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MRI Insights in Hypomyelinating Disorders With Early Myelination Disturbances

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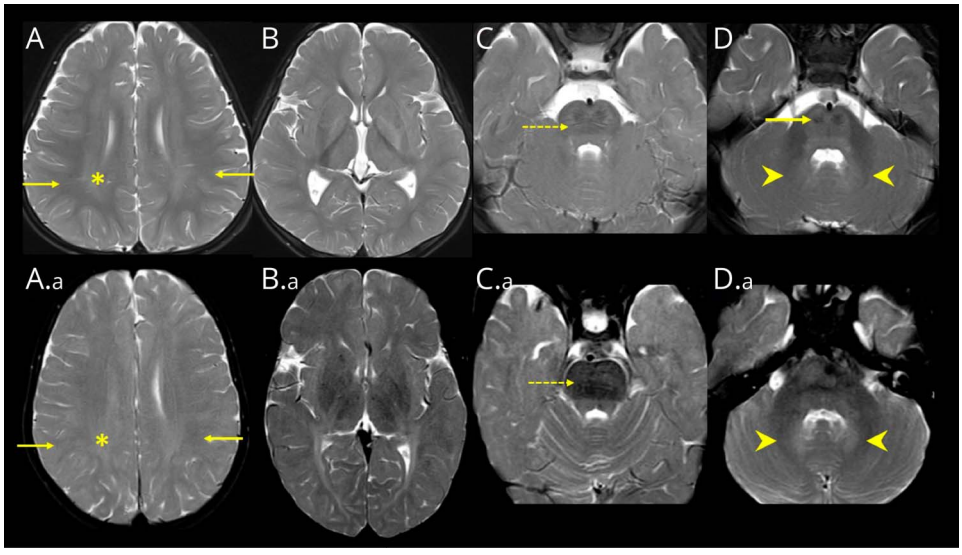
A 5-year-old boy presented with a slowly progressive spastic ataxic syndrome since the age of 8 months. Targeted genetic testing confirmed a homozygous nonsense pathogenic variant c.121A>T(p.Lys41Ter), in the *NKX6-2* gene. We compare the MRI findings with those of a companion case of hypomyelination of early myelination structures (HEMS) in a 4-year-old child.

Hypomyelinating disorders selectively affecting early myelinating machinery lead to characteristic MRI phenotypes with poorer myelination of early myelinating structures.[1] While HEMS serves as a prototype, a newer disorder due to *NKX6-2* variants has recently emerged.[1,2]

There are several similarities in their MRI appearances (Figure 1), but they differentially affect some structures (Figure 2) such as the ventrolateral nucleus of thalamus (VLT) and posterior limb of internal capsule (PLIC). Involvement of VLT in *NKX6-2* (relative sparing in HEMS) and PLIC in HEMS (relative sparing in *NKX6-2*) highlights that structures myelinating at

Figure 1 MRI Overlaps



NKX6-2 (upper panel) and HEMS (lower panel)—Axial T2WI show hypomyelination as mild hyperintensity in the central hemispheric white matter (asterisk A, A.a), pons (dashed arrow C, C.a), and dentate nucleus (arrowhead D, D.a). Better myelination of the pontine corticospinal tracts is noted in NKX6-2 (thick arrow, D).

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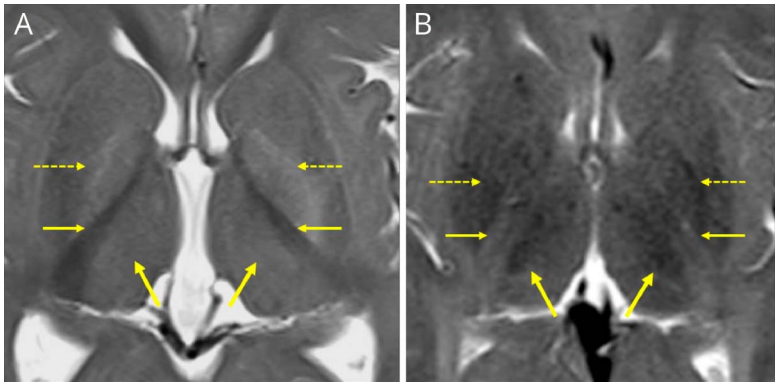
Figure 2 Distinct Structural Involvement



Note the trilaminar appearance (hyperintense rims flanking middle hypointense signal) of the PLIC fibers in HEMS (arrow, B) and normal myelination in NKX6-2 (arrow, A). Also note a better myelinated hypointense ventrolateral thalamus (VLT, thick arrows) and globus pallidus (dashed arrows) in HEMS (B) vs diffuse hyperintensity in NKX6-2 (A).

different periods in fetal life (VLT at 25–28 weeks gestation, and PLIC at 35–36 weeks gestation) may be differentially vulnerable in early hypomyelinating disorders.[1,2]

MRI findings support the distinct roles that *NKX6-2* plays during early and later stages of myelination and may allow distinction from other hypomyelinating leukodystrophies.

Author Contributions

P. Malik: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. B.S.U.: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. B.B. Mathew: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. M. Thomas: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. S. Yoganathan: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data.

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