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SCIENTIFIC LETTER

A Call for Increased Focus on Fractures in Congenital Myopathy Infants

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To the Editor: Pathogenic mutations in RYR1 gene classically lead to Central Core Disease (CCD), whose manifestations include polyhydramnios, decreased fetal movement, hypotonia, respiratory distress, delayed motor skills and muscle weakness [1]. The low incidence of CCD combined with the multisystem involvement might cause fractures to remain unknown or under exposed to the healthcare providers. We aim to explain the mechanism of fracture in a patient at our center.

The proband is a female newborn, born at 39+6 wk via. cesarean section for polyhydramnios. At birth the patient presented with bradycardia, respiratory failure requiring invasive ventilation, marked generalized hypotonia and weakness, severe dysphagia and funnel chest. She had myopathic facies, generalized muscle weakness and total immobility of four limbs. Fracture of the left humerus and right femur were found at 8 d of age. Exome sequencing of the proband revealed two missense mutations in the RYR1 gene (c.14645C>T, p.T4882M and c.2792T>C, p.L931P). Muscular biopsy at the age of 2 mo confirmed CCD. The fractures healed 1 mo after possible treatment strategies (vitamin D, calcium, splint fixation, Hegu point acupuncture). During the stay in NICU, she had been breathing with the aid of invasive ventilation for 60 d, followed by lasting continuous positive airway pressure (CPAP) ventilator assistance until death. Her clinical conditions had been increasingly severe, with worsening respiratory failure and she died at 8 mo of age.

However, unlike fractures at birth reported in the previous cases [1, 2], our patient revealed fractures at 8 d of age. The molecular mechanisms of fracture can be explained by the following reasons. Firstly, myokines that are expressed in atrophic muscle, lead to decreased bone mineral density and long bone fractures [3]. Secondly, skeletal genesis and embryonic physeal growth require viable contracting skeletal muscles [4]. The findings of this study advise to routinely assess bone quality in patients with RYR1-related congenital myopathies.

Declarations

Conflict of Interest None.

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