Case Report

Leukoencephalopathy with Calcifications and Cysts in a Child with Progressive Hemiparesis—A Case Report

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INTRODUCTION

Leukoencephalopathy with calcifications and cysts (LCC) or Labrune syndrome is a rare autosomal recessive disorder with a striking radiological appearance and a progressive clinical course. The large nodular morphology and central distribution of calcifications in LCC are key distinguishing features in its diagnosis and differentiation from other calcifying and cystic leukoencephalopathies. Herein, we present a case of a 9-year-old boy with this rare disorder.

CASE REPORT

A 9-year-old boy, born of a nonconsanguineous marriage, presented for evaluation of seizure disorder and gradual progressive weakness of left upper and lower limbs of a 3-year duration. The seizures were generalized tonic-clonic in nature with one to two episodes per month and without any preceding aura. The left hemiparesis was gradual in onset and slowly progressive in the course and has become severe enough to affect his daily motor activities and was associated with poor scholastic performance. No similar history was present in his family. On examination, the muscle power in the left upper and lower limbs was grade 3 (MRC scale).

A magnetic resonance imaging (MRI) of the brain was done [Figure 1], which revealed varying sized cysts in the subcortical and deep white matter of bilateral cerebral hemispheres. Few of these cysts showed internal hemorrhage with fluid-hemorrhage levels within. The susceptibility-weighted images showed evidence of calcification in bilateral basal ganglia, along the wall of the cysts and few in bilateral centrum semiovale. Nodular enhancement was noted along the regions of smaller calcifications in the parenchyma. Also, diffuse and asymmetrical T2/FLAIR hyperintensity involving the periventricular and deep white matter was noted sparing the corpus callosum and posterior fossa structures. A noncontrast computed tomography (CT) scan head [Figure 2] confirmed the dense aggregates of nodular calcifications in bilateral basal ganglia. Few curvilinear, faint, blush-like calcifications were noted at the gray–white matter junction of bilateral cerebral...
hemispheres. The genetic profiling was not done, however the neuroimaging features and clinical profile were consistent with a diagnosis of LCC.

**DISCUSSION**

LCC is a rare genetic disorder characterized by diffuse cerebral microangiopathy causing microcystic and macrocystic white matter degeneration. The earliest description of this disease was given by Labrune et al., in 1996 in a series of three unrelated children with progressive neurologic symptoms and imaging features of noncortical parenchymal cysts, calcifications, and diffuse white matter hyperintensities.

LCC is characterized pathologically by angiomatous-like blood vessels, gliosis, and Rosenthal fiber deposition. It usually affects children, however, late-onset presentations in adulthood have also been described. It is now well established that LCC is an...
autosomal recessive disease with mutations involving the *SNORD118* gene.\[^3\] The clinical presentation of LCC is variable and consists of progressive cognitive slowing, seizures, pyramidal/extrapyramidal, and cerebellar symptoms. The neurodeficits are initially mild, but progressive and usually requires surgical intervention once the cysts become large enough to produce mechanical complications.\[^4\]

The imaging appearance of LCC consists of extensive, asymmetric, and predominantly central white matter hyperintensity on T2WI; coarse bulky calcifications in basal ganglia, dentate nuclei, and brainstem; and intraparenchymal cysts.\[^4\] The calcifications in LCC have been characteristically described as large, bulky, nodular, dense rock-like aggregates in central gray nuclei and spot-like calcification in deep white matter.\[^4,5\] Calcifications bearing this morphology were present in our case. Additionally, our case also showed curvilinear faint/blush-like calcifications along the gray–white matter junction of both cerebral hemispheres. Such a morphological pattern of calcification at the gray–white matter junction has not been described in previous reports of LCC.

The neuroimaging differentials of intracranial calcifying diseases with white matter changes and cysts include Coats plus syndrome, *COL4A1* mutation-related disease, Aicardi–Goutieres syndrome (AGS), and TORCH infections.

Coats plus syndrome is characterized by bilateral retinal telangiectasia, exudative retinopathy, intracranial calcification, leukoencephalopathy, and intraparenchymal cysts. Owing to similar radiopathological features, Coats plus syndrome and LCC were previously considered as two different manifestations of a common entity and were clubbed together as “cerebroretinal microangiopathy with calcification and cysts” phenotype.\[^6\] However, Coats plus syndrome was recently found to have a separate genetic origin (*CTCI* gene mutation) and is now considered a different entity from LCC.\[^7\] The important differentiating feature is the presence of bilateral retinal telangiectasia with exudation in Coats plus syndrome which is not described in LCC.

*COL4A1* mutation-related disorders are rare, genetically inherited small vessel disease causing microhemorrhages and ischemic injury to brain parenchyma in the perinatal or postnatal period resulting in a porencephalic cyst, periventricular leukomalacia, and fine periventricular, basal ganglia and deep white matter calcifications. *COL4A1* mutation affects the vascular basement membrane of multiple systems, especially the eyes and kidneys. Hence, nonneurologic features such as reduced vision, retinal arterial tortuosity, retinal microhemorrhages, congenital cataracts, renal cysts, proteinuria, and hematuria may be present and help to differentiate it from LCC which is devoid of extraneurologic manifestations.\[^8\] In contrast to LCC, the calcifications in *COL4A1* mutation-related disease are fine and punctate, the cysts communicate with the ventricles, and the periventricular white matter is atrophied.\[^5\]

In AGS, the calcium deposits are small and punctate, white matter abnormalities are usually symmetric with associated cerebral atrophy.\[^5\] Besides, AGS typically presents in the first year of life, unlike in the present case where the age of onset of symptoms was 6 years.

TORCH infections, particularly cytomegalovirus infection, may present with periventricular and basal ganglia calcifications, patchy white matter changes, cortical malformations, predominant anterior temporal cystic abnormalities, microcephaly, and cerebral atrophy. In LCC, the white matter changes are diffuse, the cysts are more central in location (within the basal ganglia), and there are no associated cortical malformations or cerebral atrophy.\[^5\]

LCC can cause mechanical complications like hydrocephalus or mass effect due to the progressively expanding cysts. Such large cysts need surgical removal.\[^9\] Anti-vascular endothelial growth factor (VEGF) therapy has been reported as useful in decreasing the size of these cysts.\[^10\]

To summarize, LCC is a rare disorder with progressive neurodegeneration and characteristic radiologic abnormalities. In addition to the bulky central calcifications characteristic of LCC, our case also demonstrates curvilinear blush-like calcification along the gray–white matter junction. Identification of key imaging features of LCC aids in its accurate diagnosis and differentiation from other disorders, especially in children.

**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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Conflicts of interest
There are no conflicts of interest.

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