Gene. 2012 Sep 18. pii: S0378-1119(12)01110-9. doi: 10.1016/j.gene.2012.09.029. [Epub ahead of print]

A novel heterozygous mutation of the AIRE gene in a patient with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APECED).

Fierabracci A, Bizzarri C, Palma A, Milillo A, Bellacchio E, Cappa M.

Source

Immunology Area, Bambino Gesù Children's Hospital IRCCS, Rome, Italy. Electronic address: alessandra.fierabracci@opbg.net.

Abstract

BACKGROUND: Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APECED) is an autosomal recessive disease due to mutations of the autoimmune regulator (AIRE) gene. Typical manifestations include candidiasis, Addison's disease, and hypoparathyroidism. Type 1 diabetes, alopecia, vitiligo, ectodermal dystrophy, celiac disease and other intestinal dysfunctions, chronic atrophic gastritis, chronic active hepatitis, autoimmune thyroid disorders, pernicious anemia and premature ovarian failure are other rare associated diseases although other conditions have been associated with APECED.

CASE PRESENTATION: What follows is the clinical, endocrinological and molecular data of a female APECED patient coming from Lithuania. The patient was affected by chronic mucocutaneous candidiasis, hypoparathyroidism and pre-clinical Addison's disease. Using direct sequencing of all the 14 exons of the AIRE gene in the patient's DNA, we identified in exon 6 the known mutation c.769 C>T (p.Arg257X) in compound heterozygosity with the newly discovered mutation c.1214delC (p.Pro405fs) in exon 10. The novel mutation results in a frameshift that is predicted to alter the sequence of the protein starting from amino acid 405 as well as to cause its premature truncation, therefore a non-functional Aire protein.

CONCLUSIONS: A novel mutation has been described in a patient with APECED with classical clinical components, found in compound heterozygosity with the c.769 C>T variation. Expanded epidemiological investigations based on AIRE gene sequencing are necessary to verify the relevancy of the novel mutation to APECED etiopathogenesis in the Lithuanian population and to prove its diagnostic efficacy in association with clinical and immunological findings.