Skin Biopsy Used for the Diagnosis of Hereditary Diffuse Leukoencephalopathy With Spheroids

Author(s):
Chengyuan Song, Dr¹; Fengjuan Wu, Dr¹; Yiming Liu, Dr¹; Xinwei Wu, Dr¹; Yuying Zhao, Dr¹,²

Corresponding Author:
Yuying Zhao, zyy72@126.com

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Affiliation Information for All Authors: 1. Department of Neurology, Qilu Hospital, Shandong University, Jinan, Shandong, 250012, China; 2. Research Institute of Neuromuscular and Neurodegenerative Diseases and Department of Neurology, Qilu Hospital, Shandong University, Jinan, Shandong, 250012, China.

Equal Author Contribution:
Chengyuan Song and Fengjuan Wu contributed equally.

Contributions:
Chengyuan Song: Drafting/revision of the manuscript for content, including medical writing for content
Fengjuan Wu: Drafting/revision of the manuscript for content, including medical writing for content
Yiming Liu: Study concept or design
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Hereditary diffuse leukoencephalopathy with spheroids (HDLS) is a rare leukodystrophy of the central nervous system. We present two patients from unrelated families with late-onset HDLS. Patient 1 was a 50-year-old woman who developed blurred speech and difficult dressing at 48 and epilepsy and uroclepsia one year later. Patient 2 was a 51-year-old man with a 10-month history of slurred speech and cognitive decline. Both patients had several brain MRI studies that showed persistent patchy hyperintensities on DWI images (Figure 1). These imaging findings lead us to perform genetic testing. We identified two “likely pathogenic” variants of c.2264T>C (p.Leu755Pro) (patient 1) and c.1957T>C (p.Cys653Arg) (patient 2) in the CSF1R gene. Skin biopsy revealed the characteristic swelling of unmyelinated axons (spheroids) (Figure 2). Although brain biopsy is the gold standard for the diagnosis of this condition, skin biopsy may be an effective and efficient alternative for diagnosing HDLS.
References

Figure 1: MRI analysis of two patients.

A. Patient 1

B. Patient 2

Lateral ventricle enlargement and brain atrophy (A, B). Patchy hyperintensity around periventricular (red arrows) and subcortical (green arrows) on DWI images and corresponding decreased ADC signal (blue arrows).
Figure 2: Electron microscopic findings of skin biopsy.

The axons (arrows) of unmyelinated nerve fibers were enlarged by numerous dense substances and swollen spheroids (patient 1/A and patient 2/B).
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