Leukoencephalopathy with brain calcifications and cysts with SNORD188 mutations: a case report

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Background

Leukoencephalopathy with cerebral calcifications and cysts (LCC), also known as Labrune syndrome, and Coats plus syndrome, are cerebral microangiopathies characterized by angiomatous-like blood vessels with gliosis and Rosenthal fiber deposition. LCC and Coats plus were originally considered to be the same clinical entity termed cerebroretinal microangiopathy with calcifications and cysts (CRMCC), but recent evidences suggest that they are genetically distinct. Mutations in CTS telomere maintenance complex component 1 (*CTC1*) have been found in Coats plus syndrome, and mutations in small nucleolar RNA, C/D box 1 (*SNORD118*) gene have been recently associated to Labrune syndrome. *SNORD118* encodes for nucleolar RNA (snoRNA), box C/D U8, a vertebrate-specific factor, critical for maturation of the 5.8S and 28S ribosomal RNAs (rRNAs).

Materials and methods

We recently performed *SNORD118* gene analysis in two siblings, came to our observation 15 years ago, with Labrune syndrome phenotype.

Clinical and Genetic Results

The proband, at the time of evaluation, was a 23 y-old male. He experienced recurrent left-sided convulsive seizures at two months of age. At the age 11 y a slowly progressive motor and cognitive impairment was observed. Neurological examination showed a severe bilateral pyramidal syndrome and dystonic posture on the left arm. A brain Computerized Tomography (CT) scan at 15 years showed multifocal areas of calcifications in the basal ganglia, subcortical white matter, diffuse hypodense lesions in the white matter and a small left frontal cystic lesion. Brain Magnetic Resonance Imaging (MRI) showed areas of calcifications in the basal ganglia, subcortical white matter of the hemispheres and right dentate nucleus, hyperintensity of the white matter of both hemispheres, sparing the U fibres and corpus callosum, paratrigonal and corona radiata cysts. Enhancement was observed in the white matter and around the cysts and the calcifications. Magnetic Resonance Spectroscopic Imaging (1H-MRSI) showed significant increases in lactate inside the cerebral cysts. Ophthalmological findings were normal. His younger brother was examinated at the age of 19. His past history, neuroimaging features, and neurological examination were overlapping to that of his brother. The mutational analysis of *SNORD118* gene revealed the presence of two heterozygous mutations: n.57 G>A and n.*10G>T, already reported as pathogenic.

Conclusion and Discussion

To our knowledge this is the first report of *SNORD118* gene mutations in Italian patients. We suggest to screen for *SNORD118* in all patients with cerebral calcificationsuggestive of Labrune phenotype

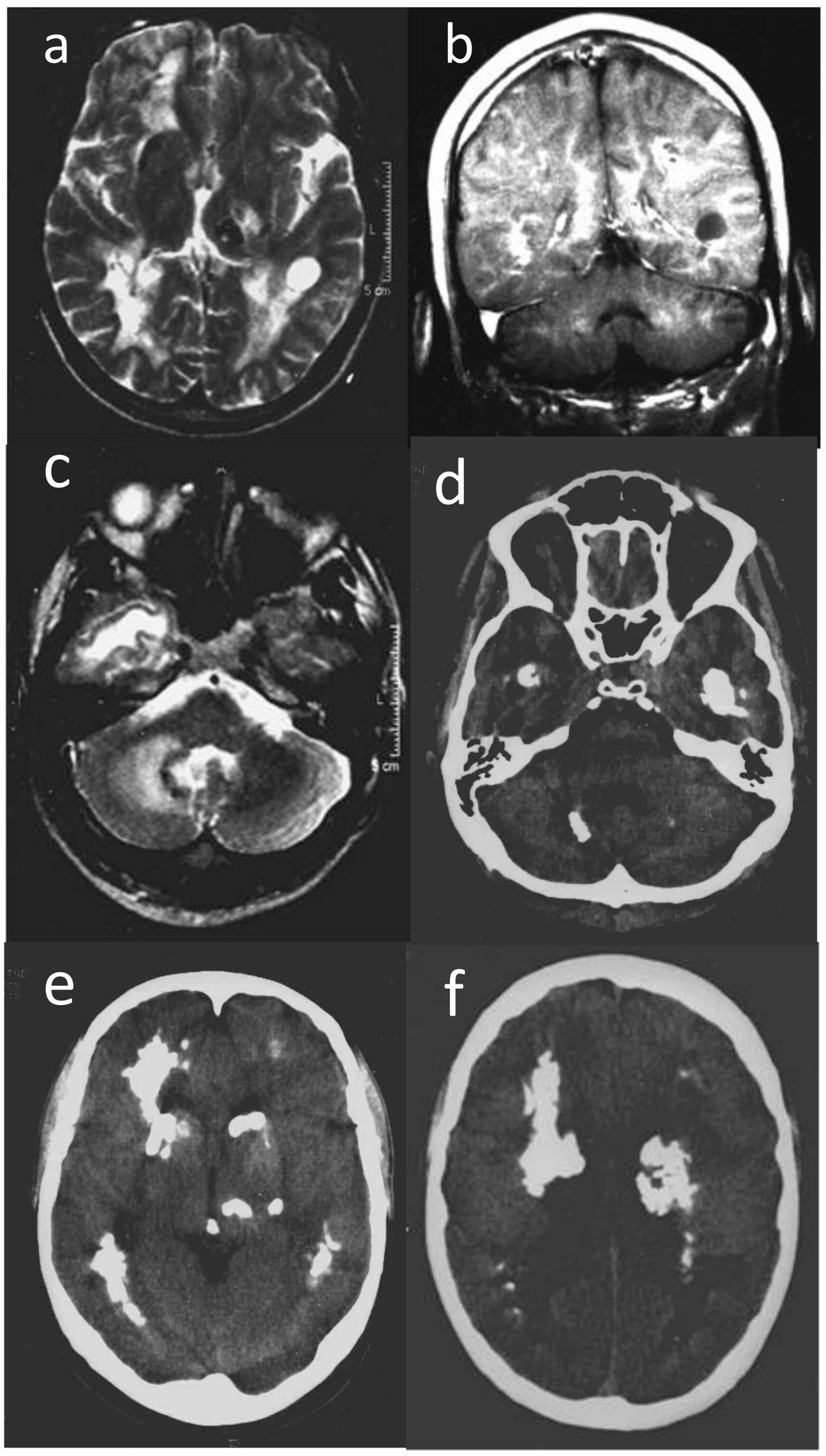

Figure 1: a-c) Axial T1-weighted brain MRI; b) Coronal fluid-attenuated inversion recovery (FLAIR) brain MRI; d-f) non consecutive brain CT scans

References: 1) Labrune P, at al. Extensive brain calcifications, leukodystrophy, and formation of parenchymal cysts: a new progressive disorder due to diffuse cerebral microangiopathy, Neurology. 46 (1996)1297-1301. 2) Jenkinson EM, et al. Mutations in *SNORD118* cause the cerebral microangiopathy leukoencephalopathy with calcifications and cysts. Nat Genet. 48 (2016)1185-1192. 3) Iwama K, et al. Identification of novel *SNORD118* mutations in seven patients with leukoencephalopathy with brain calcifications and cysts, Clin. Genet. (2017)