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Identification of C.430C>T Mutation Leading to Diagnosis of Alstrom Syndrome via Genetic Analysis

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Introduction

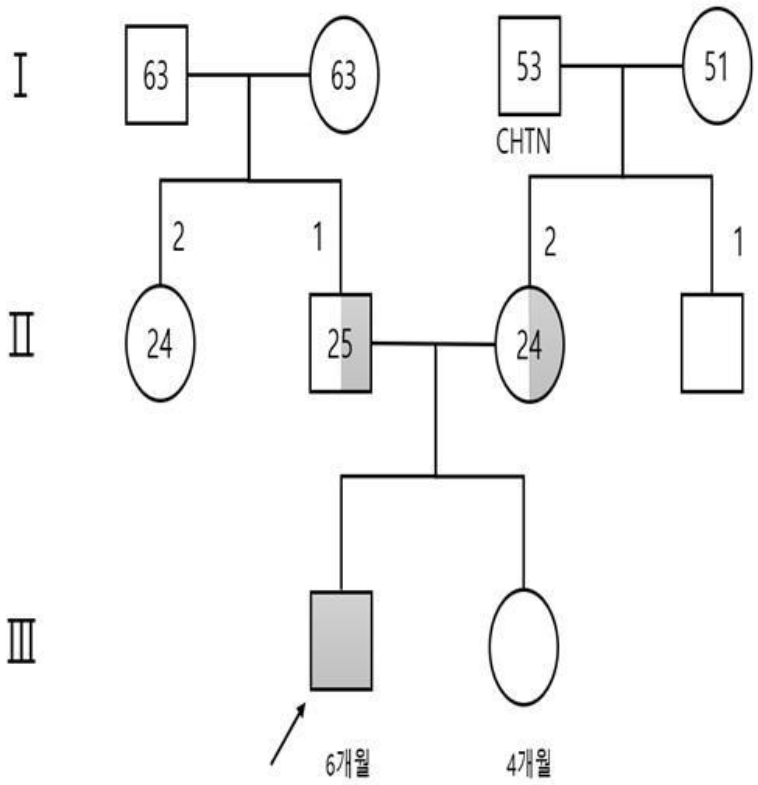
Alstrom syndrome (ALMS1) is a rare autosomal recessive disease associated with ALMS1 gene mutation located at Chromosome 2 (2p13). Patients with Alstrom syndrome usually become blinded due to progressive visual cell atrophy and sometimes sensorineural hearing loss occurs. By the age of 10 type 2 DM occurs accompanied child obese. During the period from infant to adolescent 70% patients occurs with dilated myocarditis. Also, abnormalities in renal, pulmonary, urinary function are common and progressive systemic fibrosis occurs. Here we present a case of Alstrom syndrome early diagnosed via genetic analysis.

Case report

The male patient was referred from pediatrics to rehabilitation medicine and medical genetics due to facial deformity at 6 months. Patient's mother was diagnosed in poly hydramnios and gestational diabetes. He was delivered by C-Sec at 34 weeks 5 days. Patient's weight was 2400g at the time of delivery and patient is preterm and low-birth weight baby. Because of dyspnea and cyanosis with chest retraction in neonatal room, the patient was moved to intensive care unit and received ventilator care. Echocardiography revealed Patent Ductus Arteriosus(PDA), Atrial Septal Defect(ASD), Mitral Regurgitation(MR), Tricuspid Regurgitation(TR) in this patient. However, PDA and ASD were closed spontaneously and MR and TR showed improvement in follow up Echocardiography. There was no abnormality in ophthalmic examination for retinopathy of prematurity. On physical examination, height and weight were below 25th percentile and occipital-frontal circumference was below 3rd percentile. On oral examination, the patient had high arched palate and capillary hemangioma in cervical area. Also, microretrognathia and simian line were showed. Given the family history and physical examination, we arranged a chromosomal microarray for the patient that yielded a normal result. Diagnostic exom sequencing (DES) was performed on the subject identified c.430C>T and c.12155_12158delinsACAT mutation in ALMS1 gene. So, we performed the genetic study including patient's parents and sister. We found c.12155_12158delinsACAT mutation from father and c.430C>T mutation from mother. We could not find any mutation for his sister. There was no abnormality in hearing test to evaluate sensorineural hearing loss observed commonly in Alstrom syndrome. So, we recommended regular check up and educated neuromuscular stimulation exercise.

Conclusion

The patient was referred to us due to facial deformity, microencephaly and microretrognathia and diagnosed as Alstrom syndrome at 9 months earlier than the average age of diagnosis (> 2 years). The patient showed c.430C>T and c.12155_12158delinsACAT mutation simultaneously in ALMS1 gene. We thought that parents had a individual different allele mutation and the patient was inherited indivisually. To the best of our knowledge, c.430C>T mutation is the first molecular genetic analysis of Alstrom patient.



Three generation pedigree of the patient's family. Filled symbols represent affected members, open symbols represent unaffected members. Circles and squares represent females and males, respectively.