Labrune syndrome: A unique leukoencephalopathy

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Clinical Case

A 10-year-old male child weighing 23 kg, born of nonconsanguinous union with no perinatal complications first sought medical attention for headache of 1 year duration which was predominantly in the frontal and occipital region, throbbing in nature, almost continuous, which interfered with her sleep and studies. Cough worsened the headache. He was admitted to our facility following aggravation of headache with recurrent bouts of vomiting and focal seizures typified by left hemifacial clonic movements. General physical was unremarkable. The visual examination did not reveal telengiectasias, exudates, retinopathy, optic atrophy, or any other relevant findings. Neurological examination revealed a fully conscious and alert child with mildly increased muscle tone, brisk deep tendon reflexes, bilateral extensor plantar response, subtle signs of neck rigidity and positive Kernig's sign and symmetrical cerebellar signs in the form of limb dysmetria, intention tremor, and gait ataxia. There was history of antitubercular therapy taken for 9 months for tubercular lymphadenitis at the age of 2 years.

Complete blood count, sedimentation rate, liver and renal function tests, serum calcium, phosphate, alkaline phosphatase levels, chest radiograph, and abdominal sonogram were within normal limits. Serological tests for hydatid, toxoplasma, cysticercosis, cryptococcosis, cytomegalovirus immunodeficiency, and human virus (HIV) were negative.

Computed tomography (CT) topogram revealed luckenschadel skull with intracranial calcification [Figure 1a]. Axial sections of brain revealed extensive calcification involving bilateral deep cerebellar nuclei, gray and white matter junction and bilateral gangliocapsular region and thalami [Figure 1b-d]. Magnetic resonance imaging (MRI) of the brain revealed extensive T2 and fluid-attenuated inversion recovery hyperintensity involving bilateral periventricular white matter with sparing of subcortical U-fibers and corpus callosum [Figure 2 a-d] with cystic changes and obstructive hydrocephalus [Figure 3a-d]. The calcification seen in CT showed hypointense signal intensity on T2-weighted image (WI), gradient echo (GRE), T1-WI with blooming on GRE [Figure 4a and b].

The clinical and radiological picture was classical of leukoencephalopathy, cerebral calcifications and cysts (LCC) with features of obstructive hydrocephalus. A ventriculo-peritoneal shunt was advised by the neurosurgery team, but the family was not willing for any invasive procedures. The patient was started on valproic acid and acetazolamide which produced good symptomatic relief.

Discussion

The association of extensive cerebral calcification, white matter changes, and cysts is an entity described by Labrune *et al*., in 1996[1] as LCC. It is extremely rare with only 10 cases reported so far in the medical literature. It has been reported from around the world in children and adults, with onset up to 59 years. The ubiquitous presentation with seizures and progressive neurodeficit in a child invites a huge list of differential diagnoses, but the classical radiological features make the diagnosis of LCC unmistakable.[2]

Close differentials include parasitic infections such as hydatid, cysticercosis, and cryptococcosis. In neurocysticercosis,

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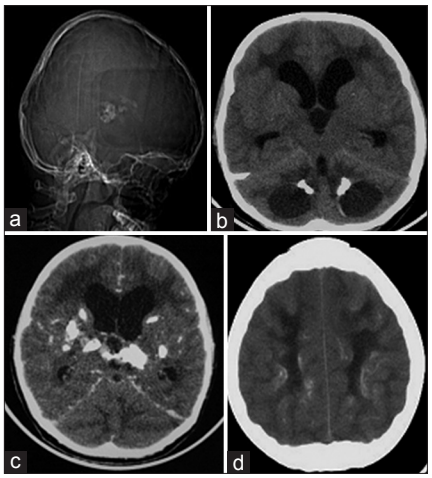

Figure 1: (a) Computed tomography topogram revealed luckenschadel skull with intracranial calcification. (b) Non contrast axial computed tomography image showing calcification of the Dentate nuclei. (c) Non contrast axial computed tomography images showing exuberant calcification in bilateral Gangliocapsular region, Thalamus (red arrows) and (d) grey-white matter junction

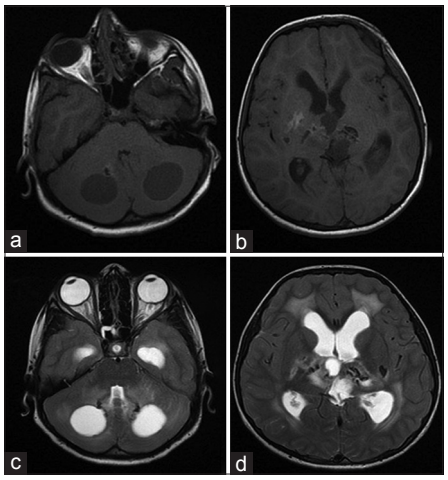

Figure 3: T1-weighted (a and b) and corresponding T2-weighted (c and d) images showing cysts in bilateral Cerebellar hemispheres (white arrow), above the third ventricle and in the region of Pineal gland. There is also associated obstructive hydrocephalus

there are multiple cystic lesions with variable parenchymal calcification.[3] Gelatinous pseudocyst and parenchymal calcification are reported in HIV patients with cryptococcosis.[4] However, no serologic evidence was found for these infections and in addition, leukoencephalopathy is not a characteristic feature of these entities. Other diseases which show extensive basal ganglia and cerebellar nuclei calcification like Fahr's disease do not have other features such as cystic lesions and leukoencephalopathy. To the best of our knowledge, ours is probably the first case of a child reported in Asia. Our patient presented with raised intracranial pressure and cyst related mass effects, which are the main presenting features of LCC. Etiopathogenesis of LCC is still a matter of debate. Obliterative microangiopathy has been found to be the basic abnormality in histopathological examination. It is postulated that cyst

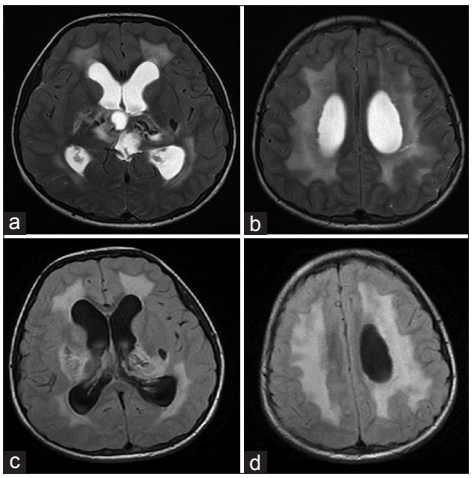

Figure 2: T2-weighted (a and b) and corresponding fluid-attenuated inversion recovery (c and d) images showing diffuse white matter hyperintensity suggesting leukoencephalopathy

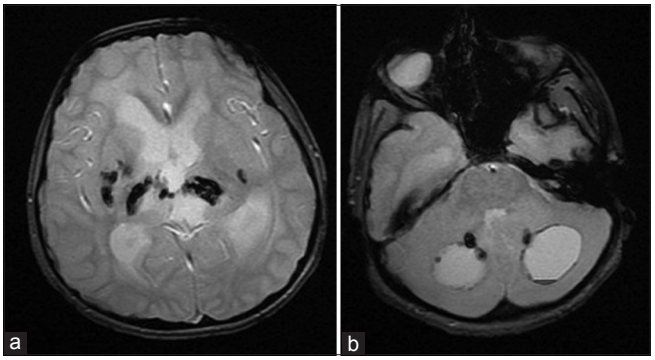

Figure 4: (a and b) magnetic resonance imaging shows blooming in bilateral Basal Ganglia, Thalami and Dentate nuclei on gradient echo images suggesting calcification

formation is due to necrotic process secondary to obliterative microangiopathy and calcification seen is dystrophic in nature.[5] White matter changes are a result of changes in water content rather than a primary abnormality of myelination. Clinical presentations are myriad and include convulsions, pyramidal, extrapyramidal cerebellar features, cognitive decline, retinal microangiopathy, and dystonia. Progression and severity can be variable. Calcifications are reported predominantly in basal ganglia but can also occur in cerebellum and cerebral cortex.[6] Parenchymal cysts can occur both in cerebral hemispheres and infratentorial compartment. White matter changes are seen predominantly in relation to the cysts and in the periventricular location.[7] Similar leukoencephalopathy, cysts, and calcification have been reported in few cases in association with Coat's disease, an emerging entity described as "Coat's plus."[8] Coat's disease is unilateral retinal telangiectasia with exudation commonly occurring in boys sporadically without systemic features. However, in Coat's plus, there is bilateral retinal telangiectasia with exudation along with systemic features in the form of LCC. However, in our case, examination of eyes revealed no retinal abnormality. Another entity which deserves a special mention is cerebroretinal microangiopathy with calcifications and cysts.[7] This includes both LCC and Coat's plus diseases. A certain degree of overlap has been

seen in anecdotal reports between these two entities, but the identification of the CTC1 gene has endowed a distinct genetic identity for the latter. The commonality remains at the level of the pathophysiological mechanisms especially the presence of obliterative microangiopathy. However, further studies are needed to validate this concept.[8]

Conclusion

We can say that, even though this triad of CT/MRI findings has been observed in other diseases, it is fairly characteristic to allow the diagnosis of Labrune syndrome to be made. This is only the second report of this distinct neuro-radiological constellation from the subcontinent.[9] Another noteworthy previously unreported feature of the present case was the presence of multiple cysts in both the supra and infratentorial compartments along with other typical findings of Labrune syndrome.

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Conflicts of interest
There are no conflicts of interest.

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