Stroke

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Bone marrow transplant restores Cerebrovascular Reactivity (CVR) in Sickle Cell Disease (SCD): a case presentation

K Alhadid (Toronto) M Kirby-Allen (Toronto) G DeVeber (Toronto) W Logan (Toronto) N Dlamini (Toronto)*

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Background: A diagnosis of SCD in childhood confers a 200-fold increase in the risk of arterial ischemic stroke. Blood flow velocity measures provide better identification of ischemic risk compared to angiography. This indicates that steno-occlusive arteriopathy is not the singular causative factor. Cerebrovascular reactivity allows for augmentation of cerebral blood flow when needed. Kosinski et al in 2016 demonstrated a direct correlation between CVR and hematocrit levels in SCD. We report a case where CVR persistently normalized in an SCD patient following bone marrow transplant therapy (BMT). *Methods:* A nine-month-old SCD patient presented with right AIS. Angiography revealed a bilateral Moya-Moya like arteriopathy. A TCD study was normal while a CVR-MRI study revealed markedly impaired reactivity in the entire anterior circulation. Haemaglobin-S at that time was 20.2 %. BMT was performed at age four due to frequent sickle cell crises. *Results:* One year post-transplant, CVR had dramatically improved in areas previously shown to have impairment (haemoglobin-S 0%). Neuroimaging five years post-transplant showed no further arteriopathy and persistently normalized CVR. *Conclusions:* BMT therapy resulted in the arrest of progressive intracranial arteriopathy and persistently restored vascular reserve. SCD might not only produce global hematological effects but also triggers local processes such as endothelial dysfunction and vascular inflammation that impair cerebrovascular function.

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Intracranial hemorrhage as initial presentation of sagittal sinus thrombosis: review of 3 cases

*JY Chu (Toronto)**

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Background: Intracranial hemorrhage due to sagittal sinus thrombosis is an unusal inital clinical presentation and a series of 3 cases is presented. *Methods:* A retrospective study of stroke patients seen at the William Osler Health System between 2014 -2016. *Results:* 1: 43 y.o. female presented with headaches and right hemiparesis. CT and MRI/MRV showed L. parietal intra-cerebral hemorrhage and sagittal and transverse sinus thrombosis. She was treated with IV heparin and subsequent oral Warfarin but developed symptomatic left subdural hematoma which was successfully evacuated. Hypercoagulable workup was negative. Subsequent MRI/MRV showed resolution of her sinus thrombosis and received asparin only since. 2: 45 y.o. male presented with generalized seizure 10 days following a motor vehicle accident. Initial CT showed focal right frontal subarachnoid hemorrhage and subsequent MRI/MRV confirmed extensive sagittal sinus thrombosis. He was treated with IV heparin and subsequent Warfarin without any complications. 3: 32 y.o. male presented with generalized seizure. CT and MRI/MRV confirmed a large right temporal lobe intra-cerebral hemorrhage and extensive right transverse sinus and straight sinus thrombosis. He was successfully treated with IV heparin followed by oral Warfarin. *Conclusions:* Despite intracranial hemorrhage in patients with cerebral sinus venous thrombosis, they could be managed successfully with anticoagulation therapy and with careful clinical and neuro-imaging monitoring.

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Next-generation sequencing to determine a genetic cause of familial intracranial aneurysms

E Hitchcock (Vancouver) J Diamond (Vancouver) P Eydoux (Vancouver) K Townsend (Victoria) Y Shen (Vancouver) S Jones (Vancouver) GJ Redekop (Vancouver) WT Gibson (Vancouver)*

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Background: Approximately 12-15% of patients with intracranial aneurysms (IA) have affected first-degree relatives, and are considered to have familial intracranial aneurysms (FIA). Individuals with FIA are at higher risk for aneurysm formation and subarachnoid hemorrhage. *THSD1* is the only gene to be associated with nonsyndromic FIA at this time. Our study aims to find rare DNA variants that are major risk factors for FIA in our cohort of patients. *Methods:* To date we have enrolled 37 affected and 31 unaffected people from 16 families. We have done exome or genome sequencing on at least 1 person from each of 12 families. *Results:* A rare p.(R686W) variant in *THSD1* was found in 1/12 families, but did not cosegregate fully with disease. While less attractive as the primary cause of FIA, we cannot rule out the potential modifying effects of *THSD1* p.(R686W) in this family. A second candidate, an extracellular matrix gene within a chromosomal region previously implicated by familial mapping studies, contains rare variants in 4/12 of our families. All four variants are predicted to be damaging. *Conclusions:* Alongside environmental risk factors, individual FIA families may also have complex rare variant contributions to their disease, such as digenic and multi-locus contributions.

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Software algorithms for atrial fibrillation screening with wearable devices: a systematic review

GA Jewett (Calgary) S Crooks (Calgary) JL Sapp (Halifax)*

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Background: Atrial fibrillation (AF) is an important risk factor for ischemic stroke but has no recognized screening method. Wearable devices have the potential to provide near continuous monitoring to detect AF. This systematic review evaluates the current state of software capable of detecting AF using wearable devices. *Methods:* We conducted a systematic search using PRISMA method of Medline, CENTRAL, PubMed and trial registries up to January 15, 2017. Abstracts and titles were screened, and relevant articles reviewed fully. English articles were selected if reporting on (1) software for AF detection (2) using heart rhythm signal, (3) theoretically applicable to wearable technology. Quality was evaluated with Cochrane GRADE. *Results:* Of 269 unique abstracts, 54 were identified for full review. 20 studies met inclusion criteria for algorithm accuracy analysis. Sensitivity and specificity ranged from 87.0 - 97.6% and 89.0 - 99.6%, respectively. 4 studies analyzed signal acquired using