Wishbone Sign in GM1 Type III Gangliosidosis

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A 19-year old gentleman presented with progressive generalized dystonia for the past 10 years with onset in the right lower limb. Thereafter, he developed left lower limb dystonia 1 year later and dystonia of both upper limbs 2 years later. The dystonia was non-task-specific and was initially present on action but progressed to presence at rest as well. He developed speech disturbance for the past 8 years and became anarthric in the next 2 years. He also developed neck dystonia and dysphagia 2 years back and blepharospasm 1 year ago. He had no cognitive impairment, seizures, slowness, stiffness, myoclonus, or tremors and was born to non-consanguineous parents with normal birth and developmental history. His younger brother and sister were similarly affected.

Examination revealed generalized dystonia (blepharospasm, upper and lower facial, lingual, retrocollis, truncal, and all four limbs) and thoracic scoliosis. He had no organomegaly and a normal fundus examination.

Juvenile onset generalized dystonia causes like Wilson's disease, KMT2B mutations, neurodegeneration with brain iron accumulation (NBIA) spectrum disorders, GM1 gangliosidosis, and dopa responsive dystonia were considered. Magnetic resonance imaging (MRI) brain revealed bilateral posterior putamen volume loss with hyperintensity on T2 weighted imaging (T2WI) [Figure 1a], and susceptibility weighted imaging (SWI) revealed blooming of the globus pallidus in the "wishbone pattern" [Figure 1b]. Chest X-ray revealed thoracic scoliosis with platyspondyly. Routine blood investigations were normal, and Wilson's disease work-up was negative. Exome sequencing revealed pathogenic compound heterozygous variants in the *GLB1* gene on exon 4 (c.442C > T) and exon 13 (c. 1325G > A), clinching the diagnosis of GM1 type III gangliosidosis. He was treated with levodopa and trihexyphenidyl with mild symptomatic improvement.

GM1 gangliosidosis is a rare lysosomal storage disorder with autosomal recessive inheritance caused by beta-D-galactosidase enzyme deficiency.[1] It occurs due to *GLB1* gene mutations on chromosome 3, leading to a generalized accumulation of sphingolipids, glycoproteins, and keratan sulfate and leading to various neurological and skeletal manifestations. The clinical phenotypes vary according to the age at symptom onset [infantile (type I), juvenile (type II), and adult (type III)].[2] Type III disease usually presents between the first and fourth decades with prominent neurological findings. Generalized dystonia and severe speech abnormality (progressing to anarthria) are the most common clinical presentations.[1] Facial dystonia is prominent (both upper and lower faces) along with skeletal abnormalities like flattened vertebral bodies, scoliosis, and dysplasias.[1] The "wishbone" pattern is formed by iron deposition in the medial (GPi) and lateral (GPe) parts of the globus pallidus (separated by the internal medullary lamina) making the forked ends, along with downward extension to the anterior substantia nigra and red nucleus forming the stem of the wishbone. The posterior putaminal T2 hyperintensity is probably caused by neuronal loss with secondary gliosis and gangloside storage.[3]

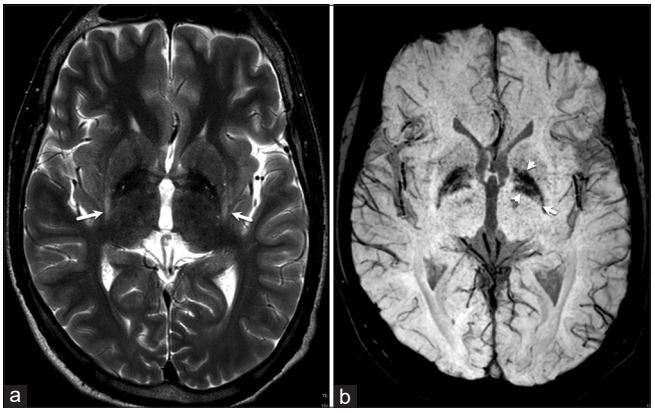

Figure 1: Axial T2-WI (a) shows bilateral symmetrical atrophy and hyperintensities (arrows) of posterior putamen, which have been described in type III GM1 gangliosidosis. Axial SWI image (b) reveals 'wish bone' pattern of hypointensities secondary to mineral deposition in the globes pallidi, forming the fork (arrowheads) and substantia nigra, red nuclei, forming the stem (short arrow)

The combination of the putaminal finding on T2WI and the wishbone pattern of iron deposition on SWI is highly suggestive of adult-onset (type III) GM1 gangliosidosis.[4,5]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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