Optic nerve demyelination as the presenting feature of adrenoleukodystrophy in a child

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Adrenoleukodystrophy (ALD) is an x-linked recessive lipid storage genetic disorder due to modifications in the ABCD1 (ATP-binding cassette) gene, resulting in defective peroxisomal β-oxidation and the excessive collection of very-long-chain fatty acids (VLCFAs) in tissues and plasma.[1] It causes progressive demyelination of the nervous system and manifests as dementia, behavioral changes, gait disturbances, sensory disturbances, and visual loss.[2] It can also present as a primary adrenal insufficiency resulting in hyperpigmentation in the skin and testicle. The incidence rate of ALD is 1 in 20,000 population.[3] Childhood ALD is the most common variant, and it primarily presents with either neurological symptoms or adrenal insufficiency.[4] Visual disturbance eventually develops due to optic atrophy.[2] We report a case of childhood adrenoleukodystrophy presenting with visual disturbances as the first symptom without any neurological signs.

A 9-year-old boy presented with acute painless gross diminution of vision in both eyes for 5 days. He was born of a non-consanguineous marriage and was developmentally normal. No associated ocular complaints were preceding or concurrently associated with this episode. There were no focal neurological deficits or neuropsychiatric symptoms. Neurological examination was normal; motor examination showed normal power and tone in all four limbs. The sensory system and gait were normal, and there were no cerebellar signs. On ophthalmic examination, uncorrected visual acuity (UCVA) was recorded to be finger counting close to face (FCCF) in both eyes. Refraction was emmetropic. The ocular position was orthotropic, and the extraocular movements were full, free, and painless. Anterior segment examination was within normal limits, and pupillary reactions were brisk. Fundus examination of both eyes was normal [Fig. 1a and 1b]. The visual evoked potential (VEP) showed delayed N2P2 latency with reduced amplitude in RE (N2P2 peak at 136.9 ms, amplitude: 1.59) and reduced N2P2 latency with reduced amplitude in LE (N2P2 peak 72.2 ms, amplitude: 2.35) [Fig. 1c]. Magnetic resonance imaging [Fig. 2] of the brain revealed bilateral, symmetric, and confluent T2/FLAIR hyperintensities/T1 hypo intensities with no significant diffusion restriction noted involving the periventricular, deep white matter of the parieto-occipital-temporal regions. The involved white matter showed trizonal distribution in the form of central T2 hyperintense, intermediate less T2 signal intensity changes, and the peripheral zone of serpiginous post-contrast enhancement. No abnormal STIR hyperintense signal was noted along bilateral optic nerves, and the orbits were normal.

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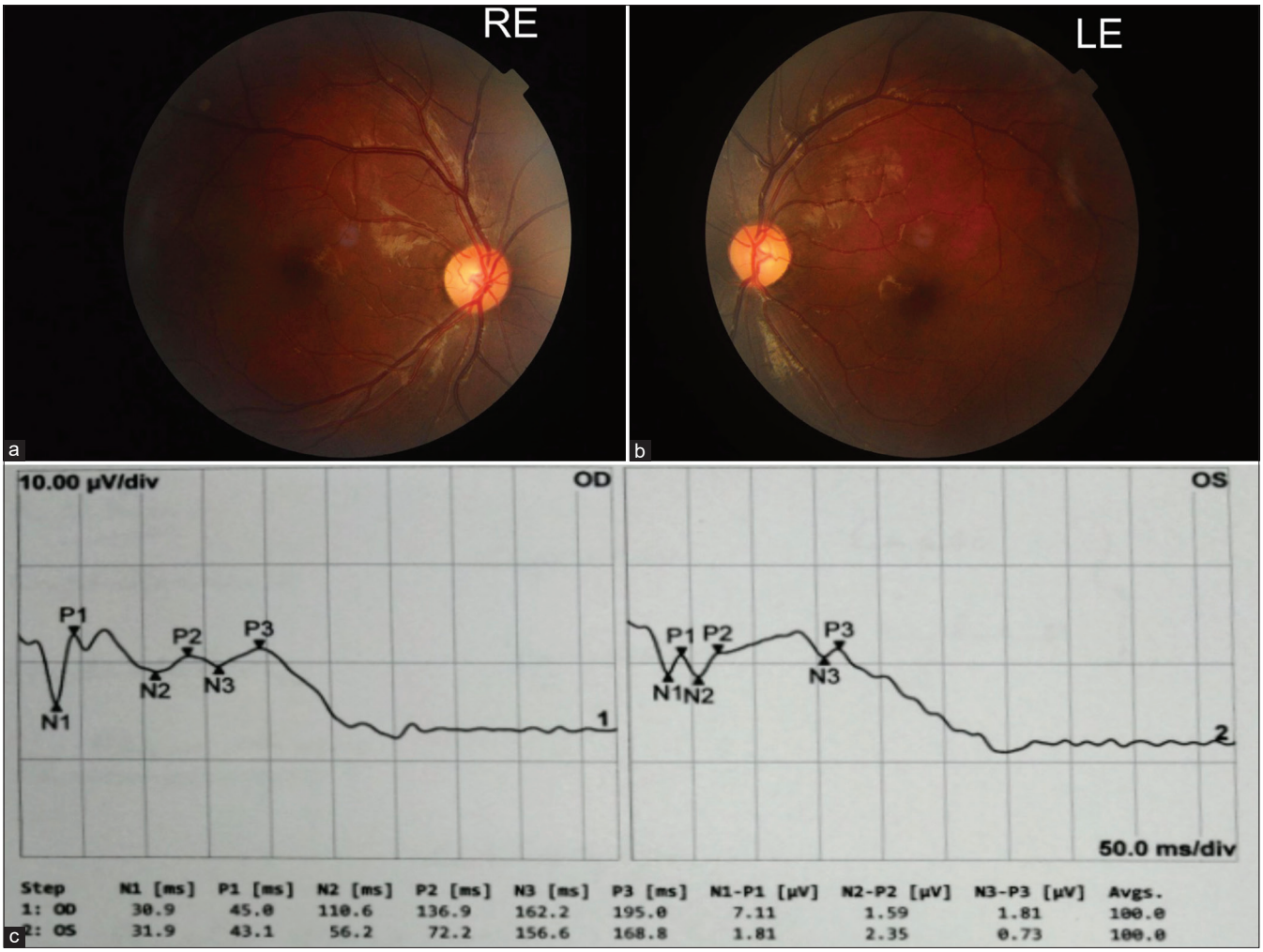

Figure 1: Fundus images (a) and (b) of both eyes showing normal disc and macula without any evidences of disc pallor, (c) visual evoked potential showing abnormal latency with reduced amplitude

Magnetic resonance spectroscopy (MRS) of the involved areas showed decreased NAA with elevated choline/NAA ratio and increased lactate peak [Fig. 3]. CSF analysis did not yield any significant findings. Serum cortisol levels (7–9 am) were below the normal reference range (2.21 µg/dl), and serum ACTH levels were highly elevated (162 pg/ml). Complete blood count and other biochemical tests were within the normal range. Based on the clinical presentation and classical MR imaging and spectroscopy finding, the diagnosis of adrenoleukodystrophy was established. Although a trial of pulse dose intravenous methylprednisolone 30 mg/kg/day in two divided doses for 3 days followed by oral steroids tapered for 3 weeks were prescribed, seeing no improvement in the visual acuity, the steroids were discontinued. The child has been kept in close monitoring for the last 1 year, and on the last follow-up visit, the child seems to develop some abnormal repetitive movements in both upper limbs.

Discussion

Adrenoleukodystrophy most commonly affects the myelin in the CNS, the adrenal cortex, and the Leydig cells in the testes.[5] Four significant disease variants have been described in the literature: neonatal ALD, childhood ALD, adrenomyelopathy (AMN), heterozygote carrier, and Addison's phenotype. Among all the variant childhood, ALD is the most common type, presenting 33%–35% of all cases. It appears at 4–8 years of age. The child often presents with progressive cognition difficulties, hearing loss, motor function loss, and permanent disability within 2 years of presentation. The patients develop visual disturbances due to optic atrophy in months to years. Progressive vision loss is caused by demyelination of the central nervous system involving the optic tracts.[2,5,6] The demyelination of the neural optic pathway results in cellular death of retinal ganglion cells demonstrable on optical coherence tomography as bilateral thinning of the RNFL around disc and loss of macular thickness and volume.[7] Traboulsi EI *et al*.[2] described the ocular manifestation in 15 ALD patients and strabismus (10/15), followed by pale optic discs (7/15); macular pigmentary changes were the most common findings.

ALD causes severe demyelination in the occipital and posterior parietal areas and is characterized by peripheral zones of active demyelination and central zones of almost total myelin loss with prominent perivascular round cell infiltration.[8] The diagnosis of leukodystrophies is based

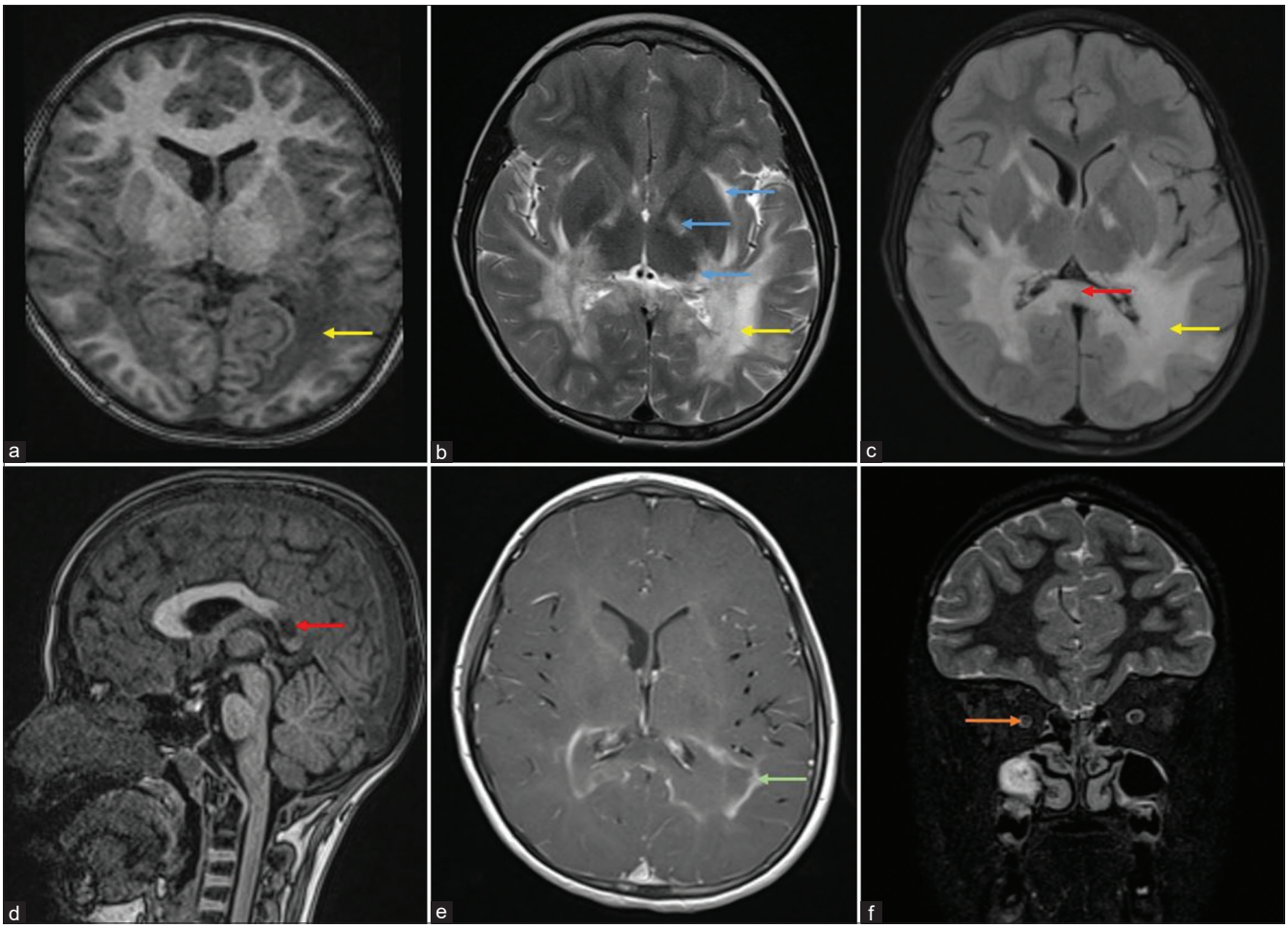

Figure 2: Magnetic resonance imaging of brain shows bilateral symmetric confluent areas of hypointensities on T1 (a) and hyperintensities on T2 (b) and FLAIR sections (c) involving parieto-occipital white matter (yellow arrows), splenium of corpus callosum (c, d-red arrow), external capsule, internal capsule, pyramidal tracts, and lateral geniculate area of the thalamus (B-blue arrows). Post-contrast study (e) shows typical peripheral enhancement (green arrow) at the mid-zone of the parieto-occipital white matter suggesting active inflammation. STIR coronal image (f) showing subtle hyperintensity involving bilateral optic nerves (orange arrow)

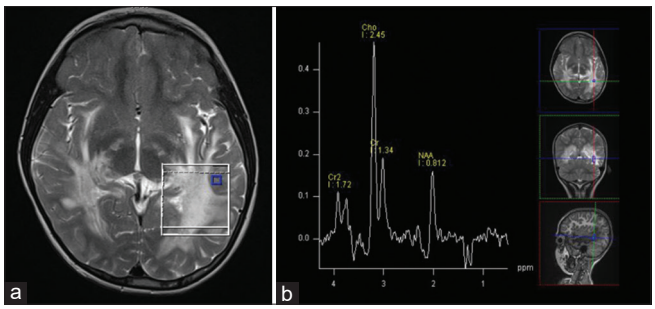

Figure 3: Magnetic resonance spectroscopy (MRS) images (a) and (b) of the involved areas and margins showed decreased NAA with elevated choline/NAA ratio and increased lactate peak

on distinctive clinical features, biochemical markers, magnetic resonance imaging; the latest modalities such as magnetic resonance spectroscopy also have a distinct role. MR imaging of the patient showed bilateral symmetric and confluent T2/FLAIR hyperintensities/T1 hypo intensities involving the periventricular, deep white matter of the parieto-occipital-temporal regions, corticospinal tracts at the posterior internal capsule, thalami, brain stem (midbrain, pons, and medulla), and in the spinal cord which is similar to the findings described by Patel *et al*.[9] and Santosh Rai *et al*.[10] Kim *et al*.[11] specified that brain MRI is an important tool for early detection and differentiation from other neurodegenerative disorders at presentation as well as follow-up evaluation. Magnetic resonance spectroscopy (MRS) of involved region showed decreased NAA with elevated choline/NAA ratio and increased lactate peak, which is a diagnostic sign of adrenoleukodystrophy. MR spectroscopy can be regarded as a useful, noninvasive tool to monitor these patients.[12] Other leukodystrophies such as metachromatic leukodystrophy or multiple sclerosis can mimic a similar clinical presentation, but the classical MRI pattern helps in diagnosing this condition. We need to keep a very close follow-up for these patients as they are very likely to develop neurological disability within two years.

Statements

Statement of ethics

Written informed consent for publication (including the images) has been obtained from the parent of the patient. All

procedures carried out were in accordance with the tenets of the Declaration of Helsinki. Institute Ethics Committee approval is not required for a case report according to the Indian Council of Medical Research guidelines.

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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Conflict of interest

There are no conflicts of interest.

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