Background and Aims

Coats plus syndrome (OMIM # 612199) is a highly pleiotropic disorder particularly affecting brain, eye, bone and gastrointestinal tract, caused by mutations in the CTC gene. We describe the phenotype of a patient with severe growth failure where whole exome sequencing (WES) revealed compound heterozygosity for two mutations in the CTC1 gene.

Results

Sequencing data of WES of patient and parents were analysed with a stringent post-sequencing annotation pipeline including de novo, X-linked recessive and recessive modes of inheritance filters. The recessive inheritance filter revealed a paternally (c.1617+5G>T) and maternally (c.724_727del p.Lys242Leufs*41) inherited pathogenic variant in the CTC1 gene (NM_025099.5). Mutations in this gene are known to cause Cerebroretinal Microangiopathy with Calcifications and Cysts 1 (CRM1C, Coats plus syndrome; OMIM#612199). The c.724_727del p.Lys242Leufs*41 variant has been described in various patients. The c.1617+5G>T variant has not been reported. Splice Predict software predicts the loss of the splice donor site which probably results in an in-frame skip of exon 10 (Fig 10).

Conclusions

Multiple characteristics (SGA, progeroid appearance, cerebral calcifications of the basal ganglia, osteopenia, bone anomalies, fractures, growth failure, anaemia, sparse hair) are consistent with Coats Plus Syndrome, but this patient is the first to present with extreme short stature, complete hypergonadotropic hypogonadism and thumb anomalies. Retinal and gastrointestinal features are absent. These observations confirm the large phenotypic variability of the syndrome and also illustrates the importance of performing WES in the diagnosis of children with extreme short stature.

References


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