BPAN: the only X-linked dominant NBIA disorder.

Abstract:

Beta-propeller protein-associated neurodegeneration (BPAN) is the most recently identified subtype of neurodegeneration with brain iron accumulation (NBIA), being unique with respect to the underlying disease genetics, the associated clinical presentation, and the suggested pathomechanism. Mutations in X-chromosomal WDR45 arise de novo; however, the dominant pattern of inheritance is unusual for an X-linked disorder and additional mechanisms such as X-inactivation or somatic mosaicism are likely to contribute to the phenotype that is indistinguishable between males and females. The course of the disease is two-staged with developmental delay and intellectual disability in childhood and a second phase of rapid neurological deterioration characterized by parkinsonism and dementia occurring in adolescence or early adulthood. At this time, neuroimaging findings are characteristic and provide excellent diagnostic guidance. There is increasing evidence that human WDR45 deficiency impairs autophagy, thereby raising the possibility that this rare disorder will offer insights into more common neurodegenerative disorders such as Parkinson or Alzheimer disease.