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Variable Expressivity in Type 2 Familial Partial Lipodystrophy Related to R482 and N466 Variants in the LMNA Gene

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Abstract

Patients with Dunnigan disease (FPLD2) with a pathogenic variant affecting exon 8 of the *LMNA* gene are considered to have the classic disease, whereas those with variants in other exons manifest the "atypical" disease. The aim of this study was to investigate the degree of variable expressivity when comparing patients carrying the R482 and N466 variants in exon 8. Thus, 47 subjects with FPLD2 were studied: one group of 15 patients carrying the N466 variant and the other group of 32 patients with the R482 variant. Clinical, metabolic, and body composition data were compared between both groups. The thigh skinfold thickness was significantly decreased in the R482 group in comparison with the N466 group (4.2 ± 1.8 and 5.6 ± 2.0 mm, respectively, p = 0.002), with no other differences in body composition. Patients with the N466 variant showed higher triglyceride levels (177.5 [56-1937] vs. 130.0 [55-505] mg/dL, p = 0.029) and acute pancreatitis was only present in these subjects (20%). Other classic metabolic abnormalities related with the disease were present regardless of the pathogenic variant. Thus, although FPLD2 patients with the R482 and N466 variants share most of the classic characteristics, some phenotypic and metabolic differences suggest possible heterogeneity even within exon 8 of the *LMNA* gene.

Keywords: DXA; Dunnigan disease; LMNA; body composition; laminopathies; lipodystrophy; variable expressivity.