Pineal Hyperplasia, Insulin-Resistant Diabetes Mellitus, and Somatic Abnormalities

Alternative Names
Rabson-Mendenhall Syndrome
Mendenhall Syndrome

Record Category
Disease phenotype

WHO-ICD
Endocrine, nutritional and metabolic diseases > Diabetes mellitus

Incidence per 100,000 Live Births
Unknown

OMIM Number
262190

Mode of Inheritance
Autosomal recessive

Gene Map Locus
19p13.2

Description
Rabson-Mendenhall Syndrome is rare syndrome of extreme insulin resistance. It is characterized by severe insulin resistance leading to postprandial hyperglycemia and fasting hypoglycemia. The onset of the disease is very early, with affected patients experiencing intrauterine and postnatal growth retardation. They suffer from pineal hyperplasia, impaired linear growth, fat and muscle tissue hypoplasia, abnormal dentition, and ectodermal tissue overgrowth.

Diagnosis of the condition is based on the findings of fasting hypoglycemia, postprandial hyperglycemia, and hyperinsulinemia. Differential diagnoses include the more severe Donohue Syndrome and the clinically less severe type A insulin resistance diabetes mellitus with acanthosis nigricans (Iran Type A). Treatment is usually with high doses of insulin and/or recombinant IGF1. Most patients tend to die before reaching their 30s due to diabetic ketoacidosis.

Molecular Genetics
Rabson-Mendenhall Syndrome is transmitted as an autosomal recessive trait. Mutations in the INSR gene are causal for this condition. The INSR gene codes for the human insulin receptor, which is a critical component in the insulin receptor signaling pathway. This pathway has many regulatory roles in numerous cellular contexts, such as proliferation, differentiation, growth, and survival. INSR mutations resulting in Rabson-Mendenhall Syndrome have been shown to affect the number of mature receptors present on a cell, the affinity of these receptors for binding of insulin, and/or tyrosine kinase activity.

Epidemiology in the Arab World

United Arab Emirates
Bastaki et al (2016) described the first molecularly diagnosed case of Rabson Mendenhall Syndrome from the UAE. The 5-year old male patient was born to consanguineous parents and presented with short stature, hirsutism, and development and speech delay. He had coarse facies with a short hirsute forehead, synophrys, flared nares, short philtrum, thick lips, and irregular teeth with caries. Acanthosis nigricans was seen on the nape, behind the ears, axilla, and the inguinal region. Penis was large with deep and numerous scrotal rugae. US Abdomen showed medullary nephrocalcinosis. Biochemical analysis revealed random glucose at 150 mg/dl, insulin at >250 mIU/l, IGF1 at 32.8 ng/ml, and IGFBP3 at 995 ng/ml. Molecular analysis revealed the presence of a novel homozygous variant in the INSR gene in the patient.

References
Bastaki F, Nair P, Mohamed M, Khadora MM, Saif F, Tawfiq N, Al-Ali MT, Hamzeh AR. Identification of a Novel Homozygous INSR Variant in a Patient with Rabson-Mendenhall Syndrome from the United Arab Emirates. Horm Res Paediatr. 2016 Jun 22. PMID: 27326825

Related CTGA Records

Insulin Receptor

External Links

http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=769

https://ghr.nlm.nih.gov/condition/rabson-mendenhall-syndrome

Contributors

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