Reversible MRI brain changes in hypermanganesaemia with dystonia 1 with EDTA therapy

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DESCRIPTION

Two sisters in their late and mid-30s, respectively, with history of consanguineous parentage presented with cockwalk gait, progressive generalised dystonia and dysarthria from 4 years of age. Both sisters are well educated and have completed their graduation. There was no evidence of cognitive decline or neuropsychiatric manifestations. MRI brain showed symmetrical T1-weighted hyperintensities involving bilateral basal ganglia, predominantly globus pallidus, cerebral peduncles, dorsal pons and dentate nuclei (figure 1A–D).

Genetic testing revealed SLC30A10 mutation causing hereditary hypermanganesaemia with dystonia 1 (HMNDYT1).

With the diagnosis of inherited metabolic disorder with hypermanganesaemia, both patients were treated with disodium edetate dehydrate (EDTA) therapy (monthly pulse of 20 mg/kg two times per day for 5 days, premedicated with 100 mg of hydrocortisone and pheniramine 45.5 mg) along with symptomatic therapy for dystonia. Two years after the start of the chelation therapy, complete resolution of the MRI alterations was seen (figure 1E–H). Patient's disease course halted and symptoms improved.

Formal assessment applying Burke Fahn Marsden scale[1] demonstrated marked improvement (movement scale—improved from 90 to 56.5, disability scale—improved from 21 to 18) in the younger and more affected sibling. Elder sister did not show progression in the symptoms and her disability had improved, but it did not reflect on the scale (movement scale—21, disability scale—6).

HMNDYT1 is an autosomal recessive disorder caused by mutation in SLC30A10 gene, which encodes a membrane-bound transporter responsible for the efflux of excess Mn2 + from the cytosol. The disorder is characterised by typical cockwalk gait, generalised dystonia, parkinsonism in adulthood, polycythaemia, hepatomegaly and cirrhosis with relative sparing of the cognitive abilities. Deposition of the paramagnetic metal in the brain leads to characteristic T1-weighted hyperintensity in the globus pallidus with corresponding T2-weighted hypointensity on the MRI.[2] Chelation therapy has the potential to revert the imaging changes, resolve the neurological symptoms and halt the liver disease. Patients with polycythaemia can benefit from oral iron supplementation as iron competes with Mn for binding and uptake at various transporters.[3]

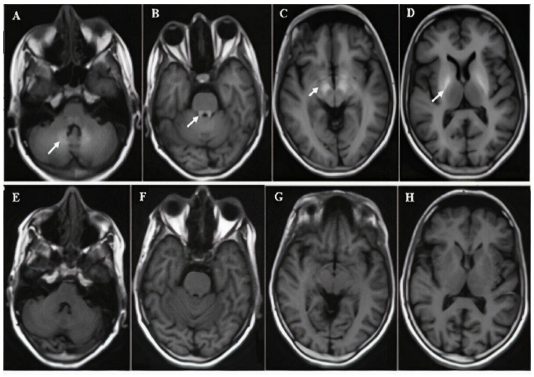

Figure 1 (A–D) T1-weighted MRI shows hyperintensity (white arrows) of the bilateral dentate nucleus of the cerebellum (A), dorsal pons (B), cerebral peduncle (C) and the globus pallidus (D). (E–H) T1-weighted MRI after 2 years of EDTA chelation therapy shows complete resolution of the previous hyperintensities involving the dentate nucleus (E), dorsal pons (F), cerebral peduncle (G) and the globus pallidus (H).

Patient's perspective

We both have been under treatment for over 2 years. We have great respect and regards for the team. We have been explained about the nature of the illness and are satisfied with the treatment going on and trust our team of neurologists. We expect to improve over a period of time.

Learning points

- T1-weighted hyperintensities involving the basal ganglia in a patient with movement disorder can be a clinching point in the diagnosis of inherited movement disorder with manganese deposition.
- Patients with hereditary hypermanganesaemia may benefit from EDTA chelation therapy.

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