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KEY WORDS:

A RARE COEXISTENCE OF TGM1-RELATED LAMELLAR ICHTHYOSIS AND DUCHENNE MUSCULAR DYSTROPHY: CASE REPORT

Dr. Chiranjeevi.B Post graduate, department of neurology, Madurai medical college, India

Dr.R.kishore* MD, DM (Neuro), Professor, Department of neurology, Madurai medical college, India *Corresponding Author

Dr.R.subramanian MD, DM (Neuro),Assistant professor, department of neurology, Madurai medical college, India

Dr.S.senthur Raja Pandiyan MD, DM (Neuro), Assistant professor, department of neurology, Madurai medical college, India

INTRODUCTION:

Autosomal recessive congenital ichthyosis (ARCI) is a group of inherited keratinization disorders usually manifested as generalized scaling and skin barrier defective function from birth. TGM1(Transglutaminase-1 enzyme) gene mutations are among the most common causes of lamellar ichthyosis. Duchenne muscular dystrophy (DMD) is an X-linked recessive dystrophin gene related disorder, which leads to progressive proximal muscle weakness begins in early childhood.

The coexistence of these two ,congenital ichthyosis and muscular dystrophy is extremely rare presentation. However, advances in next-generation sequencing have increasingly identified patients with dual molecular diagnoses involving two unrelated genetic disorders.

We report a 13-year-old boy with congenital lamellar ichthyosis who later developed progressive proximal muscle weakness.

CASE DESCRIPTION:

A 13-year-old male child born to non-consanguineous parents presented with insidious onset gradually progressive neurological weakness in the difficulty getting up from sitting posture and walking.

Since birth, he had generalized scaling over the body and was clinically diagnosed as congenital lamellar ichthyosis. There was no history of blistering skin lesions. Developmental milestones were reportedly normal during early childhood, and he remained ambulant without difficulty until around 6–7 years of age.

Later, he gradually developed difficulty in getting up from the floor and climbing stairs. Subsequently, he developed difficulty in raising both upper limbs above the head suggestive of proximal upper limb weakness. distal weakness was also noted later in the due course.

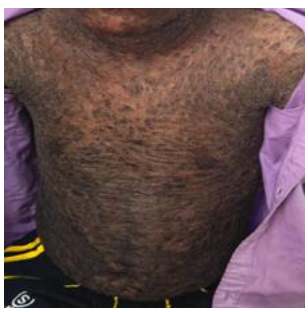
There was no history suggestive of sensory involvement, cranial nerve involvement, bowel or bladder disturbances, seizures, cognitive decline, or respiratory complaints.There was no similar family history.On neurological examination:Higher mental functions and cranial examination were normal. Tone was decreased in both upper and lower limbs. Proximal muscle weakness was noted in both upper and lower limbs. Mild distal weakness was present. Sensory examination was normal. Bilateral plantar responses are flexor. Cerebellar and autonomic examinations were in normal limits.

Routine metabolic screening was unremarkable. Echocardiography showed preserved left ventricular systolic function with an ejection fraction of 60%. Serum creatine kinase levels were high.

In view of congenital ichthyosis with progressive muscle weakness, differential diagnoses including Chanarin-Dorfman syndrome, ichthyosis-associated myopathy, and muscular dystrophy were considered.

Whole exome sequencing with copy number variation analysis revealed:
1. A homozygous missense variant in the TGM1 gene: it is associated with autosomal recessive congenital ichthyosis.
2. A hemizygous pathogenic deletion involving exons 5–7 of the DMD gene consistent with Duchenne muscular dystrophy.

The presence of two independent pathogenic variants suggested as a dual molecular diagnosis rather than a single syndromic disorder.



DISCUSSION:

Congenital lamellar ichthyosis due to mutation in TGM1 gene is typically restricted to cutaneous manifestations and is not usually associated with any primary muscle involvement. Therefore, the later onset progressive proximal weakness in this child prompted evaluation for an independent neuromuscular disorder.

Duchenne muscular dystrophy typically presents between 3–7 years of age with proximal lower limb weakness, difficulty rising from the floor, climbing stairs, and progressive involvement of shoulder girdle musculature. The identified exon 5–7 deletion in the DMD gene is a known pathogenic out-of-frame deletion associated with dystrophinopathy.

This case highlights the importance of considering dual genetic diagnoses in patients with complex phenotypes that cannot be fully explained by a single disorder.

Gene and Transcript	Exon/Intron Number	Variant Nomenclature	Zygosity	Classification	OMIM Phenotype	Inheritance
TGM1 (NM_000359.3)	Exon 4/Exon 15	c.892G>A p.Gly298Ser [274x /274x]	Homozygous	Uncertain significance	Ichthyosis, congenital, autosomal recessive 1	Autosomal recessive

CONCLUSION:

This case illustrates a rare coexistence of TGM1-related congenital lamellar ichthyosis and probable Duchenne

muscular dystrophy due to DMD exon 5–7 deletion. The report emphasizes the utility of comprehensive genomic analysis in patients with overlapping dermatological and neuromuscular phenotypes and underlines the importance of considering dual molecular diagnoses in atypical clinical presentations.

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