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RESEARCH ARTICLE

SKELETAL ANOMALIES AND BEYOND: A CASE REPORT OF DYGGVE MELCHIOR CLAUSEN DISEASE WITH SMITH MCCORT DYSPLASIA

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Abstract

Dyggve Melchior Clausen (DMC) syndrome is an unusual form of uncommon autosomal recessive skeletal dysplasia.After its first occurr ence in 1962, there has only been a hundred case reports to date with a mean incidence rate of0.1 per million.[1] This article presents an account on a rare case report of Dyggve-MelchiorClausen disease combined with Smith Mccort Dysplasia.

Introduction:-

The Disorder or diseasein question, as outlined by Dyggve et al., is similar to MorquioUllrich disease.2 In 1968, the McKusickNathans Institute of Genetic Medicine pinpointed DMC syndrome to be a unique Mendelian disorder.3 The result of the mutation of DYM gene is DMC syndrome, found at 18q12-12.1. These mutations are passed on autosomal recessively and result in inferior functionality of Dymeclin protein. 5 6 A related disorder, Smith-McCort dysplasia (SMC) also has mutations in the DYM gene.

Nonetheless, as opposed to DMC syndrome, SMC is not linked with intellectual disability.8 The vast majority of mutations in DMC cause a disease that is associated with a loss of the cellular functions, but SMC mutations are mostly missense mutations, which is an indication of a remaining Dymeclin activity leading to a milder phenotype as there is no loss of neurological development. Accurate diagnosis typically requires a comprehensive evaluation including clinical, biochemical, radiological, and genetic investigations. This report presents a case of a genetically confirmed diagnosis of DMC syndrome.

Case Report:-

A 6 years old girl had a diagnosis of the Dyggve-Melchior-Clausen syndrome with SmithMcCort dysplasia features. She had broken upper front toothbecause of trauma suffered half a year earlier. She is the first child of a 30-year-old father and a 22-year-old mother. There was no reported family history of consanguinity. She was born via cesarean section with a birth weight of 3 kg. Developmental delays and growth retardation were first noted at the age of two. Initial differential diagnoses included Morquio syndrome, mucopolysaccharidosis type VI, and spondyloepiphyseal dysplasia. However, laboratory evaluations (including growth hormone, thyroid, renal, and liver function tests) were within normal limits. Genetic analysis confirmed a homozygous variant c.705_708dup in exon 8 of the DYM gene, confirming the diagnosis of Dyggve-Melchior-Clausen syndrome.

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Radiographic Findings:
- Irregular metaphyseal surfaces
- Medially deviated femoral necks
- Pointed femoral heads
- Broad ribs
- Deep sacrosciatic notch
- Platyspondyly
- Irregular iliac bone surfaces

Orthopedic Manifestations:
- Pigeon-shaped chest
- Flaring of lower ribs
- Short neck and chest
- Flat feet
- Genu valgum
- Limited joint extension

Extraoral Findings:
- Mandibular prognathism
- Coarse facial features
- Microcephaly
- Atlantoaxial instability

Intraoral Findings:
- Poor oral hygiene indicating inconsistent care
- Oblique fracture with pulpal exposure in tooth 51
- Deep dentinal caries in teeth 54, 55, 64, 65, 74, 75, 84, and 85
- Dentinal caries in teeth 53 and 63
- Open bite with severe tongue thrusting
- Maxillary occlusal radiograph showed deviated nasal septum, suggestive of skeletal abnormality

Due to atlantoaxial instability, tooth extraction required pediatric clearance, given the high risk of neck injury. The procedure was challenging due to the child's lack of cooperation. Postoperatively, the child was friendly but exhibited repetitive speech and poor attention span.

Dental hygiene and dietary counseling were provided, and continuous monitoring was advised.

Discussion:-

DMC syndrome is an increasingly severe spondyloepimetaphyseal dysplasia with coarse facial features and the intellectual disability that is differentiated with others including the syndrome of MPS IV (Morquio disease). Although, there may be an overlapping of skeletal abnormalities, lack of mucopolysaccharidurіa and corneal clouding with other characteristic radiological findings, favours the diagnosis of DMC.3 Similar to Smith-McCort dysplasia, mutations in the same DYM gene but genetically distinct, are not, in most cases, associated with intellectual13 Dyggve-Melchior-Clausen (DMC) syndrome is a rare autosomal recessive disease, which results in progressive spondyloepimetaphyseal dysplasia (SEMD), coarse facial profile and mental retardation.

It has similar skeletal abnormalities with the Morquio disease (mucopolysaccharidosis type IV, MPS IV), and this condition usually causes mix up to differences in diagnosis. Nonetheless, some important characteristics could be identified in order to distinguish DMC and MPS IV as well as other SEMDs. The lack of clouding of the cornea, lack of mucopolysaccharidurіa, the presence of intellectual disability, and the radiological features that are unique to syndrome characterize DMC syndrome in differentiating with those of MPS IV. Even though their skeletal structures are also related in some ways, like the formation of spinal and pelvic abnormalities, these factors are important clinical indicators toward a proper diagnosis. Skeletal manifestations in DMC involve abnormal development of the spine, pelvis, and epiphyses, leading to growth delays and functional impairments.

Radiographic features commonly include platyspondyly, irregular iliac bones, pointed femoral heads, and broad ribs. These abnormalities obstruct normal skeletal growth and contribute to orthopedic complications such as genu valgum, joint stiffness, and limited mobility. 9 The severity of SEMD symptoms can vary widely among affected

individuals. While some may present with mild skeletal abnormalities and preserved function, others may suffer from more debilitating structural and neurological impairments. In this reported case, the patient showed both classical skeletal and neurological features of DMC, alongside a confirmed homozygous mutation in exon 8 of the

DYM gene, reinforcing the diagnosis. Coarse facial features were observed in all patients with Dyggve-Melchior-Clausen (DMC) syndrome under study, with severity increasing with age and being more pronounced in males than in females. A prominent mandible is a common craniofacial trait associated with DMC syndrome. 14’15’16This contrasts with Morquio disease, where joint hyperextensibility is a defining feature, whereas restricted joint movement is characteristic of DMC. [14]

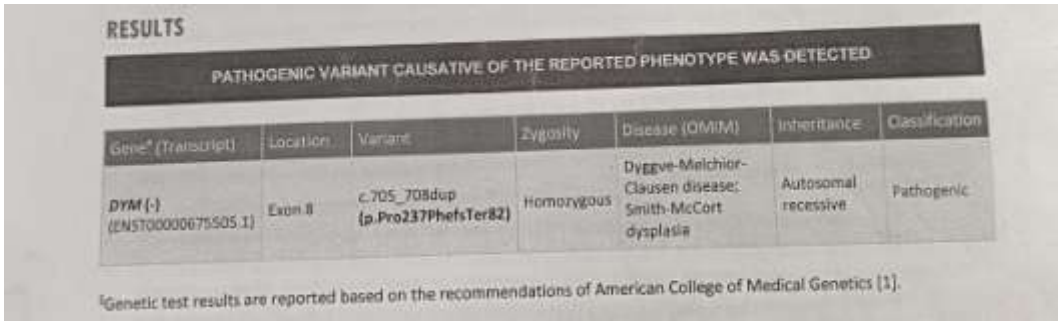
The pathophysiology of DMC syndrome remains incompletely understood, but some studies suggest a disruption in proteoglycan metabolism. 17 According to Engfeldt et al., elevated levels of glycosaminoglycans (GAGs) were found in cartilage samples from DMC patients. Additionally, they noted that proteoglycan monomers exhibited a reduced ability to reaggregate with hyaluronic acid chains, implicating impaired extracellular matrix integrity. However, this hypothesis is not universally accepted. Beck et al.

found that fibroblasts from DMC patients exhibited normal proteoglycan breakdown, suggesting that the underlying defect may not lie in proteoglycan catabolism18. Moreover, Roesel et al. reported elevated plasma and urinary levels of pipecolic acid in a child with DMC syndrome, despite other peroxisomal function tests being within normal ranges19. This finding raises the possibility of subtle metabolic involvement in DMC syndrome, though further research is needed. Management of DMC syndrome is primarily supportive and symptomatic. Orthopedic interventions are often required in cases with scoliosis, hip dysplasia, or significant joint deformities. Early initiation of speech-language therapy, physical therapy, and educational support is essential to maximize developmental outcomes and address cognitive impairments where present.

Interdisciplinary care—involving pediatricians, geneticists, orthopedists, dentists—is crucial for optimizing care delivery and improving qualityof life.Importantly, genetic counseling plays a vital role. DMC syndrome is inherited in an autosomal recessive pattern with a 25% recurrence risk in consanguineous unions.Carrier screening prenatal or preimplantation genetic testing and family education are essential components of reproductive planning and informed decision-making. Empowering families with knowledge about inheritance patterns and available options supports better long term outcomes and planning

Conclusion:-

For children with developmental delays, speech issues, craniofacial problems, and dental irregularities, a complete, multidisciplinary approach is essential. Ongoing education and preventative initiatives are also critical.



RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene* (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
DYM (-) (ENST00000675505.1)	Exon 8	c.705_708dup (p.Pro237PhefsTer82)	Homozygous	Dyggve-Melchior-Clausen disease; Smith-McCort dysplasia	Autosomal recessive	Pathogenic

*Genetic test results are reported based on the recommendations of American College of Medical Genetics [1].

Fig 1: Genetic report

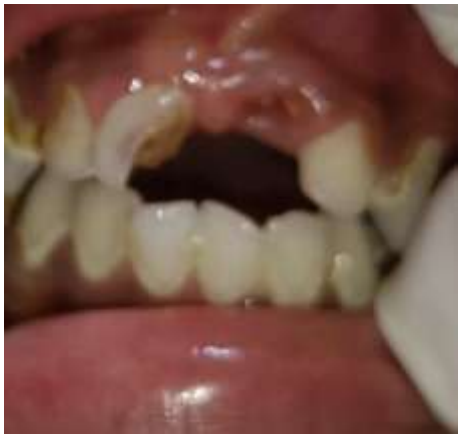
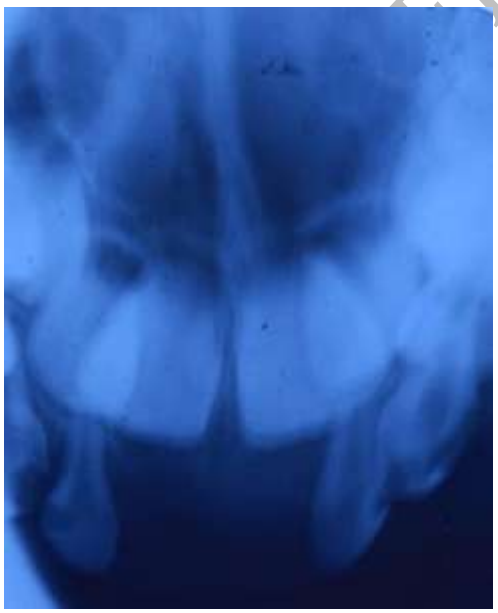


Fig 2;Intra oral view



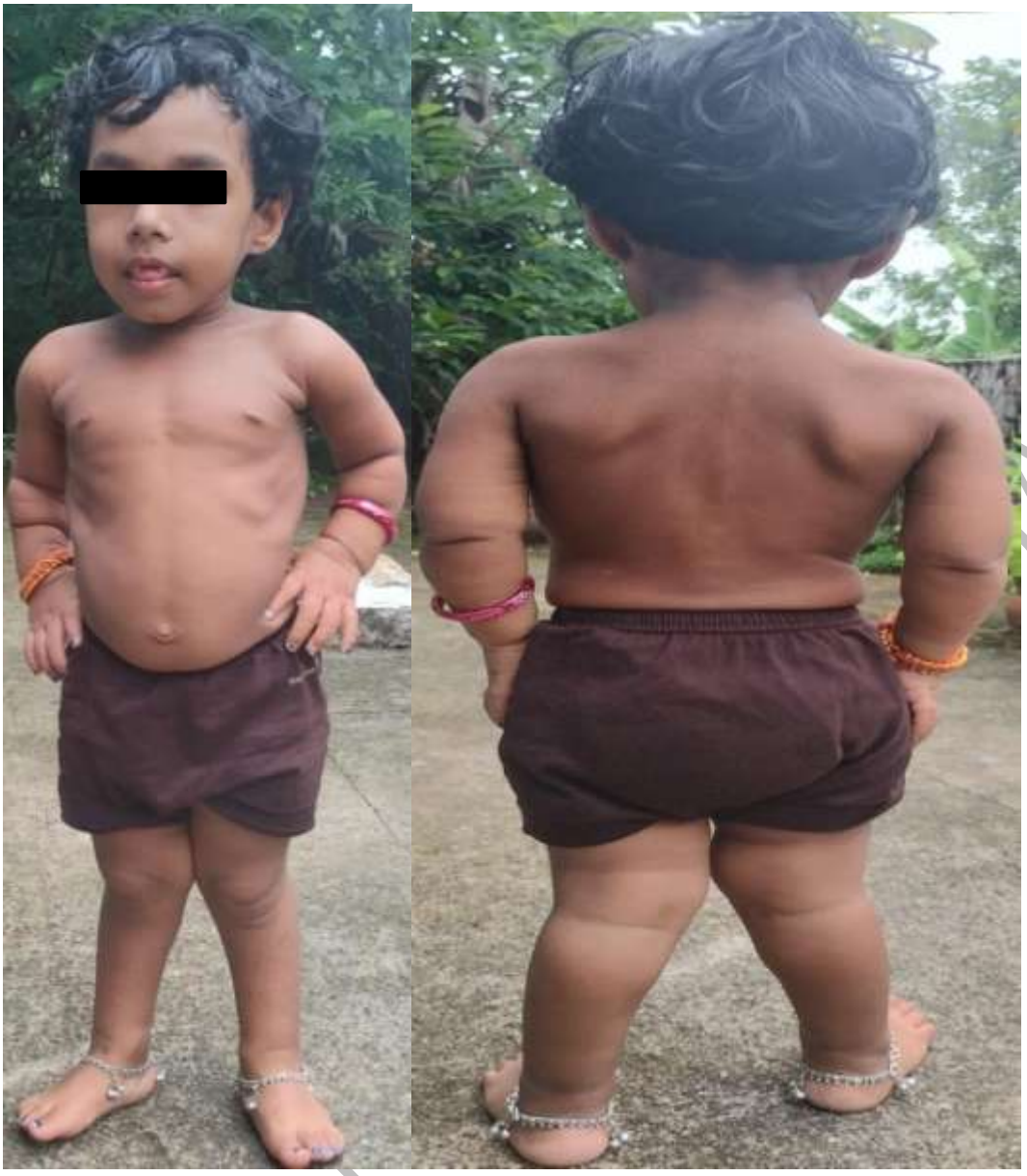


Fig 4:Clinical anterior and posterior picture with distinct facial dysmorphism

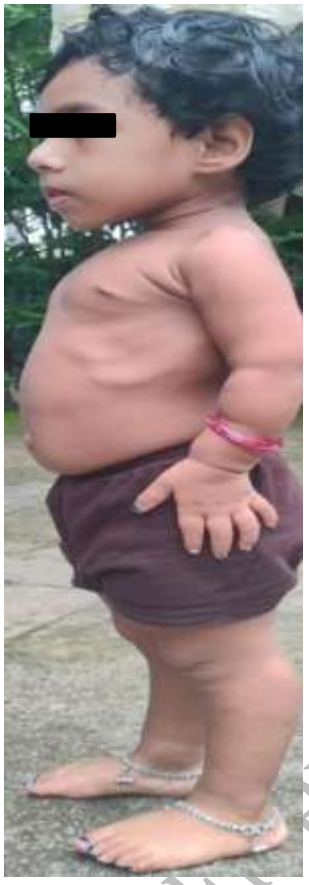


Fig5: Clinicalaterapicturewithdistinctfacialdysmorphism

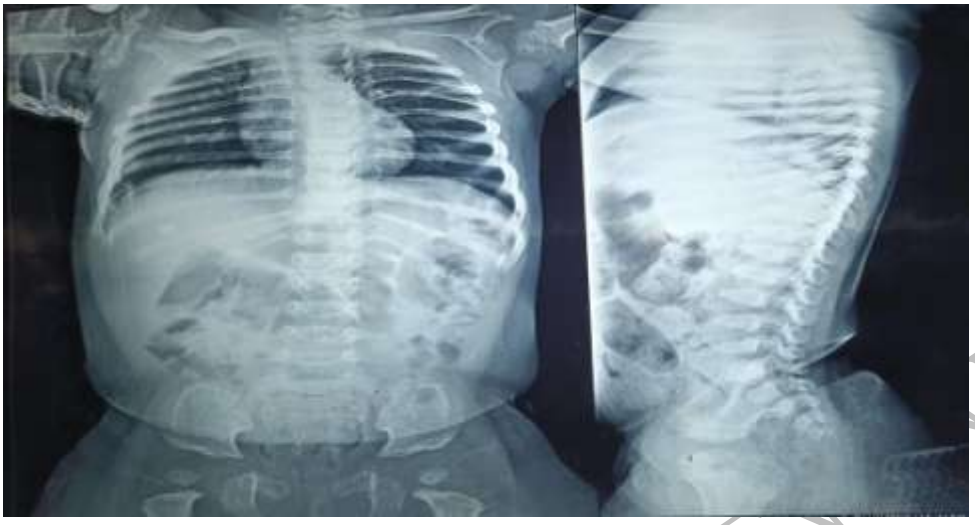


Fig 6:Radiographic features showing platyspondyly and irregular vertebral endplates

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