Journal of Clinical & Experimental Pathology

Lynds, J Clin Exp Pathol 2023, 13:1

Commentary Open Access

Symptoms and Genomics Analysis of Dubowitz Syndrome

Zennifer Lynds*

Department of Internal Medicine, St. Joseph's Hospital and Medical Center, Phoenix, Arizona, USA

Corresponding author: Zennifer Lynds, Department of Internal Medicine, St. Joseph's Hospital and Medical Center, Phoenix, Arizona, USA, E-mail: zenniferlynds@harvard.edu

Received: 02-Dec-2022, Manuscript No. JCEP-22-77635; **Editor assigned:** 06-Dec-2022, PreQC No. JCEP-22-77635 (PQ); **Reviewed:** 27-Dec-2022, QC No. JCEP-22-77635; **Revised:** 05-Jan-2022, Manuscript No. JCEP-22-77635 (R); **Published:** 13-Jan-2022, DOI:10.4172/2161-0681.23.13.428.

Citation: Lynds Z (2023) Symptoms and Genomics Analysis of Dubowitz Syndrome. J Clin Exp Pathol. 13: 428.

About the Study

Dubowitz Syndrome (DubS) is a distinguishable syndrome characterised by a distinct facial appearance and growth and development deficits. Over 200 people have been diagnosed with Dubowitz or a "Dubowitz-like" condition, but no single gene has been identified as the cause. We executed Exome (ES) or Genome Sequencing (GS) on 31 people who had been clinically diagnosed with DubS. A presumptive molecular diagnosis was made in 13/27 (48%) families after genome-wide sequencing, rare variant filtering, and computational and Mendelian genomic analyses. Biallelic variants in SKIV2L, SLC35C1, BRCA1, and NSUN2 were identified, as well as de novo variants in ARID1B, ARID1A, CREBBP, POGZ, TAF1, HDAC8, and copy-number variation at 1p36.11 (ARID1A), 8q22.2 (VPS13B), Xp22, and Xq13 (HDAC8). Variants with unknown significance in known disease genes, as well as genes with unknown significance, were found in 7/27 (26%) of the additional families. Only one gene, HDAC8, could account for the phenotype in multiple families (N=2). Except for two, all of the genomic diagnoses were for genes discovered or conditions recognised since the advent of next-generation sequencing. Overall, the DubS-like clinical phenotype is associated with extensive locus heterogeneity, and molecular diagnoses are for emerging clinical conditions with features that overlap the DubS phenotype. There was no single gene identified as being responsible for the majority, or even a significant minority, of people clinically diagnosed with DubS. The lack of a common cause could be explained by the fact that we sequenced a clinically heterogeneous cohort, DubS is genetically heterogeneous, or DubS as a clinical entity is a nonspecific collection of relatively common clinical features. DubS have historically been associated with mild intellectual disability, short stature, microcephaly, a sloping forehead, ptosis, telecanthus, eczema, and a high-pitched voice.

However, no formal phenotypic criteria exist to diagnose this syndrome. We acknowledge that the lack of strict phenotypic criteria for diagnosis, as well as reliance on the clinical impression of the referring physician, is a limitation of any DubS study. Nonetheless, it is a well-studied syndrome and appears in several editions of Smith's recognizable patterns of human malformation, so most clinical geneticists should be familiar with it. The molecular diagnoses made and candidate genes nominated in this study provide insight into shared disease mechanisms and pathways between DubS cases and other syndromes. We see that the DubS phenotype can be explained by Fanconi anaemia, Coffin-Siris syndrome, or Cornelia de Lange syndrome. Individual cases of DubS in our cohort could be explained by other syndromes that share common biological processes, such as DNA repair and chromatin remodelling. Another key message from this project is that people who were thought to have DubS were frequently found to have alternative diagnoses, despite being diagnosed by experienced clinicians. These diagnoses tended to fall into broad categories in this study, including genes for (a) chromatin remodelling and transcription, which are typically de novo dominant, and (b) DNA repair genes, which are typically autosomal recessive. If DubS is a possibility, a thorough clinical evaluation of these syndromes should be performed. We have ruled out the diagnosis of DubS in a large proportion of people by providing alternative diagnoses through molecular means. Furthermore, the lack of compelling variants in shared genes in the remaining individuals leads us to conclude that the majority of people diagnosed with DubS do not have a shared syndrome.