Immunodeficiency, Common Variable, 8, with Autoimmunity

Alternative Names
CVID8

Record Category
Disease phenotype

WHO-ICD
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism > Certain disorders involving the immune mechanism

Incidence per 100,000 Live Births
0-1

OMIM Number
614700

Mode of Inheritance
Autosomal recessive

Gene Map Locus
4q31.3

Description
CVID8 is a phenotypically heterogeneous disorder caused by immunological dysfunction. Immunoglobulin levels are very low in affected individuals. The disorder is characterized by recurrent bacterial infections, particularly of the respiratory tract; inflammation or infection of the gastrointestinal tract, resulting in frequent bouts of diarrhoea; and an abnormal accumulation of immune cells resulting in lymphadenopathy and splenomegaly. Patients may also develop auto-immune disorders such as immune thrombocytopenia purpura, autoimmune hemolytic anemia, rheumatoid arthritis or non-Hodgkin's lymphoma.

CVID8 affects both men and women equally and symptoms may have an onset anytime between childhood and adulthood. Prognosis of the disorder depends on the severity and recurrence of secondary illnesses. Diagnosis of the disorder is made by measuring immunoglobulin and B cell levels in the blood. The genetic cause of CVID has only been discovered in about 10% of cases, making it difficult to diagnose the disorder through genetic analysis alone. Primary treatment for CVID consists of intravenous immunoglobulin therapy as well as antibiotics to treat infections. In certain cases, a splenectomy may be required.

Molecular Genetics
CVID8 follows an autosomal recessive pattern of inheritance. While more than 13 genes have been associated with common variable immune deficiency, CVID8 is caused by mutations in the LRBA gene. Although the function of LRBA is yet to be determined, it is believed to be involved in signal transduction and vesicle trafficking. More than a dozen homozygous mutations in the LRBA gene have been found to result in CVID8. Most of these mutations result in little to no expression of the LRBA protein.

Epidemiology in the Arab World

Lebanon

Alkhairy et al. (2016) described a 6-year-old Lebanese girl born to consanguineous parents. She first presented at the age of 3-years with dental abscesses. She also had recurrent otitis media which required an adenoidectomy and caused hearing loss. Subsequent investigations at 4 years of age found bilateral pulmonary nodules, hepatosplenomegaly and thrombocytopenia along with pulmonary, retroperitoneal and mesenteric lymphoadenopathy. Subsequent to seizures, an MRI revealed a subcortical lesion in the left parietal lobe. CSF culture was positive for Staphylococcus aureus. She also suffered from pneumonia. At age 5, she endured intermittent arthralgia and was found to have hypogammaglobulinemia. Due to hypersplenism she had a splenectomy and was diagnosed with Castleman's disease of the hyaline-vascular type. A genetic analysis revealed a novel LRBA mutation (c.2963delT) resulting in a frameshift deletion and premature truncation (p.N988fs*7).

References

Alkhairy OK, Abolhassani H, Rezaei N, Fang M, Andersen KK, Chavoshzadeh Z, Mohammadzadeh I, El-Rajab MA, Massaad M, Chou J, Aghamohammadi A, Geha RS, Hammarström L. Spectrum of Phenotypes Associated with Mutations in LRBA. J Clin Immunol. 2016; 36(1):33-45. PMID: 26707784.

Related CTGA Records

Lipopolysaccharide-Responsive, Beige-Like Anchor Protein

External Links

http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/common-variable-immune-deficiency/
https://ghr.nlm.nih.gov/condition/common-variable-immune-deficiency#
https://rarediseases.org/rare-diseases/common-variable-immune-deficiency/

Contributors

Sayeeda Hana: 17.10.2016