Cerebral Venous Sinus Thrombosis in a patient with Smith Magenis Syndrome

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Background

- Smith Magenis syndrome (SMS) is a complex genetic developmental disorder, typified by a microdeletion of chromosome band 17p11.2. This chromosome encodes for multiple genes including the retinoic-acid-induced 1 (RAI1) gene. SMS is a rare disorder with ongoing exploration of multi-systemic manifestations.
- We report a case of a 25-year-old female with SMS who was diagnosed with Cerebral Venous Thrombosis (CVT). Our hope is to contribute to the literature in regards to multi-systemic manifestations of SMS.

Case Presentation

A 25-year-old female with SMS presented with complaints of lethargy, vomiting, diarrhea, and abdominal pain for the past few days. She was diagnosed and managed for proctocolitis.

On hospital day 2, patient was noted to be increasingly altered with decreased responsiveness, however, maintaining a Glasgow Coma Scale (GCS) of 11. Stroke alert was initiated. Tenecteplase was not recommended as patient was out of window period. Computed Tomography (CT) of the brain without contrast revealed findings concerning for CVT and venous infarct. CT brain venogram revealed occlusion of the inferior sagittal sinus and bilateral deep cerebral veins. Magnetic Resonance Imaging (MRI) brain with/without contrast revealed secondary venous infarcts of bilateral thalami and right basal ganglia in addition to CVT. Interventional neurology recommended therapeutic anticoagulation with intravenous heparin and no surgical intervention due to patency of the torcula and right transverse/sigmoid system.

On hospital day 4, patient's Glasgow Coma Scale (GCS) worsened to 8; she was intubated for airway protection. Electroencephalogram (EEG) revealed interictal discharges, prompting initiation of levetiracetam.

Patient had gradual improvement in neurological status and was extubated on hospital day 10.

Hematology was consulted. Lupus anticoagulant, antiphospholipid, antinuclear, and antineutrophil cytoplasmic antibodies were negative. Fibrinogen and D-dimer were within normal limits. Patient was transitioned to apixaban prior to discharge to a rehabilitation facility.

Extensive work-up outpatient was negative for any inherited or acquired hypercoagulable disorders. Patient was discharged from the rehabilitation facility with remarkable improvement.

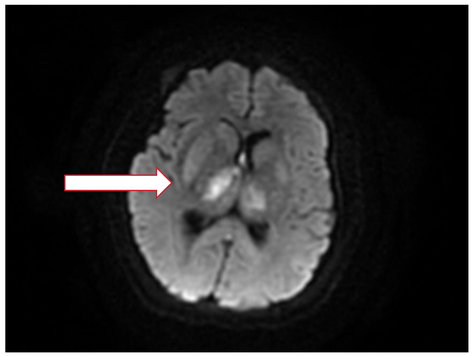

Figure 1: MRI brain with/without contrast revealed secondary venous infarcts of bilateral thalami and right basal ganglia.

Discussion

- The incidence of Cerebral Venous Thrombosis is 0.22–1.32/100,000/year (1). CVT accounts for 0.5% of all strokes (2). Risk factors for CVT include genetic hypercoagulable disorders, malignancy, pregnancy, puerperium, estrogen-containing medications, and autoimmune disorders (3).

Discussion

- CVT or any hematological manifestations of SMS has not been reported till date. SMS is a genetic disorder that is typically characterized by distinctive physical features, developmental delay, cognitive impairment, and behavioral abnormalities.
- SMS is caused by interstitial 17p11.2 deletions (90%), encompassing multiple genes including *RAI1*, or by pathogenic variants in *RAI1* itself (10%). RAI1 acts as a transcriptional regulator. The variants of *RAI1* gene have been explored with some contributing to systemic manifestations.
- Our patient was diagnosed with SMS in childhood. However, had no history of prior VT or hypercoagulable disorders. She did not exhibit classic risk factors for VT, had no family history of hypercoagulable disorders, and was not on any estrogen-containing medications. Work-up was negative for any inherited or acquired hypercoagulable disorders and autoimmune conditions including vasculitis. Possible role of *RAI1* gene variants in contributing to CVT was suspected.
- Our case :
  - Suggests association of systemic manifestations including hematological manifestations with SMS that haven't been reported till date
  - Suggests possible role of gene variants in SMS contributing to VT
  - Reiterates the importance of holding a high index of suspicion for CVT in patients presenting with stroke like symptoms and thereby ordering appropriate neuroradiodiagnostic tests.

References

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