Florid Brain Calcification in a Child with X-Linked Adrenoleukodystrophy: What Does it Signify?

A seven-year-old boy presented with poor attention span, hyperactivity, and aggression for past one month. There was no history of hearing, vision, speech, and gait disturbances or focal neurological deficits. There was no history of trauma or any similar history in the family. His 4-year-old younger female sibling was apparently healthy and asymptomatic. Generalized hyperpigmentation other than inattention was noticed during examination. Computerized tomography (CT) brain revealed hyperdensities in bilateral parieto-occipital white matter along the trigones of the lateral ventricles with suggestive demyelination in MRI [Figure 1]. With a clinico-radiological possibility of X-linked Adrenoleukodystrophy (X-ALD), the next genetic sequencing confirmed the diagnosis [a hemizygous pathogenic missense variant in exon 9 of the *ABCD1* gene (p.Arg660Trp)]. His serum ACTH was 800 pg/ml. Parental testing could not be done due to affordability issues and the parents are not planning for next pregnancy.

(X-ALD) is the commonest peroxisomal disorder. The involved *ABCD1* gene encodes a peroxisomal membrane protein involved in transmembrane transport of very-long chain fatty acids into the peroxisome, thereby causing cytosolic accumulation in the disease state.[1] Varied clinical phenotypes have been described for ALD with age: Addison-only at school age, childhood, adolescent and adult

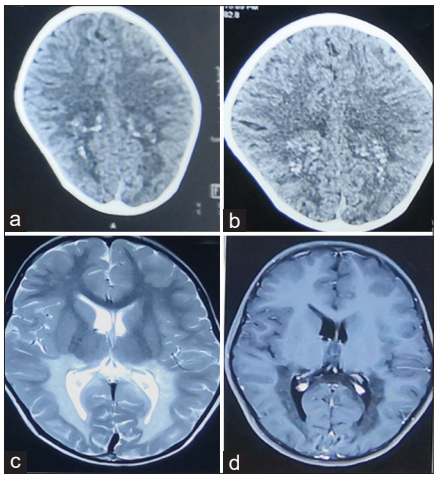

Figure 1: Neuroimaging of the index child. Contrast Computed tomography images show calcifications in bilateral parieto-occipital white matter (a, b); T2W MRI images show confluent hyperintense signal intensities in parieto-occipital periventricular white matter (c) and T1W contrast MRI images showing no contrast enhancement (d)

cerebral ALD, adrenomyeloneuropathy with or without cerebral demyelination in late adulthood, and symptomatic and asymptomatic carriers.[2] Cerebral ALD is an insidious onset (as in the index child), rapidly progressive disorder that presents with deficits in attention and reasoning and may mimic attention deficit hyperactivity disorder.[2] Brain MRI is the preferred imaging modality for the detection of progressive demyelination and evolution of the disease when compared to CT. The classic MRI findings include parieto-occipital white matter (WM) abnormalities with complete sparing of arcuate fibres. On histopathology, three zones have been described- outer active demyelination zone, middle inflammatory zone, and innermost burnt-out zone.[3] Besides, contrast enhancement has a role in determination of progression of the disease. Also, different radiological patterns have been described for X-ALD. These include – the classical parietooccipital WM involvement, frontal WM predominant, isolated involvement of tracts, and cerebellum or a combination of any of these.[4] Many of these patterns are reported with Krabbe disease which is the closest differential diagnosis.[5]

Symmetrical calcifications have been rarely reported in childhood X-ALD. If present, they are often seen in the innermost zone and may be an early sign of progression to inflammatory stage of X-ALD.[1,2,6] Intracranial calcifications have also been described in other neurodegenerative disorders such as Cockayne syndrome, Alexander disease, Krabbe disease, mitochondrial cystic leukoencephalopathies, Fabry disease and sulphite oxidase deficiency.[7] Proposed hypothesis for calcium deposition in the brain for different neurological disorders include inflammation and secondary to white matter degeneration (X-ALD, Krabbe disease), microangiopathy (mineralising microangiopathy), dystrophic process (Dural arteriovenous fistula), abnormal calcium metabolism (hypoparathyroidism), etc.[8,9]

In X-ALD, the calcifications are usually seen around the peritrigonal and periventricular regions.[10] The characteristic location of calcifications in an appropriate clinical setting may aid in narrowing the differential diagnoses. Hence, computerized tomography may help in an early diagnosis of ALD especially in resource constraint settings.

Consent

Written informed consent obtained from parents.

Ethical statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Conflicts of interest

There are no conflicts of interest.

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