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LETTER TO EDITOR

Hypomyelinating Leukoencephalopathy

اعتلال بياض الدماغ بقلة تكون المايلين

Sir,

Leukoencephalopathies in children are a heterogeneous group of disorders affecting the white matter of the brain, and often pose a major challenge to the treating physician for the appropriate aetiological diagnosis and management. Van der Knapp and others described a peculiar form of leukoenchalopathy affecting the basal ganglia and cerebellum in children with extensive hypomyelination; however, since that publication, few cases have been reported in the literature.[1] The patients described had normal births and early development followed by an extrapyramidal movement disorder in the form of dystonia, spasticity, and ataxia, with global developmental regression. Magnetic resonance imaging (MRI) of the brain showed characteristic hypomyelination with atrophy of basal ganglia and cerebellum; however, the thalamus and globus pallidus were spared. The molecular basis for the diagnosis has never been established for this disease.[4] However, histopathologyhas been able to confirm extensive myelin loss in the aforementioned areas of the brain.[2] We report a two-year-old Nigerian boy with clinical and radiological features of hypomyelination, and mild atrophy of the basal ganglia and cerebellum.

The boy was brought to our hospital by his parents due to abnormal movements of his trunk and limbs from 8 months of age. He was born full-term to non-consanguineous parents. He had a normal perinatal and postnatal history. The boy had been sent home two days after delivery and had had normal development until 8 months of age, when he had been able to sit with support and could hold objects in his hands. However, his mother noticed that, when he was crying, the boy would develop stiffness in both legs, with more stiffness on his left side. After a few months, he lost the ability to sit as the stiffness increased in severity and progressed to involve all 4 limbs. He was unable to interact with his parents and had orofacial dyskinesia which interfered with feeding. He was seen by doctors and was started on anti-epileptic drugs with no benefit. When he presented to us, he was severely malnourished and bed-ridden, with extensive orolingual dyskinesia movements. There was dystonia of both axial and appendicular integuments with intermittent opisthotonos posturing. His cognitive skills were severely compromised and he could not communicate with his parents. A neurological examination revealed normal cranial nerve function, rigidity of all four limbs including the trunk, few choreiform movements of the extremities, and normal deep tendon reflexes and flexor plantar responses. There were no Kayser-Fleischer rings, and other systemic examinations were unremarkable. A routine biochemistry and metabolic work-up, including a leukocyte enzymes estimation, an evaluation of serum copper and ceruloplasmin levels, and a human immunodeficiency virus (HIV) screening were normal. An MRI brain study revealed severe cortical atrophy with hypomyelination and atrophy of the caudate and putamen nuclei as well as the cerebellum. [Figure 1]

He was treated with carbiodopa+levodopa (sinemet) and benzodiazepine after discontinuing all anti-epileptic drugs. In the initial weeks, he showed symptomatic improvement, but the symptoms recurred despite adequate dosages of the above medications.

Our case clearly illustrates the importance of neuro-imaging in the diagnosis of hypomyelination with basal ganglia and cerebellar atrophy after ruling out other causes of dystonia with the available diagnostic tools. Leukoencephalopathies have distinctive clinical and radiological findings, and aetiological confirmation could be established with an extensive molecular genetic work-up. This would help patients acquire appropriate genetic counselling and possibly a potential curative treatment. However, in reality, more than half of these disorders remain undiagnosed because of the lack of availability of neuroimaging tools and, in such conditions, specific MRI findings could establish the correct diagnosis. Recently described leukoencephalopathies, such

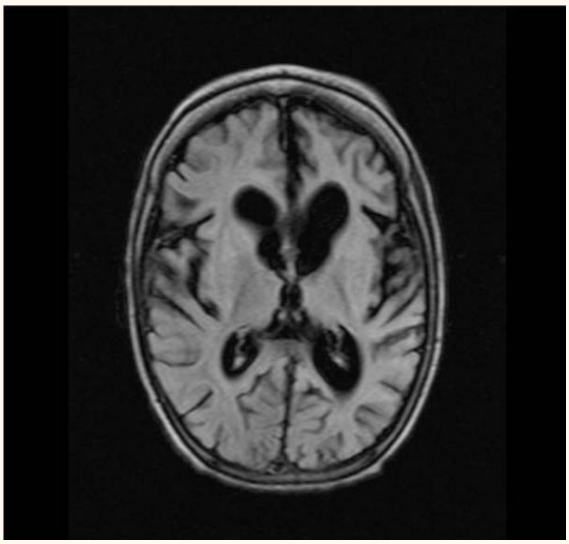

Figure 1: A magnetic resonance imaging brain scan revealing severe cortical atrophy with hypomyelination and atrophy of the caudate and putamen nuclei as well as the cerebellum.

as vanishing white matter disease, megalencephalic leukoencephalopathy with subcortical cysts, and adrenoleukodystrophy, deserve mention here for the importance of MRI in achieving a diagnosis.[5] In this context, van der Knapp *et al.* identified seven unrelated patients with extensive extra pyramidal movement abnormalities, ataxia, and spasticity.[2] An MRI brain scan revealed atrophied cerebral white matter, neostriatum, and cerebellum. Detailed metabolic work-ups were normal and none of the 7 had any history of perinatal insults. Magnetic resonance spectroscopy (MRS) showed elevated myo-inositol in the white matter, which is an indicator of gliosis. N-acetyl aspartate and choline levels were normal, suggesting that neither axonal loss nor active demyelination had occurred. They named this a distinctive leukoencephalopathy "hypomyelination with atrophy of the basal ganglia and cerebellum" (H-ABC) to indicate patients sharing these unique clinical and MR imaging features.[2]

Our patient shared some of the above clinical and radiological features of H-ABC, and we present this case to emphasise the role of neuro-imaging in the diagnosis of this recent and rare nosological entity. Levodopa and cabiodopa were found to be effective in one patient with a similar condition.[3] Unfortunately, our patient did not improve much during this treatment, although the dystonic spasms were initially alleviated.

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