Adult Onset Leuko-encephalopathy, Cerebral Calcifications and Cysts.

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ABSTRACT

Leuko-encephalopathy, brain calcifications and cysts (LCC) known as Labrune syndrome, is a rare syndrome. It is primarily described in childhood and adolescence as presenting with neurological impairment of relatively rapid progression and intra-cerebral hemorrhage that frequently leads to death. The etiology is unknown & there is no specific clinical feature suggestive of this disorder. Here in, we report a 34-year old man with LCC who had chronic Headache & neurological symptoms beginning in adulthood and discuss recently described entities in view of the relevant literature.

Keywords: Brain Calcifications & Cysts, Labrune Syndrome, Leukoencephalopathy.

INTRODUCTION

Leuko-encephalopathy, intracranial calcifications, and cysts (LCC) is a very rare cerebral disorder reported from around the world in children and adults. The clinical presentation is insidious and variable. All the reported patients have a characteristic triad of calcification in the deep cerebral nuclei and white matter, diffuse leuko-encephalopathy, and multiple cystic brain lesions on brain imaging. We report an adult case with clinical & radiologic features consistent with LCC.

CASE REPORT

A 34-year old man was referred for the evaluation of chronic headache for the past 4 years. He was born after an uneventful pregnancy. His apparently healthy parents were not consanguineous. No abnormality was found on general physical, ophthalmologic, and neurologic examinations.

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Complete blood count, sedimentation rate, liver and renal function tests, serum thyroid and parathyroid hormones, calcium, phosphate, alkaline phosphatase, and lactate levels were within normal limits. Serological tests for cytomegalovirus, toxoplasma gondii, toxacara canis and cati, hydatid cyst, and HIV 1 and 2 were all negative. Cervical, thoracic, and abdominal CT examinations showed no abnormality. Scalp EEG showed minimal slowing in background activity at the left fronto-temporal area with no epileptiform activity.

Clinically, he had slowly progressive pyramidal symptoms and normal intelligence. The initial CT showed numerous foci of calcifications scattered in the pons, cerebellum, basal ganglia and all lobes of the brain. The supra-tentorial lesions were predominantly located in the subcortical white matter. Some of the calcified lesions were associated with cystic formations and surrounding white matter edema. The largest cysts showed internal hemorrhage & fluid blood level due to hematocrit effect [Figure 1.A-F]. The diameters of the cysts ranged from 3-18 mm & calcifications from 2-10mm.

MR imaging showed more cysts associated with the calcifications than seen on CT [Figure 2.A-E]. Abnormally increased signal intensity was noted in the bulbous pons, bilateral cerebellar peduncles, both basal ganglia, as well as in both hemispheric white matter always surrounding a cyst or a focus of calcification representing vasogenic edema with evident mass effect [Figure 3.A-K].

The intensity of the cysts was higher than that of the CSF on T2-weighted and fluid-attenuated inversion recovery images [Figure 4.A-E] with ring enhancement of the cyst walls following intravenous gadolinium contrast [Figure 5.A-H & Figure 6.A-F]. Diffusion Weighted Images show no restricted diffusion [Figure 7.A-E] with increased ADC values [Figure 8.A-E].

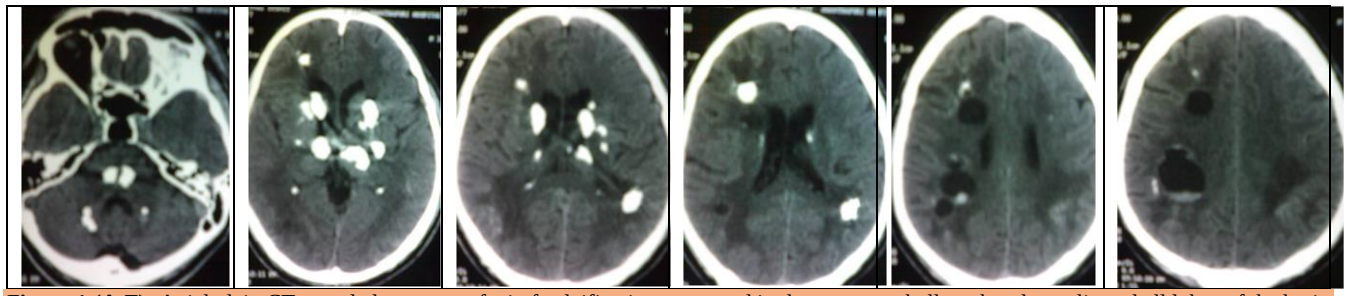

Figure 1 (A-F): Axial plain CT revealed numerous foci of calcifications scattered in the pons, cerebellum, basal ganglia and all lobes of the brain in the subcortical white matter with some of the calcified lesions associated with cystic formations and surrounding white matter edema. The largest cysts showed internal hemorrhage & fluid blood level due to hematocrit effect.

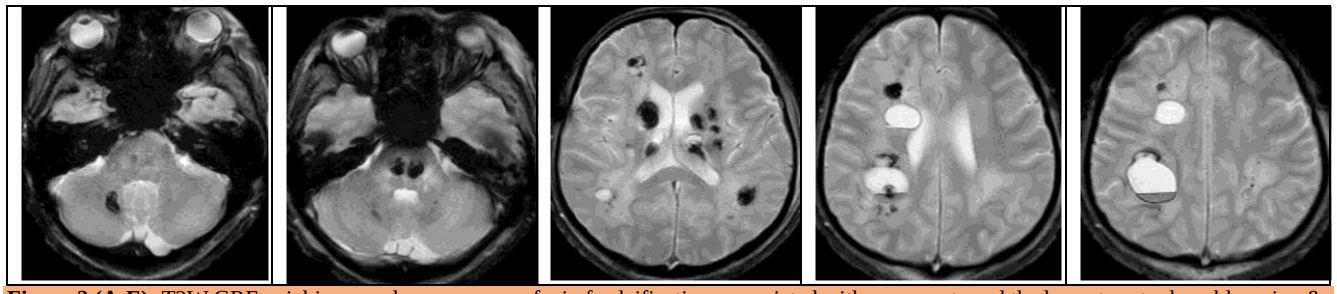

Figure 2 (A-E): T2W GRE axial images show numerous foci of calcifications associated with more cysts and the largest cysts show blooming & fluid blood level due to hematocrit effect.

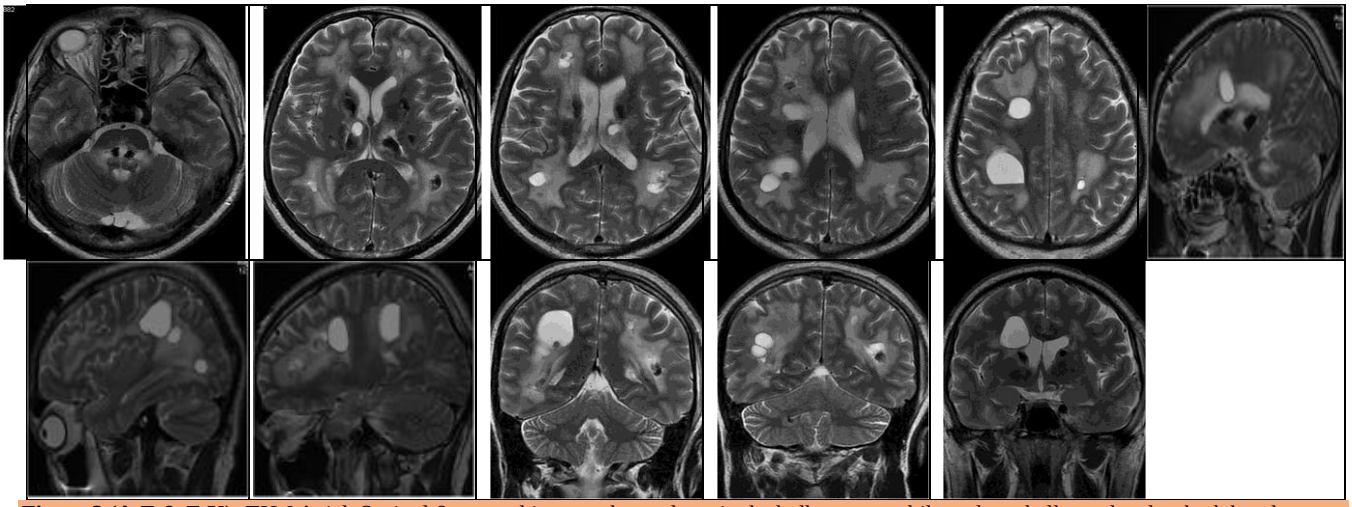

Figure 3 (A-E & F-K): T2W Axial, Sagittal & coronal images show edema in the bulbous pons, bilateral cerebellar peduncles, both basal ganglia & both hemispheric white matter surrounding a cyst or calcification with evident mass effect.

DISCUSSION

LCC was first described by Labrune et al in 1996.[1] The clinical presentation of LCC includes decline of cognitive performance, rare convulsive seizures and a mixture of extrapyramidal, cerebellar and pyramidal signs.[1,2]

Progressive calcifications in the basal and cerebellar gray nuclei and the central white matter are found on CT.

MR imaging reveals diffuse abnormal signals of the white matter on T2-weighted sequences.[1,2] A special feature is the development of parenchymal cysts in the supra-tentorial compartment and cerebellum, leading to compressive complications and surgical considerations.

It is suggested that an energy dysfunction stimulates cyst formation. This is indicated by spectroscopy studies which revealed an isolated lactate peak, reduced N-acetylaspartate and choline content.[2]

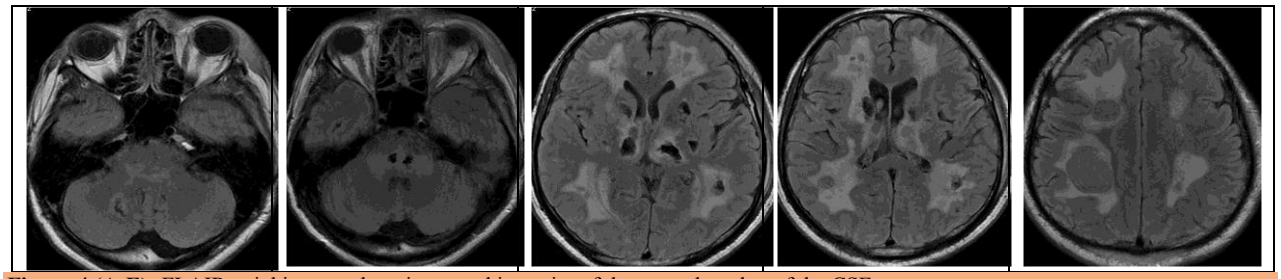

Figure 4 (A-E): FLAIR axial images show increased intensity of the cysts than that of the CSF.

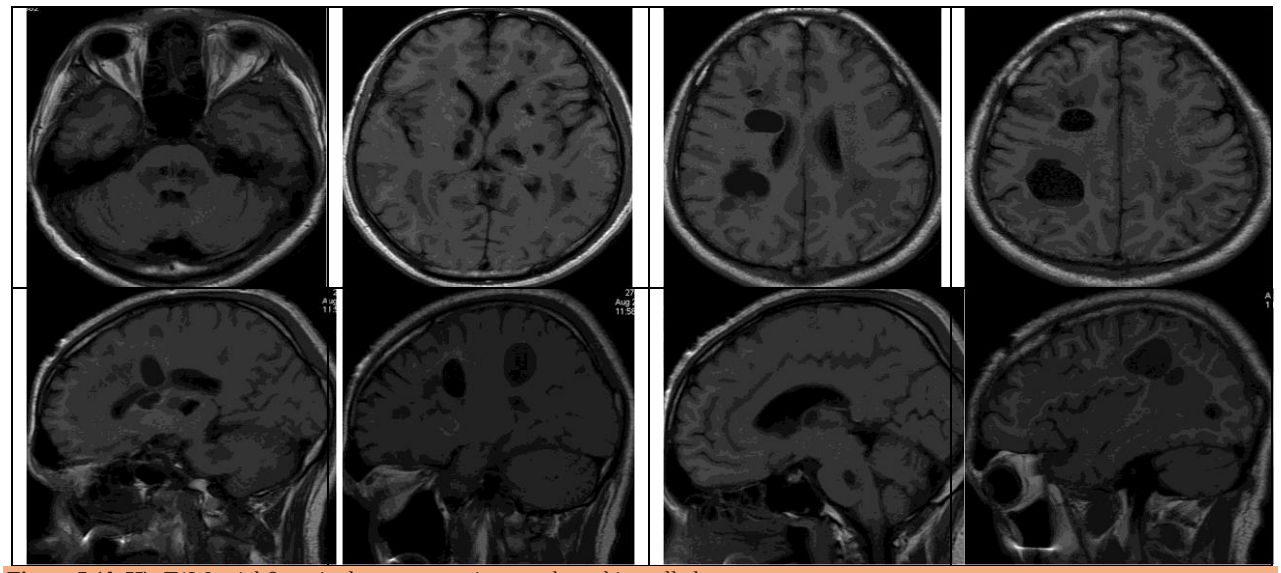

Figure 5 (A-H): T1W axial & sagittal pre-contrast images show thin walled cysts.

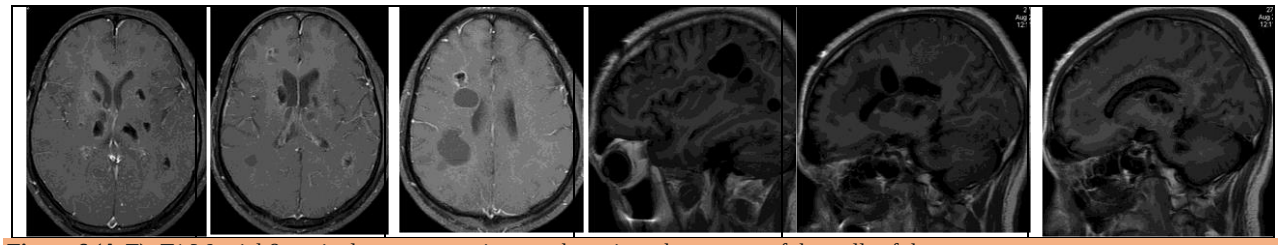

Figure 6 (A-F): T1 W axial & sagittal post contrast images show rim enhancement of the walls of the cysts

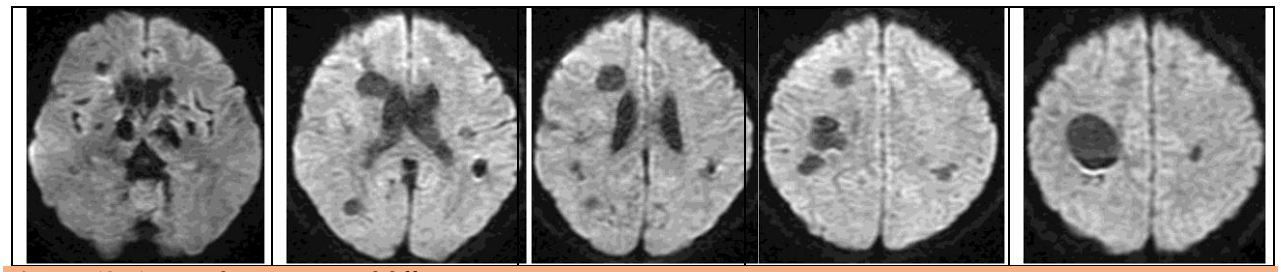

Figure 7 (A-E): DWI show no restricted diffusion.

In some cases it is difficult to differentiate from Coats plus syndrome and diagnosed as cerebro-retinal micro-angiopathy with calcifications and cysts. The most characteristic features of Coats plus syndrome are retinal telangiectasia and exudates.

Labrune et al reported the results of histo-pathologic examination in 2 of 3 patients with LCC.[1] They noted exuberant proliferation of abnormal small vessels associated with Rosenthal fibers, intense gliosis, and micro-calcifications on the specimens. According to Labrune et al, the probable primary pathologic feature is rearrangements involving the micro vessels, whereas perivascular foci of calcifications, hyaline deposits, and formation of Rosenthal fibers appeared compatible with secondary changes.

In contrast to the mild clinical course, a severe and progressive neurodegenerative process was shown in the central nervous system on neuroimaging. CT and MR imaging findings in our case were similar to those of other cases described in the literature showing increased white matter signal intensity, relatively sparing the U fibers and corpus callosum, with extensive coarse calcifications in the basal ganglia, brain stem, and subcortical white matter and the development of parenchymatous cysts.[1,2] Ring enhancement of the cyst wall that reflects disruption of the blood- brain barrier was noted on MR imaging.[1] Another additional finding noticed in our case was intra cystic hemorrhage & fluid blood level due to hematocrit effect.

Although the presence of cysts, calcification, and peri-focal white matter edema suggests a parasitic infection namely, cysticercosis or echinococcus alveolaris infection[3], no serologic confirmatory evidence was found in our patient.

Kaffenberger et al. suggested that distinct but overlapping pathophysiological mechanisms (demyelination and edema) lead to leuko-encephalopathy, calcifications and cysts.[4]

Berry-Candelario et al. suggested that these abnormalities may constitute an umbrella term that encapsulates distinct disease entities, including micro-angiopathy, aberrant myelination, or multiple central nervous system injuries or insults in the context of congenital abnormalities. Because of the rarity of the disorder and the variety of clinical manifestations, a biopsy should be performed for tissue diagnosis. Based on the existing literature, the highest diagnostic yield likely involves draining the cyst and a biopsy of the cyst wall.[5]

Armstrong et al. found both growth and shrinkage in cysts over time in their neuroimaging of a patient. They believed that the decrease in size of some cysts over time may suggest a more complex pathological finding than has been previously theorized.[6,7]

Only six cases of adult-onset LCC have been reported in the literature so far[4,8,9] and in most of these cases as in ours, there is no mention of early neurological impairment during infancy or any systemic features. Thus, we can hypothesize that the adult form presents as a much more indolent and benign disease.

Thus, this case supports the possibility of a long-lasting asymptomatic form of LCC which was diagnosed at the time of intra-cystic hemorrhage, a highly unpredictable event. This may explain the wide inter individual variability among patients with LCC.

Diagnostic imaging and follow-up are essential, while brain biopsy can be avoided as the neuroimging triad is highly characteristic.[10]

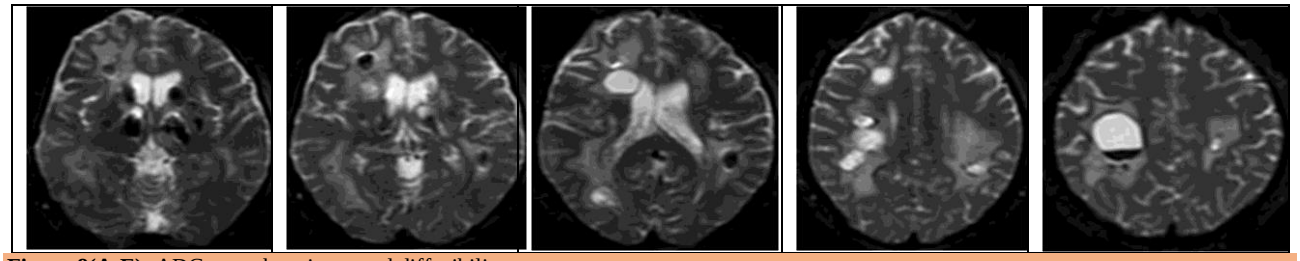

Figure 8(A-E): ADC map show increased diffusibility.

CONCLUSION

The etiology of the association of the LCC triad remains unknown but probably represents a distinct clinico-radiologic entity. The most striking histo-pathologic feature is cerebral angiomatous changes. Despite these relatively characteristic imaging and histo-pathologic findings, no uniformity on clinical features is notable.

Based on the latest findings, we believe that LCC and Coats plus syndrome are genetically distinct entities. It may be speculated that older onset age, normal intelligence, and very slow progression, as in our patient, may indicate the presence of the adult form of this rare disease. Diagnostic imaging and follow-up are essential, while brain biopsy can be avoided as the neuroimaging triad is highly characteristics.

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