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Review Article

Leukoencephalopathy with cerebral calcification and cysts: Cases report and literature review

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ABSTRACT

Background: Leukoencephalopathy with calcifications and cysts (LCC) is a rare disease in which parenchymal cysts and calcifications within a widespread leukoencephalopathy can cause a broad spectrum of neurological symptoms. We present cases with adult LCC and discuss previously described entities in relevant literature.
Case presentation: Two cases of adult-onset LCC confirmed by clinical presentations, typical neuroimaging and neuropathological findings are reported.
Literature review: A detailed search of all relevant reports published in the English language between 1996 and 2015 via PubMed (http://www.ncbi.nlm.nih.gov/pubmed) was performed, with "Leukoencephalopathy", "cerebral calcifications" and "cysts" as keywords. Including the current cases, we summarized the clinical presentations, neuroimaging features, biopsy features, and genetic features of 38 LCC patients.
Conclusion: Our findings suggested that LCC could be diagnosed by clinical presentations, neuroimaging and gene detection, and biopsy might not be necessary. Therefore, we propose a diagnostic flow chart for neuroimaging in leukoencephalopathy, cerebral calcifications and cysts.

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1. Background

Leukoencephalopathy with cerebral calcifications and cysts (LCC) is a rare disease, which was originally described in 3 patients by Labrune and coworkers in 1996 [1]. Age of onset ranges from infancy to

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adulthood, with varying clinical presentations, including seizures, cognitive decline, and pyramidal, extrapyramidal, and cerebellar signs. In this report, we present 2 cases with adult-onset LCC and discuss previously described entities in relevant literature.

2. Methods

We described the clinical presentations as well as neuroimaging and biopsy data for the 2 LCC patients, and searched all published reports concerning LCC in the English language between 1996 and 2015 via PubMed (http://www.ncbi.nlm.nih.gov/pubmed), with "Leukoencephalopathy, cerebral calcifications, and cysts" as keywords. Detailed information about the 38 patients, including the current 2 cases, are summarized in Tables 1–4.

3. Patients and literature review

3.1. Case report

Case 1. A 20-year-old previously healthy Asian woman, born to non-consanguineous parents, experienced a progressive headache with nausea and vomiting for 5 days as well as confusion for 1 day, and was admitted to the Neurology Department of our hospital in October 2015. Physical examination showed bilateral pyramidal signs and meningeal irritation symptoms. Lumbar puncture was performed, demonstrating a high intracranial pressure of over 300 mm H_2O. CSF analysis data, including white blood cell count, protein level, and IgA, IgM and IgG amounts, were unremarkable. Serological and immunological tests, including rheumatoid factor, anti-nuclear antibodies, anti-neutrophilic cytoplasmic antibodies, and anti-DNA antibodies, were all within the normal range. Assays for detecting parasitic, viral, bacterial and fungal infections showed negative results. Ophthalmologic examinations were negative as well. Brain CT (Fig. 1) revealed calcification in both thalami and the basal ganglia, as well as multiple cysts in bilateral hemispheres. The larger cyst in the left frontal lobe contained a hemorrhage, and was surrounded by a diffused edema. Magnetic resonance imaging (MRI) demonstrated that this cyst in the left frontal lobe had inhomogeneous and ring enhancements (Fig.2). T_2 weighted images revealed diffused white matter abnormalities with sparing of the gray matter. MR-angiography showed no arterial malformation or arteriostenosis. Magnetic resonance spectroscopy (MRS) revealed reduced *N*-acetyl-aspartate (NAA) and choline (Cho) levels in the regions of abnormal white matter, with no metabolites detected in the cyst. A perfusion-weighted

Table 1
The clinical presentations of LCC.

Source	Sex	Age of onset	Seizure	Ataxia	Dysarthria	HIP	Pyramidal	Extrapyramidal	Cognitive deficit	Visual impairment	Fundus	Systemic involvement
Labrune et al. (1996) [2]	F	11 yrs	+	+	+	+	+	−	+	+	NA	−
	F	3 months	+	−	+	+	+	+	+	−	−	−
	M	infancy	+	+	−	−	+	−	−	−	NA	+
Nagae-Poetscher et al. (2004) [4]	F	2 yrs	−	+	−	−	+	+	+	−	−	−
	F	0	+	+	−	+	+	+	−	−	Papilledema	−
Corboy et al. (2006) [5]	F	44 yrs	+	+	−	+	−	−	+	−	−	−
Linnankivi et al. (2006) [6]	M	14 yrs	+	+	−	−	+	−	+	+	−	−
Sener et al. (2006) [7]	M	13 yrs	+	−	−	+	+	−	−	−	−	−
Brenner et al. (2006) [8]	F	1 months	+	+	+	−	+	+	+	−	−	−
Wargon et al. (2008) [10]	F	30 yrs	−	−	−	−	+	−	−	−	−	−
Briggs et al. (2008) [11]	M	8 yrs	−	+	+	+	+	+	−	−	−	−
Marelli et al. (2008) [12]	F	27 yrs	−	+	+	+	+	−	+	−	−	+
	M	12 yrs	+	+	−	−	+	−	+	−	−	−
Kaffenberger et al. (2009) [13]	F	59 yrs	−	−	+	−	+	+	+	−	−	−
Kleinschmidt-Demasters et al. (2009) [14]	M	40 yrs	−	+	+	−	+	−	−	−	−	−
	F	52 yrs	−	−	−	+	−	−	−	−	−	−
Daglioglu et al. (2009) [15]	F	26 yrs	−	+	−	+	+	−	−	−	Papilledema	−
Armstrong et al. (2009) [16]	F	30 months	+	−	+	−	+	−	+	+	NA	−
Ummer et al. (2010) [17]	M	50 yrs	−	+	−	+	+	−	−	−	Papilledema	−
Berry-Candelario et al. (2011) [18]	M	24 yrs	−	+	−	−	−	−	−	−	−	−
Gulati et al. (2011) [19]	M	31 yrs	+	−	−	−	+	+	−	−	−	−
Coeytaux et al. (2011) [20]	F	14 yrs	−	+	−	−	+	−	+	−	−	−
Bertotti et al. (2011) [21]	M	child	−	+	−	+	+	−	+	−	−	−
Pessoa et al. (2011) [22]	M	24 yrs	+	−	−	−	+	−	−	−	NA	−
Labauge et al. (2012) [23]	M	37 yrs	−	−	−	−	+	−	+	−	−	−
Osman et al. (2012) [26]	F	2 yrs	+	−	+	−	+	+	−	−	−	−
Dusak et al. (2012) [27]	M	20 yrs	+	−	−	−	−	−	+	−	−	−
Banks et al. (2013) [30]	F	65 yrs	−	−	−	−	+	−	−	−	−	−
Wang et al. (2013) [31]	M	19 yrs	−	−	−	−	+	−	−	+	−	−
Ooba et al. (2013) [32]	M	1.5 months	+	+	−	−	+	+	+	−	−	−
Ogles et al. (2014) [33]	F	25 yrs	−	−	−	−	+	−	−	−	−	−
	F	3 months	+	−	−	−	−	−	+	−	−	−
Karlinger (2014) [34]	M	10 yrs	+	−	−	−	+	+	+	−	−	−
Li et al. (2015) [35]	F	21 yrs	−	−	−	−	−	−	−	+	−	−
Liu et al. (2015) [36]	F	19 yrs	−	−	−	+	−	−	−	−	Papilledema	−
	F	34 yrs	−	−	−	−	+	−	−	−	−	−
Present case	F	20 yrs	−	−	−	+	+	−	−	−	−	−
	F	25 yrs	−	−	−	−	+	−	−	−	NA	−

NA: not available.