PUF60-related developmental disorder (Verheij syndrome)

https://pubmed.ncbi.nlm.nih.gov/37303278/

PUF60-related developmental disorder (also referred to as Verheij syndrome), resulting from haploinsufficiency of PUF60, is associated with multiple congenital anomalies affecting a wide range of body systems. These anomalies include ophthalmic coloboma, and congenital anomalies of the heart, kidney, and musculoskeletal system. Behavioral and intellectual difficulties are also observed. While less common than other features associated with PUF60-related developmental disorder, for instance hearing impairment and short stature, identification of specific anomalies such as ophthalmic coloboma can aid with diagnostic identification given the limited spectrum of genes linked with this feature. We describe 10 patients with PUF60 gene variants, bringing the total number reported in the literature, to varying levels of details, to 56 patients. Patients were recruited both via locally based exome sequencing from international sites and from the DDD study in the United Kingdom. Eight of the variants reported were novel PUF60 variants. The addition of a further patient with a reported c449-457del variant to the existing literature highlights this as a recurrent variant. One variant was inherited from an affected parent. This is the first example in the literature of an inherited variant resulting in PUF60-related developmental disorder. Two patients (20%) were reported to have a renal anomaly consistent with 22% of cases in previously reported literature. Two patients received specialist endocrine treatment. More commonly observed were clinical features such as: cardiac anomalies (40%), ocular abnormalities (70%), intellectual disability (60%), and skeletal abnormalities (80%). Facial features did not demonstrate a recognizable gestalt. Of note, but remaining of unclear causality, we describe a single pediatric patient with pineoblastoma. We recommend that stature and pubertal progress should be monitored in PUF60-related developmental disorder with a low threshold for endocrine investigations as hormone therapy may be indicated. Our study reports an inherited case with PUF60-related developmental disorder which has important genetic counseling implications for families.