Cerebrovasc Dis 2013;35:396–397

DOI: [10.1159/000348312](https://doi.org/10.1159/000348312)**A Case of Late-Onset Leukoencephalopathy, Calcifications, and Cysts Presenting with Intracerebral Hemorrhage Resembling a Neoplasm**Garrett P. Banks^a, Shennan A. Weiss^a, David Pisapia^b,
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In 1996, Labrune et al. [1] described a clinical entity in 3 children with multiple calcifications in deep gray structures, leukoencephalopathy, and parenchymal cysts on neuroimaging. Brain biopsy demonstrated irregular calcified small arteries. Subsequently more than 10 adult patients with identical neuroradiological features have been reported [2–10]. While some patients demonstrate pathological findings similar to the childhood form of the syndrome, others exhibit thickened, hyalinized large blood vessels and surrounding gliosis [10]. Clinically, these patients have diverse findings ranging from subtle deficits to chronic seizures and dystonia. Several of these patients have presented with intracerebral hemorrhage (ICH) [3, 6, 8].

Case Report

A 71-year-old woman with a past history of hypertension, prior ischemic stroke with mild residual left hemiparesis 6 years prior and poorly differentiated ovarian carcinoma in remission for 18 years presented with subacute worsening left hemiparesis and headache for 3 weeks.

On admission, the patient was hypertensive (159/78 mm Hg), mildly confused, and presented with left hemineglect and spastic left hemiparesis. Neuroradiological studies are displayed in figure 1. Computed tomography showed a 26-cm³ right frontoparietal ICH with surrounding edema throughout the right hemisphere and a 1-cm midline shift. Calcifications in the cerebellum and basal ganglia, as well as extensive white matter hypodensities were noted both on admission as well as 6 years prior. Magnetic resonance imaging (MRI) demonstrated increased fluid-attenuated inversion recovery both surrounding the hemorrhage with contrast enhancement and in the bilateral periventricular white matter hyperintensities. T2 images showed increased intensity, consistent with cysts, posterior to the left frontal horn and in the left cerebellum. All of

these findings, except for the hemorrhagic mass, were seen 6 years prior on an MRI scan performed for left-sided weakness. In 2006, MR spectroscopy of the right leukoencephalic region demonstrated a reduced N-acetyl aspartate/choline ratio, but no lactate peak. Cerebral angiography showed normal arterial and venous phases.

The patient underwent a right hemispherectomy and eventual resection of the hemorrhagic mass. Biopsy was notable for gliosis and thickened blood vessels, but no amyloid deposition or malignancy. A follow-up MRI demonstrated resolution of the hemorrhage and surrounding edema. Complete body positron emission tomography demonstrated no regions of hypermetabolism.

Discussion

The patient presented with an initial clinical presentation and imaging concerning for a hemorrhagic brain tumor, with brain biopsy and positron emission tomography demonstrating no evidence of malignancy. The patient's imaging was notable for white matter disease, cystic changes, and subcortical calcifications, all evident 6 years before her ICH. These neuroradiological findings have been previously described in adults and children and are collectively termed Labrune syndrome. The underlying cause of Labrune syndrome is unknown. Genes linked to deep white matter hyperintensity, such as CST3 (cysteine protease inhibitor cystatin C), are candidates [9]. The patient's hemorrhage and white matter disease could normally be ascribed to aggressive atherosclerosis or cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, however neither etiology is associated with cystic changes or calcifications. Labrune syndrome is a rare disorder that can present with a hemorrhagic brain lesion and should be considered in the differential diagnosis after more common etiologies have been ruled out [10]. The genetic basis of Labrune's disease is unclear.

References

- 1 Labrune P, Lacroix C, Goutieres F, Laveaucoupet J, Chevalier P, Zerah M, Husson B, Landrieu P: Extensive brain calcifications, leukodystrophy, and formation of parenchymal cysts: a new progressive disorder due to diffuse cerebral microangiopathy. *Neurology* 1996;46:1297–1301.
- 2 Osman NI, Lorincz MT, Hulsing KL, Gebarski SS: Leukoencephalopathy, cerebral calcifications, and cysts: case report. *Clin Neurol Neurosurg* 2012;114:806–809.
- 3 Corboy JR, Gault J, Kleinschmidt-DeMasters BK: An adult case of leukoencephalopathy with intracranial calcifications and cysts. *Neurology* 2006;67:1890–1892.
- 4 Kaffenberger T, Valko PO, von Meyenburg J, Barath K, Hewer E, Heppner FL, Jagella CE, Horst A, Siccoli MM: A case of late onset leukoencephalopathy with cerebral calcifications and cysts in a 59-year-old woman. *Eur J Neurol* 2009;16:278–281.

Fig. 1. a Axial fluid-attenuated inversion recovery images demonstrate bilateral asymmetric periventricular white matter hyperintensities prior to presentation. **b** Axial T2-weighted images demonstrate a cystic mass posterior to the left frontal horn. **c** Axial

T1-weighted post-gadolinium MR shows gadolinium enhancement of the hemorrhagic region at presentation. **d** Axial computed tomography images show stable basal ganglion calcifications and ICH at presentation.

- 5 Wargon I, Lacour MC, Adams D, Denier C: A small deep infarct revealing leukoencephalopathy, calcifications and cysts in an adult patient. *J Neurol Neurosurg Psychiatry* 2008;79:224–225.
- 6 Gulati A, Singh P, Ramanathan S, Khandelwal N: A case of leukoencephalopathy, cerebral calcifications and cysts. *Ann Indian Acad Neurol* 2011;14:310–312.
- 7 Berry-Candelario J, Kasper E, Eskandar E, Chen CC: Neurosurgical management of leukoencephalopathy, cerebral calcifications, and cysts: a case report and review of literature. *Surg Neurol Int* 2011;2:160.
- 8 Bertotti MM, Linhares MN, Ferreira R, Santos DS, Athayde AT, Mussi AC, Moritz JW, Jung TS, Schroeder HK, Rodrigues IK: Leukoencephalopathy, cerebral calcifications, and cysts: entity that can mimic a neoplasm. *Arq Neuropsiquiatr* 2011;69:717–722.
- 9 Mitaki S, Nagai A, Sheikh AM, Terashima M, Isomura M, Nabika T, et al: Contribution of cystatin C gene polymorphisms to cerebral white matter lesions. *Cerebrovasc Dis* 2011;32:489–496.
- 10 Kleinschmidt-DeMasters BK, Cummings TJ, Hulette CM, Morgenlander JC, Corboy JR: Adult cases of leukoencephalopathy, cerebral calcifications, and cysts: expanding the spectrum of the disorder. *J Neuropathol Exp Neurol* 2009;68:432–439.