Case Report

Transaminitis in a Three-year-old Boy with Duchenne Muscular Dystrophy

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Abstract

Duchenne muscular dystrophy (DMD) is a fatal X-linked genetic disease of the neuromuscular system and is the most serious type of muscular dystrophy in humans. The disease is characterized by progressive muscular atrophy and a poor prognosis. The incidence rate is 1/3500, and symptoms appear at age of 5 years-old. Some patients present with abnormal aminotransferases as the first symptom. In addition to the clinical characteristics and genetic history, electromyography examination, muscle biopsy, serum enzyme examination, and measures of creatine kinase (CK), CK isoenzyme, and serum lactate dehydrogenase are important features of auxiliary examination. Clinicians who encounter unknown causes of transaminitis should consider the possibility of DMD. We describe here a 3 year-old pediatric patient with increased aminotransferases who had elevated CK and a family genetic history but without liver damage on computed tomography. He was suspected as having inherited the disorder and was finally diagnosed as having DMD by next-generation sequencing.

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Case report

On August 22, 2019, a 3 year-old male received an annual physical examination at his local hospital. His blood tests showed alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels of 588 U/L and 492 U/L, respectively, negativity for serum hepatitis B surface antigen and positivity for hepatitis B surface antibody, and normal serum total bilirubin. Thereafter, on October 1, 2019, blood ALT and AST levels were 580 U/L and 302 U/L, respectively, and B ultrasonic examination revealed thickening of the intra-hepatic bile-duct wall and echo. He was admitted to the Department of Infectious Diseases, Shunde Hospital of Southern Medical University on October 1, 2019.

Keywords: Transaminitis; Duchenne muscular dystrophy; Gene sequencing.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, CK isoenzyme; DMD, Duchenne muscular dystrophy.
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Since onset of the disease, he has had a good appetite and normal mood, no headaches or dizziness, no chest tightness or pain, no shortness of breath, no abdominal pain or distension, no skin itching, no bleeding from the mouth or nose, normal sleep patterns, normal urination and defecation, no weight loss, and has been able to carry out daily activities as normal. An investigation of the boy's family history revealed that his grandfather had chronic hepatitis B. The patient's uncle became weak and a little unsteady on his feet at 7 years-old, then became paralyzed and died at the age of 17 (unknown cause of death). Another of the boy's uncles and the uncle's son had "congenital lameness" (no specific information). The second child of the patient's mother died when she was 30-weeks pregnant.

Physical examinations, including of the nerve and muscular systems, found no abnormalities. Biochemical tests showed his ALT and AST to be 526 U/L and 408 U/L, respectively. All hepatitis viral markers, including cytomegalovirus and Epstein-Barr virus, were negative on PCR and immunoblot assay. Ceruloplasmin, blood copper, r-glutamyl transpeptidase, and alkaline phosphatase levels were normal. Autoimmune liver disease antibodies were negative. Creatine kinase (CK) and CK isoenzyme (CK-MB) were 42320 U/L and 700 U/L, respectively, and 3-hydroxybutyrate dehydrogenase was 1840 U/L. Serum lactate dehydrogenase was 2496 U/L and free fatty acids levels were 63 μmol/L. His upper abdomen was normal on computed tomography scan, chest x-ray and electrocardiograph findings were normal, and the heart was normal on ultrasound examination.

The primary diagnosis was liver impairment (description of cause pending). After admission, the boy was treated with vitamins and other regimens to decrease blood aminotransferases. Blood tests were repeated on October 22, 2019, and they showed his CK to be 21755 U/L, CK-MB to be 311.7 U/L, ALT to be 430 U/L, AST to be 319 U/L, and lactate dehydrogenase to be 1207 U/L. Liver and muscle biopsies were refused by his parents. His blood sample was sent to MyGenostics (Beijing, China) for genetic disorder testing, and gene sequencing showed a DMD gene exon 8-43 hemizygous deletion (Fig. 1). To ensure the best treatment, the boy was transferred to Guangzhou Children's Hospital for further medical care.

Discussion

DMD is the most common type of progressive muscular dystrophy.[1,2] The disease is characterized by progressive muscular atrophy and a poor prognosis. The gastrocnemius muscles of patients undergo pseudohypertrophy, tendon reflex weakening or disappearance, and proximal

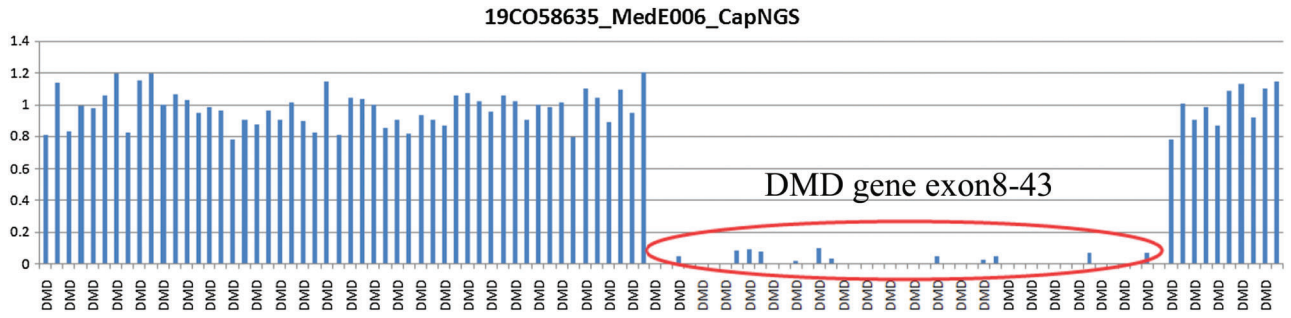

Fig. 1. Next-generation sequencing results.
DMD gene deletion of exon 8-43 was hemizygous.

myasthenia. As the disease progresses, the patients may lose their ability to walk before or around 12 years of age and die of respiratory failure or heart failure when approximately 20 years-old. The incidence rate of DMD is about 1 in 3500 newborn boys, and symptoms start to appear at 5 years of age. Patients are usually male but some female carriers are affected by partial inactivation of the X chromosome; DMD is an X-linked-recessive inherited disease.[3,4] At present, approximately 60-70% of the known pathogenic genes of DMD are deletion mutations of one or more exons, 5-10% are repetitive mutations, and 25-35% are point mutations (single base mutations or small base insertion/deletion mutations). Currently, there are no specific treatments available clinically.[2,5] Traditional methods, including acupuncture, massage, functional training, and traditional Chinese medicine, can maintain and enhance muscle strength, and some later-stage cases need orthopedic treatment. Glycine, glutamic acid, vitamin E, and hormones have no positive effect. Muscle strength increases within half a year after cell transplantation[6–8] but the long-term effects are not ideal. Additionally, the potential use of gene therapy is still under exploration.[9,10]

In clinical practice, it is difficult to explain the phenomena of liver injury and myocardial damage using routine biochemical tests and liver protection treatment. When there are no other reasons for auxiliary examination, CK levels can be further investigated.[11] It is easy to ignore the early-stage symptoms of the disease, which could be misdiagnosed as viral hepatitis, drug-induced liver injury, etc. Detailed physical examination is very important in the diagnosis of DMD. The extensive application of next-generation gene sequencing provides promise for the early diagnosis of many diseases, including DMD.[12,13] Early intervention is highly advantageous for maintaining the normal functions of organs, and delaying disease progression.

Conclusions

DMD is a serious genetic disease of childhood. Gene sequencing is crucial for early diagnosis.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study design (JD), analysis and interpretation of data (QX, YF, JL,QC), manuscript writing and critical revision (JD).

References

[1] Verhaart IEC, Aartsma-Rus A. Therapeutic developments for Duchenne muscular dystrophy. Nat Rev Neurol 2019;15:373–386. doi: 10.1038/s41582-019-0203-3.
[2] Mercuri E, Bönnemann CG, Muntoni F. Muscular dystrophies. Lancet 2019; 394:2025–2038. doi: 10.1016/S0140-6736(19)32910-1.
[3] Aartsma-Rus A, Ginjaar IB, Bushby K. The importance of genetic diagnosis for Duchenne muscular dystrophy. J Med Genet 2016;53:145–151. doi: 10.1136/jmedgenet-2015-103387.
[4] Chemello F, Bassel-Duby R, Olson EN. Correction of muscular dystrophies by CRISPR gene editing. J Clin Invest 2020;130:2766–2776. doi: 10.1172/JCI136873.
[5] Ryder S, Leadley RM, Armstrong N, Westwood M, de Kock S, Butt T, *et al*. The burden, epidemiology, costs and treatment for Duchenne muscular dystrophy: an evidence review. Orphanet J Rare Dis 2017;12:79. doi: 10.1186/s13023-017-0631-3.
[6] Sun C, Serra C, Lee G, Wagner KR. Stem cell-based therapies for Duchenne muscular dystrophy. Exp Neurol 2020;323:113086. doi: 10.1016/j.expneurol.2019.113086.
[7] Meng J, Sweeney NP, Doreste B, Muntoni F, McClure M, Morgan J. Restoration of functional full-length dystrophin after intramuscular transplantation of foamy virus-transduced myoblasts. Hum Gene Ther 2020;31:241–252. doi: 10.1089/hum.2019.224.
[8] Blau HM, Daley GQ. Stem cells in the treatment of disease. N Engl J Med 2019;380:1748–1760. doi: 10.1056/NEJMra1716145.
[9] Duan D. Systemic AAV micro-dystrophin gene therapy for Duchenne muscular dystrophy. Mol Ther 2018;26:2337–2356. doi: 10.1016/j.ymthe.2018.07.011.
[10] Fernández-Ruiz I. New developments in gene editing for Duchenne muscular dystrophy. Nat Rev Cardiol 2020;17:200–201. doi: 10.1038/s41569-020-0350-7.
[11] Ndrepepa G, Kastrati A. Creatine kinase myocardial band - a biomarker to assess prognostically relevant periprocedural myocardial infarction. Int J Cardiol 2018;270:118–119. doi: 10.1016/j.ijcard.2018.07.077.
[12] Ebrahimzadeh-Vesal R, Teymoori A, Azimi-Nezhad M, Hosseini FS. Next Generation Sequencing approach to molecular diagnosis of Duchenne muscular dystrophy; identification of a novel mutation. Gene 2018;644:1–3. doi: 10.1016/j.gene.2017.12.009.
[13] Okubo M, Minami N, Goto K, Goto Y, Noguchi S, Mitsuhashi S, *et al*. Genetic diagnosis of Duchenne/Becker muscular dystrophy using next-generation sequencing: validation analysis of DMD mutations. J Hum Genet 2016;61: 483–489. doi: 10.1038/jhg.2016.7.