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CASE REPORT

An uncommon case with coexistence of Down syndrome and Duchenne muscular dystrophy

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ABSTRACT

Down syndrome and Duchenne muscular dystrophy are not uncommon hereditary diseases in children. This case report presents a five-year-old male child with Down syndrome who exhibited elevated transaminase levels, hypotonia, proximal muscle weakness, and motor developmental delay. Genetic analysis confirmed a hemizygous duplication in exons 8-18 of the DMD gene, establishing the diagnosis of Duchenne muscular dystrophy. This rare coexistence highlights the importance of evaluating additional genetic disorders, particularly muscular dystrophies, in Down syndrome patients presenting with muscle weakness or elevated transaminase levels. Early diagnosis and a multidisciplinary approach are of critical importance.

Keywords: Children, Down syndrome, Duchenne muscular dystrophy.

Down syndrome (DS) is one of the most common chromosomal abnormalities in humans. It is characterized by phenotypic features such as typical facial appearance, mild-moderate mental retardation, short stature, as well as susceptibility to autoimmune diseases.[1] Muscular dystrophies are genetic diseases that occur as a result of mutations in the gene encoding the dystrophin protein. Duchenne muscular dystrophy (DMD) is the most common inherited muscle disease in children.[2] In this case report, DMD in a child with the diagnosis of DS and the frequency of coexistence of the two diseases were examined.

CASE REPORT

A five-year-old male patient with DS was admitted to our institution for further investigation due to elevated serum transaminase levels. Down syndrome was not detected during routine pregnancy screening and was diagnosed after birth. The parents were not related, and the child was the first child of the family. The mother was 26 years old, and the father was 28 years old. The patient did not have a family history of DS and any genetically inherited disease. The patient had been unable to walk since birth. Physical examination revealed characteristic facial features of DS, cryptorchidism, weak reflexes, hypotonia, and proximal muscle weakness. The laboratory evaluation showed the following: white blood cell count, 10.5×10^3/uL; hemoglobin, 12.3 g/dL; platelet, 316×10^3/µL; aspartate aminotransferase, 359 U/L; alanine aminotransferase, 379 U/L; albumin, 4.1 g/dL; gamma-glutamyl transferase, 12 U/L; creatine kinase (CK), 35970 U/L; lactate dehydrogenase, 1413 U/L; serum myoglobin, >1000 mcg/L. The family did not give written consent for a muscle biopsy. After obtaining written informed consent from the family, the DNA sample obtained from peripheral blood was analyzed by multiplex ligation-dependent probe

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amplification. Hemizygous duplication in exons 8 through 18 of the DMD gene was detected, confirming the diagnosis of DMD.

After the diagnosis, the patient was followed up in the pediatric neurology and physiotherapy and rehabilitation clinics. Genetic counseling training was given to the parents.

DISCUSSION

Down syndrome, one of the most common chromosomal abnormalities in humans, occurs in approximately 1 in 1000 live births each year, and is caused by a triple repeat (trisomy) on chromosome 21.[3] It is characterized by a typical facial structure, mild to moderate mental retardation, physical growth retardation, congenital heart defects, hypothyroidism, and other autoimmune diseases.[1]

Dystrophinopathies are a group of muscle diseases affecting males that develop as a result of mutations in the gene on the X chromosome that encodes the protein dystrophin. Two main forms have been defined: DMD and Becker muscular dystrophy (BMD).[4] Duchenne muscular dystrophy is the most common form of inherited muscle disease in children, with an estimated incidence of 1 in 3500 births. The disease appears in early childhood and progresses rapidly, with affected children becoming wheelchair-bound by the age of 12. Becker muscular dystrophy occurs in 1 in 18,518 births and is a milder form of dystrophinopathies. The dystrophin protein is partially produced. The disease progresses slowly and has a wide spectrum from asymptomatic to severe muscle weakness or dilated cardiomyopathy.[2] The Duchenne phenotype is usually caused by deletion, point mutation, and, rarely, duplication, which cause a shift of the reading frame of the mRNA transcript, respectively.[5] In a study conducted on this topic, deletions were detected in 83% of patients with DMD.[6]

Decreased muscle strength is a common condition in patients with DS. The correlation between DMD and Turner, Klinefelter, and Noonan syndromes have already been documented in the scientific literature.[7-9] The association between DS and genetic muscular dystrophy was reported only in two pediatric cases and one adult case. Cabradilla et al.[10] presented a nine-year-old male patient with DS who developed progressive muscle weakness and difficulty walking. Gowers sign was positive, CK level was 7655 U/L, and DNA sequencing revealed a hemizygous deletion in exon 51e54 of the DMD gene, confirming the diagnosis of DMD. Muscle biopsy was not performed. Lerario et al.[11] reported an eight-year-old boy with DS. The patient did not have progressive muscle weakness or gait disturbance; however, the CK level was 1775 U/L. An electromyography test revealed the presence of a myopathic pattern. A muscle biopsy was performed with parental consent. It revealed moderate dystrophic changes, including scattered round opaque fibers, rare necrotic fibers undergoing phagocytosis, and the presence of basophilic muscle fibers. Deoxyribonucleic acid analysis revealed a splice-site mutation c.1812+1G>A in intron 15, confirming the diagnosis of BMD. The mutation resulted in the skipping of exon 15. The first DS coexistence with DMD case, published in 1971, was a 21-year-old male.[12] Genetic analysis was not performed due to the circumstances available at the time.

In our case, it is noteworthy that DMD, the second rare genetic disease, was diagnosed in a five-year-old child with DS who presented with elevated transaminases. The presence of hypotonia, gait delay, and high CK and lactate dehydrogenase levels analyzed for elevated transaminases suggested DMD. Deoxyribonucleic acid analysis revealed a hemizygous duplication, confirming the diagnosis of DMD. Our case is the first reported in the literature, as the patient is younger than the previously published cases and has a rare case of hemizygous duplication of the DMD gene. Therefore, we believe this case contributes to the literature.

In conclusion, muscle strength must be closely monitored in patients with DS. In the event of weakness, it is of the utmost importance to consider any additional genetic disorders, such as muscle dystrophies.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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