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Abstract Topic: - Clinical Genetics

Abstract Title: - A Rare Genetic Disorder: Dyggve-Melchior-Clausen Syndrome Unveiled in the Indian population

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Aims: - This abstract emphasizes Dyggve-Melchior-Clausen syndrome (DMC), which is a rare autosomal recessive spinal dysplasia. The aim of the study is to signify the importance of advanced genetic testing in the diagnosis of single gene disorder in the endogamous Indian population scenario.(the prevalence of this syndrome <1/1,000,000,and there are about 100 cases reported worldwide.)

Methods: - A couple with a 3rd -degree consanguineous marriage were refereed to institute with the history of their 9 1/2 year old boy with speech delay. The boy had several clinical features, like pectus carinatum deformity, flat chest bulbous tip of nose, prominent ear, delayed milestones, absence seizures, clinodactyly, brachydactyly and short stature. A cardiovascular examination showed a hypoplastic basilar artery. The EEG showed significant additional white spread epileptiform activity in both cerebral hemispheres. The ALP (alkaline phosphatase) test results were significantly elevated. Epiphyseal widening with metaphyseal cupping was seen by X-ray. The boy's blood sample was examined for whole exome sequencing, suspecting a single gene disorder.

Results: - Approximately 100 cases of Dyggve-Melchior-Clausen (DMC) syndrome have been reported worldwide and have not been reported in India until now. Whole exome sequencing showed a variant c.1363C>T(p.Arg455Ter) in exon 12 is predicted to cause loss of normal DYM protein function through protein truncation. For this reason, this variant has been classified as lightly pathogenic.

Conclusions: - Advanced genetic sequencing, like whole exome sequencing(WES), can be used to identify single gene mutations associated with developmental disorders. By identifying this rare genetic disorder, we will hopefully help to elucidate the pathogenesis of this poorly understood bone dysplasia-mental retardation syndrome in our country.

Keywords: - Approximately 100 cases of Dyggve-Melchior-Clausen (DMC) syndrome have been reported worldwide and have not been reported in India until now. Whole exome sequencing showed a variant c.1363C>T(p.Arg455Ter) in exon 12 is predicted to cause loss of normal DYM protein function through protein truncation. For this reason, this variant has been classified as lightly pathogenic.