstrates occlusion of the SSS, right transverse and sigmoid sinus, and upper right internal jugular vein. (b) Follow up almost 2 year later demonstrates recanalization with normal enhancement in the venous sinuses.

vehicle accident and hit his head on the head-rest without any loss of consciousness. Examination showed BP=114/70, P=70, GCS=15. Normal neurological examination, no meningismus. Unenhanced CT brain showed tiny right frontal Subarachnoid Hemorrhage (SAH) and MRI/MRV showed extensive sagittal sinus thrombosis (Figures 4-6). He was started on IV Heparin with therapeutic PTT and Levetiracetam 1000 mg BID for seizure prevention. Eventually changed over to Warfarin with therapeutic INR between 2.0 to 3.0. While on Warfarin, slightly low Protein C (0.57, N>0.7) and Free Protein S (0.49, N>0.65). Anti-thrombin 3, thrombophilia gene all negative. Normal serum homocysteine. Repeat CT brain showed complete resolution of SAH. Discharged home for out-patient cognitive assessment at an Acquired Brain Injury program for rehabilitation. Serial MRV showed recanalization of sagittal sinus (Figure 7) and eventually Warfarin was stopped and kept on low dose aspirin for 2 years. He was last assessed 3 years from symptoms onset and is on Levetiracetam for seizure prevention but off aspirin with no neurological deficit.

Case 3

September 2016, 32 year old left-handed construction worker of Italian descent presented with sudden headaches and generalized seizure. Past health includes when he was 16 years old, developed pulmonary embolism treated with Warfarin. March, 2016: left leg DVT with bilateral pulmonary embolism Rx: Rivaroxaban 20 mg OD and stopped 1 week prior to admission. Ulcerative Colitis on Asacol TID. Examination: BP=120/60, P=70, GCS=15, Normal Neurological exam. Normal CBC and INR/PTT. Unenhanced CT showed right posterior temporal subdural hemorrhage (Figure 8) and MRV shows right transverse sinus venous thrombosis (Figure 9). He was started with IV Dilantin loading followed by maintenance and IV Heparin with therapeutic PTT followed by Warfarin with INR between 2.0 to 3.0. Hematology was consulted regarding hypercoagulable workup.

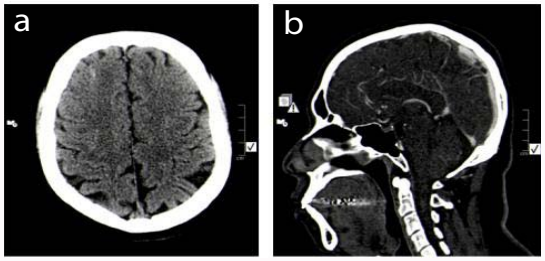

Figure 4: (a) Unenhanced CT head demonstrates subtle right frontal lobe subarachnoid hemorrhage. (b) Sagittal MPR from a code stroke CTA shows a filling defect in the SSS.

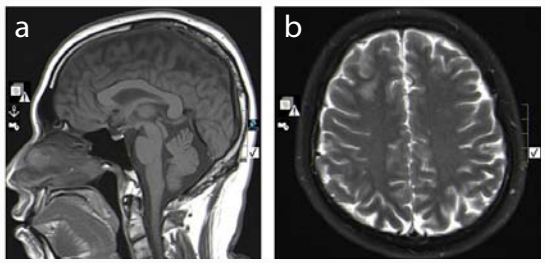

Figure 5: (a) Findings are subtle. There is mild hyper intensity in the anterior superior sagittal sinus (likely hyper acute thrombus). (b) There is edema in the right frontal lobe gyrus. The Superior Sagittal Sinus is hypointense either indicating flow void in patent part of sinus or acute thrombus which can mimic flow voids.

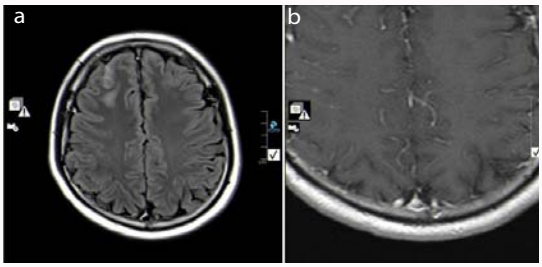

Figure 6: (a) MR Flair sequence again demonstrates the gyral edema. Hyper intensity in the sulci is in keeping with the subarachnoid hemorrhage. (b) Post contrast axial T1 images blown up at posterior SSS demonstrates enhancement of the dural sleeves around the thrombosed Superior Sagittal Sinus.

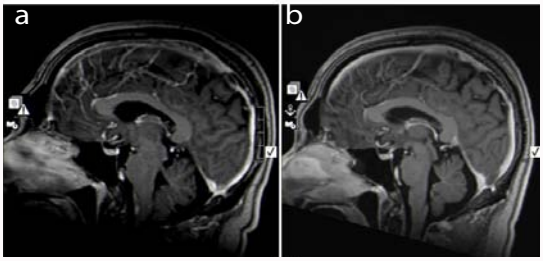

Figure 7: (a) Sagittal T1 MPR age from MRA demonstrates filling defects in the anterior and mid Superior Sagittal Sinus. (b) Follow up 6 months later shows near complete recanalization of the Superior Sagittal Sinus.

Factor V Leiden, Protein C and S all normal. Anti-thrombin III ACT slightly reduced. Switched from Warfarin to lifelong Rivaroxaban 20 mg OD and maintained on Levetiracetam 1500 mg BID for seizure prevention. Hematologist recommended life-long anticoagulation in view of recurrent venous thrombosis. Follow-up MRI/MRV showed

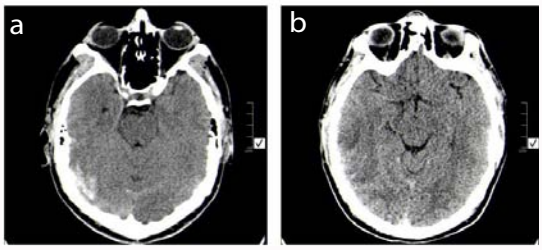

Figure 8: (a) Unenhanced CT demonstrates a right subdural hemorrhage along the tentorium. (b) More cephalad image demonstrates right temporal lobe edema, likely cytotoxic.

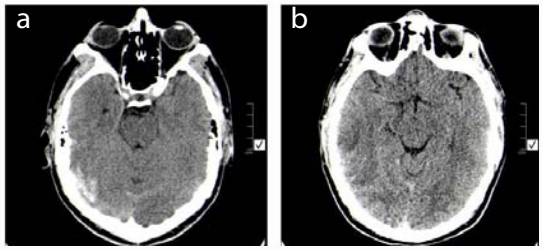

Figure 9: (a) Sagittal MPR from code stroke CTA demonstrates normal enhancement of the SSS. (b) Coronal MPR demonstrates filling defect in the right transverse sinus in keeping with thrombus. Right subdural hematoma above the right tentorium is subtle.

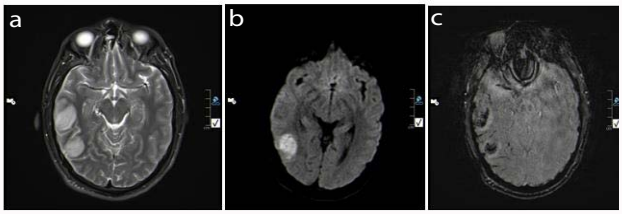

Figure 10: (a) On T2 weighting, there is edema in the right temporal and parietal lobes. (b) On diffusion weighting imaging, the posterior edema restricts diffusion in keeping with cytotoxic edema. The anterior edema does not in keeping with vasogenic edema. (c) On susceptibility weighted imaging, there is surface blooming artifact in keeping with hemosiderin deposition from petechial hemorrhages.

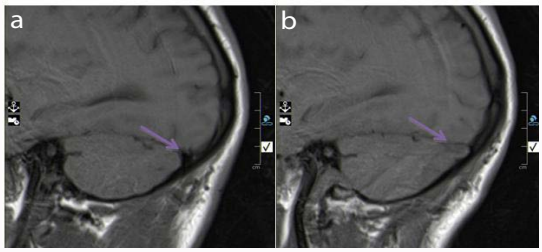

Figure 11: Sagittal T1 weighted imaging blown up at the transverse sinuses. (a) Note the normal flow void (arrow) in the left transverse sinus and the (b) lack of flow void with intermediate T1 signal in the right transverse sinus (arrow).

resolution of the right transverse sinus thrombosis (Figure 10-14). He remains stable with no neurological deficit when seen 3 years in follow up (Table 1).

Case 4

July-2017: 41 years old right-handed personal support worker of South-Asian decent with 1 week history of headaches and decrease

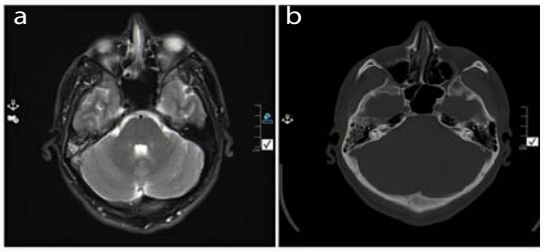

Figure 12: (a) On the axial T2, there is no flow void in the right transverse sinus due to the subacute T2 hyperintense thrombus. Note the adjacent right mastoid effusion. Venous thrombosis can be a complication of mastoiditis though in this case, (b) the CT earlier the same day demonstrated clear mastoids indicating that the effusion developed after the thrombus.

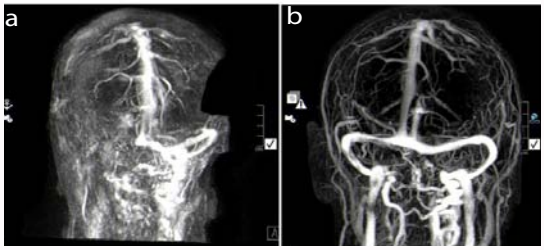

Figure 13: MRV from September 2017 and follow up MRV from 5 months later. (a) Initial coronal MIP from the MRV demonstrates occlusion of the right transverse and sigmoid sinus and upper internal jugular vein. MRV is degraded by motion artifact. (b) Follow up MRV demonstrates near complete recanalization of the venous sinuses and internal jugular vein.

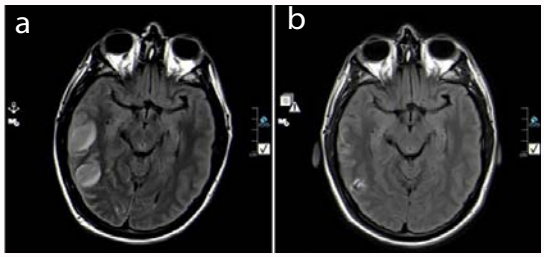

Figure 14: (a) Initial axial FLAIR demonstrates the edema in the right temporal and parietal lobes. (b) Follow up 5 months later demonstrates encephalomalacia in the area that previously demonstrated restricted diffusion (see Figure10) and normalization of the area that showed vasogenic edema.

in level of consciousness. Past health includes “Migraines” but no hypertension. Non-smoker, non-drinker. She was on Amitriptyline, Advil, Tylenol #2. Examination: GCS=8, BP=107/59, P=75, T=37C. She was drowsy but arousable with mild R. hemiparesis. CBC, INR/PTT, electrolytes, RBS, BUN, CK, Creatinine all normal. CT and CTA, MRI and MRV were done (Figure 15-17). She was treated with IV Heparin followed by oral Warfarin. When assessed by hematologist, it was decided to switch her from Warfarin to Apixaban at 5 mg BID due to concerns regarding INR monitoring. Her serial MRI/MRV had shown persistent thrombus in the left transverse sinus (Figure 17b) and encephalomalacia of left temporal lobe (Figure 18) and hence she remains on Apixaban when seen 2 years in follow-up.

Discussion

Cerebral Venous-sinus Thrombosis (CVT) is a rare cause of intracranial hemorrhage and accounts for only 0.5% to 1% of all strokes [1]. The average age of the 4 patients in this case series is

Table 1: Summary of 4 cases of ICH due to Cerebral Venous-sinus Thrombosis.

Case	Age	Sex	Location of ICH	Location of CVT	Treatment	Follow-up	Outcome
#1	43	Female	L. Parietal Ich	SST Extending to Transverse Sinus	IV Heparin-->Warfarin >ASA--> Stop	5 Years	No Deficit
#2	45	Male	R. Frontal Sah	SST Frontal-Parietal	IV Heparin-->Warfarin >ASA--> Stop	3 Years	Seizure On Keppra
#3	32	Male	R. Temporal Ich	R. Transverse Sinus Thrombosis to Proximal Jugular Vein	IV Heparin-->Warfarin >Rivaroxaban	3 Years	Lifelong Anticoagulation Seizure on Keppra Headaches
#4	41	Femal	L. Temporal Ich	L. Transverse Sinus Thrombosis to Sigmoid Sinus	IV Heparin-->Warfarin >Apixaban	2 Years	On Apixaban for Persistent Transverse Sinus Thrombosis

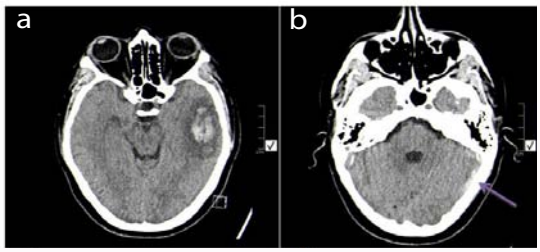

Figure 15: (a) Initial unenhanced CT brain showing moderate size left temporal intracerebral hemorrhage. (b) Left transverse sinus is hyperdense (arrow) in keeping with acute thrombus.

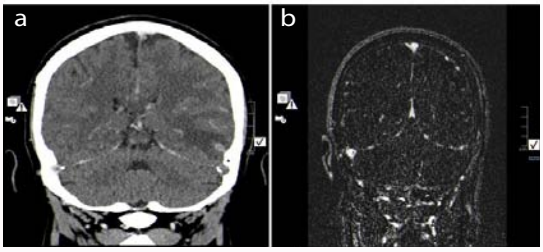

Figure 16: (a) Initial CT venogram and (b) MR venogram (from the following day) demonstrating no enhancement of the left transverse sinus in keeping with acute occlusive. Filling defect in the right transverse sinus on the CT venogram was focal and likely an arachnoid granulation.

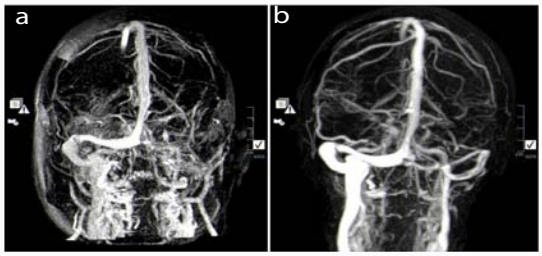

Figure 17: (a) 3D maximum intensity projection from the initial MRV demonstrates that the left transverse and sigmoid sinus are occluded. (b) MRV from 10 months later demonstrates partial recanalization of the venous sinuses though the sinuses are of smaller caliber than the other sinus.

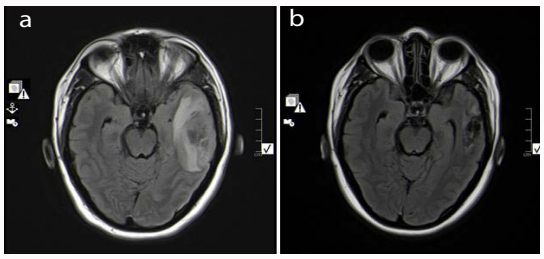

Figure 18: (a) Initial MRI demonstrates edema and hemorrhage in the left temporal lobe. (b) Follow up MRI 10 months later demonstrates encephalomalacia of left temporal lobe.

40.3 years old with equal sex distribution. There may be multiple causes of CVT but in general they are linked to the classic Virchow triad of stasis of the blood, changes in the vessel wall and changes in the composition of the blood. Risk factors for CVT can further be divided between genetic risks such as inherited thrombophilia and acquired risks such as surgery, trauma [2-7], dehydration, pregnancy, puerperium, antiphospholipid syndrome, cancer, exogenous hormones, inflammatory bowel disease as seen in case #3 in this series. Although CVT may present with a myriad of clinical symptoms, the most common one is prodromal headaches which are diffuse and may progress over days to weeks. A minority of patients may present with thunderclap headache suggestive of subarachnoid hemorrhage [8]. Even minor head trauma may be an important factor in the precipitation of CVT as in case #2 and this has also been reported by subtotal [6]. High index of suspicion should alert the clinician about CVT in those who may have past history of recurrent venous thrombosis as demonstrated in case #3 of this series. Two out of four patients in this case series presented with seizure (50%). Since 30% to 40% of patients with CVT present with ICH, it is critical to identify which ICH cases may be due to the rare cause of CVT distinct from other common causes of ICH. Immediate neuroimaging studies using CT/CTV or MRI/ MRV is recommended in patients with lobar ICH of otherwise unclear origin or with cerebral infarction that crosses typical arterial boundaries. [Class I, Level of Evidence C] [1,2] Echoplanar T2 susceptibility-weighted imaging combined with MRV are considered the most sensitive sequence to detect CVT. Routine blood work including screening for prothrombotic conditions are recommended in the initial laboratory testing but testing for thrombophilia are usually not recommended [2,3]. Once the diagnosis of CVT is established on neuro-imaging studies, intravenous anticoagulation using heparin or subcutaneous low molecular weight heparin is recommended unless there is major contraindication. It is of importance to note that ICH due to CVT is not a contraindication for anticoagulation [1-3,5]. The major reasoning behind this recommendation is that the ICH is often due to venous-sinus distention and congestion secondary to thrombosis within the venous system. Careful neurological monitoring is needed when anticoagulation is initiated and in cases which show neurological deterioration, either decompressive hemicraniectomy or endovascular mechanical thrombectomy with or without

thrombolysis can be considered [9]. Although there are no randomized controlled trial between the latter treatment compared to best medical therapy. Most patients should receive vitamin K-dependent oral anticoagulation for a period of time until there is evidence of complete resolution of the CVT on follow-up neuroimaging studies, preferably MRI/MRV. Limited data from randomized controlled clinical trials in combination with Observational studies on outcomes and bleeding complications of anticoagulation support a role for anticoagulation in the treatment

of CVT, regardless of the presence of pretreatment ICH. Data from observational studies suggest a range of risks for ICH after anticoagulation for CVT from zero to 5.4% [1]. A recent report by Mendoca et al. regarding the use of oral direct thrombin inhibitor as an alternative in the management of CVT [10]. In that series of 15 patients who were treated with dabigatran with median follow-up time of 19 months, excellent outcome was observed in 87% of patients with recanalization rate at 80%. In our case series, one patient received lifelong Rivaroxaban due to recurrent venous thrombosis while another was treated with standard dose Apixaban for up to two years without any bleeding complications or recurrence of ICH. Further randomized controlled trial of using direct oral anticoagulants compared with standard Warfarin will be needed to resolve whether the novel new oral anticoagulants can be used with better safety profile in the long-term management of patients with ICH due to CVT. It is therefore concluded that careful clinical history followed by appropriate neuroimaging studies in ICH patients secondary to CVT will require immediate parenteral anticoagulation followed by oral anticoagulation in order to achieve a favorable neurological outcome. Serial neuro-imaging studies such as using MRI/MRV are useful to guide clinicians to decide on the duration of anticoagulation for these challenging patients.

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Both Drs. Chu and Ossip have nothing to declare in terms of financial support or conflict of interests regarding this study.

Dr. Chu is responsible for the conceptualization and drafting and revision of this manuscript and Dr. Ossip is responsible for revision and review of the manuscript.

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