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DYGGVE MELCHIOR CLAUSEN DISEASE- A RARE CASE REPORT

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ABSTRACT **Introduction:** Dyggve-Melchior-Clausen syndrome (DMC) is a rare, autosomal recessive spondyloepimetaphyseal dysplasia marked by short stature, microcephaly, intellectual disability, and coarse facial features. **Case Report:** A 4 years old female child born to a 2nd degree consanguinous married couple was brought to RLJH with complaints of delayed developmental milestones and not gaining adequate height for age. **Conclusion:** Early diagnosis through clinical suspicion and genetic confirmation can improve long-term functional outcomes and guide genetic counseling

KEYWORDS : Autosomal recessive , DYM gene , spondyloepimetaphyseal dysplasia .

INTRODUCTION:

Dyggve-Melchior-Clausen (DMC) disease is a rare, autosomal recessive skeletal dysplasia characterized by spondyloepimetaphyseal involvement, microcephaly, and intellectual disability [1]. First described in 1962 by Dyggve, Melchior, and Clausen in two siblings with disproportionate short stature and mental retardation, the disorder has since been identified globally, albeit with very low prevalence due to its genetic rarity [2].

The condition is caused by mutations in the **DYM gene** located on chromosome 18q12.1, which encodes the protein **dymeclin**, involved in Golgi apparatus organization and intracellular trafficking[3]. Deficiency of dymeclin leads to disordered endochondral ossification, resulting in characteristic skeletal deformities. A related allelic disorder, **Smith-McCort dysplasia**, shares similar skeletal features but typically lacks cognitive impairment, differentiating it from classical DMC disease [4].

Clinically, patients present during early childhood with **short stature**, **delayed milestones**, **coarse facial features**, **microcephaly**, and **progressive skeletal abnormalities** including **kyphoscoliosis**, **pectus carinatum**, **genu valgum/varum**, and **joint contractures**. Radiographic findings are diagnostic and include **platyspondyly**, **irregular epiphyses**, and a **pathognomonic lacy appearance of the iliac crest** [5].

This report presents a rare case of Dyggve-Melchior-Clausen disease, highlighting its clinical presentation, radiographic features, and the importance of early recognition in resource-limited settings.

Case Report:

A 4 years old female child born to a 2nd degree consanguinous married couple was brought to RL Jalappa hospital with complaints of delayed developmental milestones and not gaining adequate height for age. The clinical evaluation revealed several dysmorphic features, including **epicanthal folds**, **hypertelorism**, **speech delay**, a **high-arched palate**, **micrognathia**, a **short neck**, **pectus carinatum**, **brachydactyly**, **waddling gait with limping**, and **pes planus**. Additionally, there was a **history of NICU admission** due to respiratory distress in the neonatal period. Radiological assessment through a **skeletal survey** demonstrated characteristic abnormalities involving the **epiphyses**, **metaphyses**, and **vertebral column**. Antenatal history was notable for **gestational diabetes mellitus (GDM)** diagnosed in the mother during the **eighth month of pregnancy**.

A comprehensive skeletal survey demonstrated platyspondyly with anterior beaking, flared iliac wings with lace-like iliac crests and early signs of thoracic scoliosis.

Genetic testing via whole-exome sequencing confirmed a homozygous pathogenic variant (LOCATION EXON 18, VARIENT: g.(?_49044213)_(49044205_49097402)del, establishing the diagnosis of Dyggve-Melchior-Clausen syndrome and thoroughly discussed with the family. **Genetic counseling** was provided to help them understand the condition and its inheritance pattern. P**renatal diagnostic options** were offered for consideration in future pregnancies.

The child was enrolled in **neurodevelopmental and physiotherapy programs** to support functional improvement. An **orthopedic consultation** was obtained to assess and monitor **spinal alignment** and **joint mobility**. A **multidisciplinary management approach** was implemented, involving specialists from **pediatrics, orthopedics, neurology**, and **clinical genetics** to ensure comprehensive care.

Fig 1 : Child with dysmorphic features stature
Fig 2 : Xrays showing features of flattened & short vertebral bodies and lacy iliac cress

DISCUSSION:

Dyggve-Melchior-Clausen (DMC) syndrome is a rare autosomal recessive skeletal dysplasia first described in 1962. In consanguineous families, the recurrence risk for autosomal recessive disorders like DMC is 25%. It is characterized by progressive spondyloepimetaphyseal dysplasia, microcephaly, intellectual disability, and distinctive facial and skeletal abnormalities. The condition is caused by **mutations in the** DYM **gene**, located on chromosome 18q12.1, which encodes the **dymeclin** protein. Dymeclin plays a crucial role in intracellular trafficking and Golgi apparatus function, particularly in cartilage and brain

tissue. Disruption of this pathway leads to defective endochondral ossification and neurodevelopmental impairment [4].

Clinically, affected children often present with **short stature**, **delayed developmental milestones**, **speech delay**, and **cognitive impairment**. Dysmorphic features such as **epicanthal folds**, **hypertelorism**, **high-arched palate**, **micrognathia**, and **short neck** are commonly observed. Skeletal abnormalities include **pectus carinatum**, **brachydactyly**, **genu varum/valgum**, **kyphoscoliosis**, **joint stiffness**, and a **waddling gait**. Radiological findings are diagnostic, revealing **platyspondyly**, **irregular metaphyses**, and the hallmark **lacy iliac crest** on pelvic radiographs [5].

The Following Are The Classic Radiological Findings:
Platyspondyly – Flattened vertebral bodies.
Lacy appearance of the iliac crest – Pathognomonic.
Epiphyseal and metaphyseal dysplasia – Irregular, delayed ossification.
Short tubular bones – With broad metaphyses.
Spinal changes – Including anterior beaking or gibbus.
Common problems in children with DMC syndrome include **motor delay**, **poor coordination**, **spinal deformities**, and in some cases, **respiratory difficulties** in infancy. Developmental and orthopedic challenges can significantly impact quality of life.

The diagnosis is based on **clinical and radiographic features**, and confirmed through **molecular genetic testing**, typically via targeted sequencing of the DYM gene. Prenatal diagnosis is possible if the pathogenic mutation is known in the family.

Management is supportive and **multidisciplinary**, focusing on **developmental therapy**, **orthopedic care**, and **regular monitoring** of skeletal progression. Physical therapy and assistive devices may be needed to support ambulation. There is no definitive cure for the syndrome. **Genetic counseling** is essential, especially for families from consanguineous backgrounds, to discuss recurrence risks and reproductive options.

Although prevention is not possible in affected individuals, **carrier screening** and **prenatal diagnosis** offer options for at-risk families. Future advances in molecular therapy may provide new treatment possibilities.

CONCLUSION :

Dyggve-Melchior-Clausen syndrome is an uncommon but distinct form of skeletal dysplasia that can often be identified based on clinical presentation. Accurate diagnosis relies on a comprehensive assessment involving clinical examination, imaging studies, and confirmatory genetic testing. It is important to distinguish this condition from other disorders with overlapping features, such as **Morquio syndrome** and **Smith-McCort dysplasia**, to prevent inappropriate management. While no definitive cure is currently available, early initiation of supportive care, including orthopedic interventions, can greatly improve functional outcomes. **Genetic counseling** plays a key role, particularly in communities where consanguineous marriages are prevalent. Ongoing advances in molecular genetics may offer promising therapeutic avenues in the future.

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