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Case Report

A novel homozygous variant of *RYR1* p.Ala3072Asp in a neonate with dusty core disease: A new entity with clinicopathological implications

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Dusty core disease (DuCD) is a recently described form of congenital myopathy with clinicopathological implications. The presence of "dusty core fibers" is the defining myopathological feature of DuCD. Most cases have a recessive inheritance and harbor *RYR1* mutations. I hereby describe a novel homozygous variant of *RYR1* p.Ala3072Asp clinicopathologically compatible with DuCD. To the best of my knowledge, this is the first documented case of DuCD from India.

Key words: congenital myopathy, dusty core disease (DuCD), RYR1.

INTRODUCTION

Congenital myopathies (CM) constitute a group of clinicopathologically and genetically distinct myopathies characterized by early-onset hypotonia and muscle weakness inherited as autosomal dominant, recessive, or X-linked patterns. The pathological abnormality common to most of the CM is the presence of hypotrophic type 1 fibers. Other findings include cytoplasmic bodies, nemaline rods, cores, tubular aggregates, central nuclei, caps, and so on. There is a high frequency of phenotypic variability and genetic heterogeneity in this group.[1] I hereby report a novel homozygous variant of *RYR1* p.Ala3072Asp clinicopathologically compatible with the recently described "dusty core disease" (DuCD), a subtype of the CM with pertinent clinical implications. To the best of my knowledge, this is the first documented case of DuCD from India.

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CLINICAL SUMMARY

A 3-day-old term male neonate with 2.5 kg birth weight born of a consanguineous marriage was floppy at birth and showed poor respiratory effort necessitating assisted ventilation, feeding difficulties, convulsions and bilateral undescended testes. Neurological examination revealed generalized hypotonia and hyporeflexia. There were no contractures, obvious deformities of limbs or spine. Ophthalmological examination revealed slightly enlarged cup with dull foveal reflex. The antenatal period was eventful with pregnancy-induced hypertension, reduced fetal movements and polyhydramnios in the third trimester. Routine blood investigations were within normal limits. Serum creatine kinase was within normal limits. Biochemical work-up for inborn errors of metabolism was negative. Magnetic resonance imaging of the brain did not show any abnormality. Examination of the mother did not reveal any facial abnormalities and her hand grip was normal. The elder female sibling had a similar presentation to the patient and died on the third day of life. Family history was consistent with an autosomal recessive pattern of inheritance (Fig. 1). The clinical manifestations of all the affected family members are summarized (Table 1). Although, the inheritance pattern was autosomal recessive, the clinical possibility of congenital myotonic dystrophy was not excluded. Subsequent genetic testing for CTG repeats was negative.

PATHOLOGICAL FINDINGS

Muscle biopsy was performed on the quadriceps. The overall myoarchitecture was altered with uniformly hypotrophic type 1 fibers. None of the degeneration, necrosis or regeneration of the myofibers, or phagocytosis, fibrosis or adipose cell infiltration in the endomysium were noted. Central nuclei were present in around 35% of fibers. Optimal cutting temperature compound-embedded frozen sections stained with hematoxylin and eosin (HE) showed an irregular granular basophilic sarcoplasmic material (Fig. 2A)