Leukoencephalopathy with calcifications and cysts associated with SNORD118 variants

Author(s):

Anna G Francis, BMBCh, MSc¹; Mihaela Boca, MD¹; Kathryn Urankar, BSc²; Anthony Cox, MBBS³; Philip Clatworthy, PhD¹; Claire Rice, PhD¹

Equal Author Contributions:

These authors contributed equally to the work

Corresponding Author:

Anna G Francis
anna.francis11@yahoo.co.uk

Affiliation Information for All Authors: 1) Neurology Dept., Southmead Hospital, Bristol, UK. 2) Pathology Dept., Southmead Hospital, Bristol, UK. 3) Department of Neuroradiology, Southmead Hospital, Bristol, UK.

Contributions:

Anna G Francis: Drafting/revision of the manuscript for content, including medical writing for content
Mihaela Boca: Drafting/revision of the manuscript for content, including medical writing for content
Kathryn Urankar: Drafting/revision of the manuscript for content, including medical writing for content; Additional contributions: Preparation of histological images
Anthony Cox: Drafting/revision of the manuscript for content, including medical writing for content; Additional contributions: MR image preparation
Philip Clatworthy: Drafting/revision of the manuscript for content, including medical writing for content
Claire Rice: Drafting/revision of the manuscript for content, including medical writing for content

Number of characters in title: 83
Abstract Word count: 100
References: 2
Figures: 2
Tables: 0
Neuroimage Legend Count: 45 (figure 1) + 28 (figure 2)

Supplemental: Consent form Word document tracking changes References Legends

Search Terms: [91] All Genetics, [120] MRI, [155] Leukodystrophies

Acknowledgements: We wish to acknowledge the West Midlands Regional Genetics Laboratory, who conducted the
genetic analysis. We also wish to thank the patient for her consent to publish her case.

**Study Funding:** The authors report no targeted funding

**Disclosures:** A Francis reports no disclosures relevant to the manuscript, M Boca reports no disclosures relevant to the manuscript, K Urankar reports no disclosures relevant to the manuscript, A Cox reports no disclosures relevant to the manuscript, P Clatworthy reports no disclosures relevant to the manuscript, C Rice reports no disclosures relevant to the manuscript.
A 67-year-old woman presented with gradually progressive gait impairment. Examination revealed left third nerve palsy, ataxia and lower limb spasticity.

Twenty-four years previously, hydrocephalus and multifocal cerebral cysts necessitated ventriculostomy and cyst biopsy (figure 1), followed by foramen magnum decompression 2 years later and, after a further 4 years, cerebellar haemorrhage evacuation.

Leukoencephalopathy with calcification and cysts, a rare, recently described autosomal ribosomopathy(1), was suspected at re-presentation on the basis of neuroimaging (figure 2). The diagnosis was confirmed following re-review of histopathology. Genetic screening detected a likely pathogenic variant in SNORD118 (n.*9C>T) and a variant of unknown significance (n.126C>T).

Progressive, multifocal symptoms are characteristic(2).
Figure 1. Histopathology of brain biopsy.

A. Gliotic brain with Rosenthal fibres (short arrows) and cysts (thin arrows) caused by microhaemorrhage secondary to underlying angiopathy (large arrow). B. Angiopathy with abnormal vessels and luminal thrombosis. C. Dystrophic calcification within the neuropil. This combination is characteristic of leukoencephalopathy with calcifications and cysts.

Figure 2. T2 weighted MRI.

Key radiological features of leukoencephalopathy with calcifications and cysts are demonstrated, with white matter hyperintensity consistent with leukoencephalopathy, calcification (confirmed on CT; dashed arrow) and cyst (solid arrow).
References:

