Grange Syndrome, Moyamoya Mimicker

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Background

Grange syndrome (OMIM#602531) is a rare autosomal recessive disorder caused by biallelic pathogenic variant of *YY1AP1*[1]. The disease has variable phenotype characterized by multifocal arterial stenosis or occlusion in the cerebral, abdominal, renal, or cardiac arteries, and hypertension, that may or may not be associated with cardiac anomalies, brachydactyly, syndactyly, bone fragility, and learning disabilities[2].

Case report

We are presenting a 13-year-old female who presented to our hospital as a case of hypertensive emergency and found to have renal artery stenosis, brachydactyly, and syndactyly. Past medical history revealed two episodes of unprovoked transient ischemic attacks. Further investigations revealed cardiac findings of left ventricle hypertrophy (ECHO), superior mesenteric artery stenosis (abdomen CT), and steno-occlusive disease of the ICA and basilar arteries [Figure 1], multifocal remote infarctions [Figure 2] and arterial stenosis [Fig 3]. Osteopenia/ osteoporosis of the femoral neck and lumbar vertebra (DXA scan). Whole exome sequencing showed a homozygous pathogenic variant of *YY1AP1*. As for managing this patient, she is on antihypertensive medication, she underwent left renal artery balloon dilatation, and she was started on aspirin for secondary stroke prevention and genetic counseling.

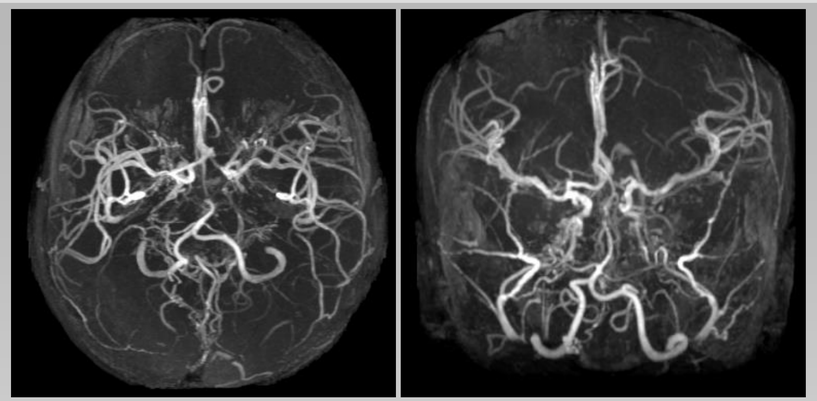

Figure 1: Brain TOF MRA MIP images axial (left) and coronal (right) showing Steno-occlusive disease of both carotids sparing the carotid terminus in contrast to moyamoya. Involvement of the basilar tip with established moyamoya like leptomeningeal collaterals.

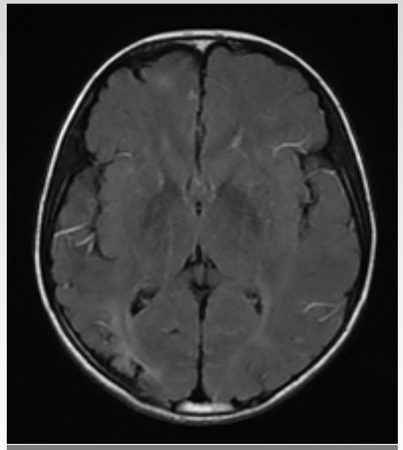

Figure 2: Barin MRI T2 flare, showing watershed infarction of the right hemisphere with gliosis and encephalomalacia. Hyperintensities within the sulci representing the leptomeningeal collaterals (ivy sign).

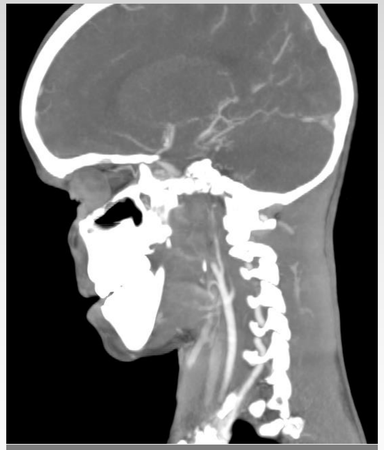

Figure 3: Neck CTA showing thread like ICA distal to the birfurcation indicative of near occlusion with distal collapse.

Discussion

Grange syndrome is an ultra-rare multisystem disorder that was first described in 1998. To date, only 15 cases have been reported world-wide[3]. Although there are some features that mimics Moyamoya disease and fibromuscular dysplasia. In the other hand, the clinical and radiological features are distinctive. Treatment is focused on symptomatic management and secondary prevention by a multidisciplinary team.

Conclusion

Grange syndrome is a well described etiology for ischemic and hemorrhagic stroke. We are highlighting the importance of genetic testing consideration as part of stroke work up in children and young adult. Although there is no curative treatment for Grange syndrome, high clinical suspicion, close follow-ups, monitoring, preventative measures and surveillance are crucial.

Take home message

Grange syndrome should be considered in a child presenting with hypertension and arteriopathy.

References:

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