

LEUKOENCEPHALOPATHY WITH CEREBRAL CALCIFICATIONS AND CYSTS IN A YOUNG ADOLESCENT FEMALE: A CASE REPORT

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ABSTRACT

Leukoencephalopathy with cerebral calcifications and cyst (LCC), also known as Labrune syndrome (first reported by Labrune in 1996), is a rare condition in which progressive parenchymal cysts and calcifications within a widespread edematous leukoencephalopathy can cause a broad spectrum of neurological symptoms.^{1,2,3,4} Till now fewer than 50 cases of LCC in literature are reported.

In this report, a new case of LCC, who presented at an age of 11 yrs at our institution in 2017 with history of GTCS, followed up with clinical, neuroradiological and histopathological findings are discussed in view of the relevant literature.

Key words: Leukoencephalopathy, cerebral calcifications, cyst, labrune syndrome

Case Report

- A 11 yr old female child was admitted to our hospital for the evaluation of generalised tonic-clonic seizures which started 1 years ago.
- She was born after an uneventful pregnancy. Her apparently healthy parents were non consanguineous. No abnormality was found on general physical, ophthalmological and neurological examinations.
- Complete blood count, ESR, liver and renal function tests, serum thyroid and parathyroid hormones, calcium, phosphate, alkaline phosphatase and lactate levels were within normal limits.
- CSF study for protein, sugar, cells, ZN and Gram stain was normal.
- Serological tests for cytomegalovirus, toxoplasma, hydatid cysts, and HIV 1 and 2 were all negative.
- Initial CT (2017) showed numerous foci of coarse calcifications scattered in dentate nuclei of cerebellum, basal ganglia and in the subcortical white matter region. Additional finding was dec-

reased attenuation of the white matter surrounding some of the lesions. There were associated cyst formation in centrum semiovale region measuring 18×16mm. seizures were controlled temporarily by carbamazepine. (Fig. 1)

One year later the patient was readmitted. Repeat CT showed progression of disease in the form new cysts formation and increase in calcification. (Fig. 2)

- MRI study revealed:
 - Cystic lesion in centrum semiovale, periventricular and basal ganglia region with largest one in left thalamus (34×33 mm) with CSF signal intensity in all pulse sequence without much post contrast enhancement.
 - GRE images show multiple focal calcifications seen in bilateral periventricular region and also in the posterior fossa.

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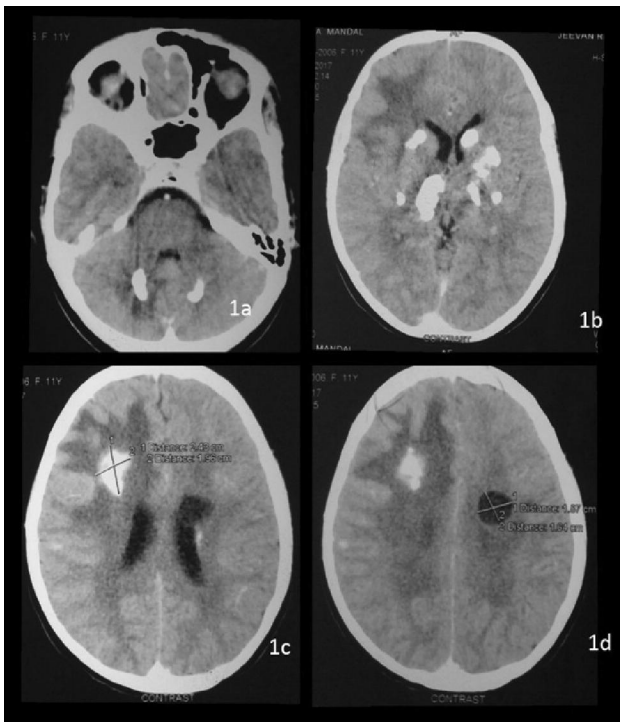


Figure 1: Axial CT showing **1a.** calcification in dentate nuclei **1b.** calcifications in bilateral basal ganglia region **1c.** a calcific lesion in right frontal region with surrounding hypodensity in white matter **1d.** a cyst with surrounding hypodensity in left centrum semiovale region.

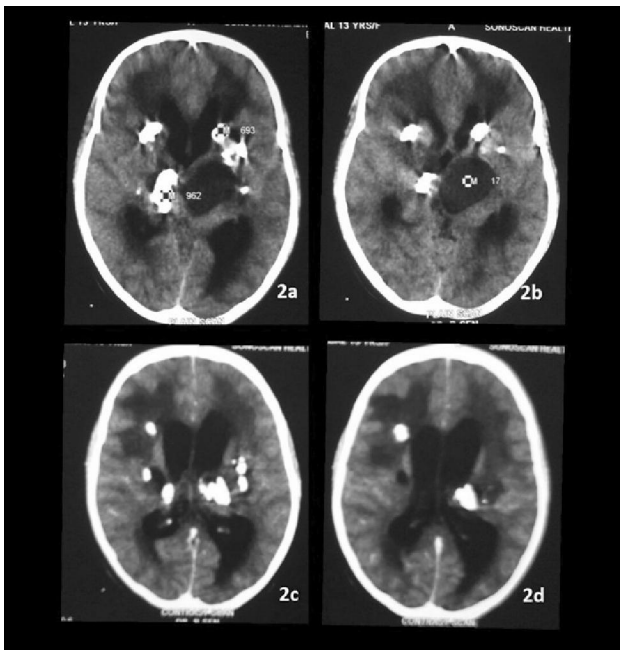


Figure 2: **2a & 2b.** multiple calcifications in bilateral basal ganglia region with a new cyst formation in left thalamic region and hypodensity in bilateral periventricular region **2c & 2d.** calcifications, cysts and hypodensity of white matter in bilateral periventricular region.

- Diffuse hyperintensity in the white matter, especially prominent around cysts (due to vasogenic edema) with relative sparing of the subcortical U fibres and corpus callosum in T2 FLAIR suggestive of leukoencephalopathy.
- MRS study revealed raised lactate peak

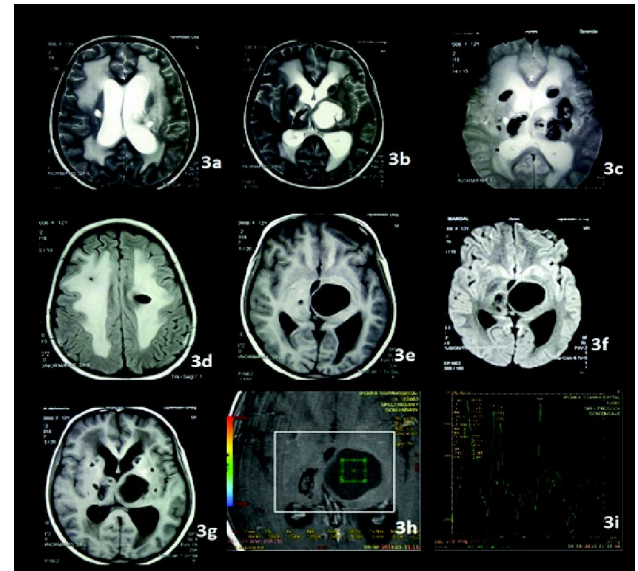


Figure 3: MRI axial sections showing **3a & 3b** (T2WI). varying sized multiple cysts and calcifications in bilateral basal ganglia and periventricular region along with long TR hyperintensity in periventricular region. **3c.** multiple foci of GRE blooming in bilateral basal ganglia **3d.** long TR hyperintensity along with cysts formation in bilateral centrum semiovale region. **3e.** T1WI showing CSF intensity inside the cysts with mild mass effect on third ventricle. **3f.** no restriction in DWI **3g.** on contrast study mild ring enhancement of few cysts. **3h & 3i.** MRS showing lactate peak at 1.25 ppm.

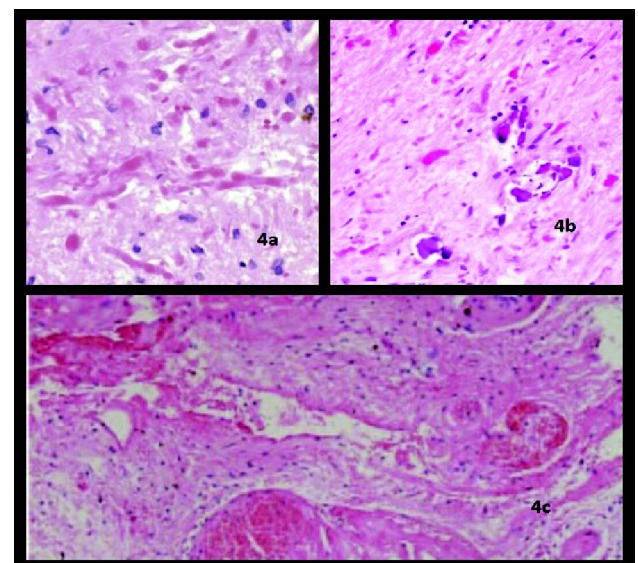


Figure 4: **4a & 4b.** there is evidence of calcification, gliosis with profuse Rosenthal fiber formation **4c.** vascular stenosis surrounded by exudation.

- Histopathology from biopsy material revealed haemorrhage with surrounding loose tissue and calcification. Edematous parenchyma with moderate gliosis and prominent angiomatous changes (numerous small tortuous blood vessels). Perivascular calcification and neutrophils were visible.
- Excluding the nearest differential diagnosis and based on typical radiological and histological findings, diagnosis of LCC was made.

Discussion

LCC is characterised by extensive brain calcifications, leukodystrophy, and formation of parenchymal cyst. The onset may occur from early infancy to adolescence with signs including cognitive decline, convulsive seizures, and pyramidal, extrapyramidal, and/or cerebellar signs. However an adult onset form is also suggested. There is a modest predilection for females.

Our patient first experienced GTCS at the age of 7 years. However there was only few episodes of seizure without any cognitive decline over the years. In contrast to the clinical course, a severe and progressive neurodegenerative process was shown in central nervous system on neuroimaging.

The probable pathophysiology as described by Labrune et al is exuberant proliferation and rearrangements involving the microvessels which leads to tissue ischaemia and hypoxia, ultimately leads to perivascular foci of calcifications, hyaline deposits, and formation of Rosenthal fibres as secondary changes.^{4,5,6}

Recently demonstrated the genetic basis of LCC to be due to mutation in SNORD 118 on chromosome 17p13 encoding the sno RNA U8. This mutation affects U8 expression, processing and protein binding and thus implicate U8 as essential in cerebral vascular homeostasis.⁷

CT and MR findings in this case were similar to those of other cases described in literature showing increased white matter signal intensity relatively sparing the U fibres and corpus callosum with extensive coarse progressive calcifications in the basal ganglia, brain stem, cerebellum and subcortical white matter and development of parenchymatous cysts.

Post contrast study showed only mild ring enhance-

ment of few cysts possibly due to disruption in blood brain barrier. DWI shows no diffusion restriction with intense blooming on GRE suggestive of calcific foci.

MR Spectroscopy of the cysts showed a doublet in 1.25 ppm representing lactate peak.

During follow up, some cysts enlarged with appearance of new cysts. Expanding cystic formations may be the consequences of progressive increase in fluid content of white matter.

Differential Diagnosis

- TORCH infections-usually subependymal pattern of calcification, cerebral cortical abnormalities are prominent.

Serology is confirmatory.

- Neurocysticercosis
- Echinococcosis
- Pseudo TORCH syndromes: COATS plus syndrome (CTC1 mutation, retinal angioma, osteopenia)
 - Aicardi syndrome
 - Adams Oliver syndrome
 - T2 deficient leukoencephalopathy
 - Baraitser-Reardon syndrome

All metabolic causes of basal ganglia calcifications (Fahr's disease, hypoparathyroidism, pseudohypoparathyroidism, pseudopseudohypoparathyroidism)

Conclusion

LCC is a rare disorder characterized by extensive white matter degeneration, asymmetric cerebral calcifications and formation of parenchymal cysts. The definitive pathogenetic mechanism still needs further research.

ABBREVIATIONS

LCC - leukoencephalopathy, calcifications and cysts

GTCS - generalised tonic clonic seizures

ESR - erythrocyte sedimentation rate

CT - computed tomography

MRI - magnetic resonance imaging

MRS - magnetic resonance spectroscopy

Conflict of Interest: None

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