HOMOZYGOUS MUTATION IN COMPLEMENT C3 GENE ASSOCIATED WITH FAMILIAL HEMOLYTIC UREMIC SYNDROME: CASE SERIES

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Introduction: Atypical hemolytic syndrome (aHUS) is a rare renal disease. It has been recognized to be due to genetic mutations in more than 60% of cases. Its pathogenesis has been characterized to be secondary to Alternative complement pathway dysregulation. We aim to report the genotypic and phenotypic features of homozygous mutation in C3 gene in three infants in three different families from the same tribe. We will go through their early sever presentations, courses, responses to treatment with anti-C5 monoclonal antibody, and their current conditions.

Methods: We retrospectively did a detailed chart review of three infants that follow up in pediatric nephrology unit in Prince Sultan Military Medical City as cases of familial aHUS secondary to homozygous mutation in C3 gene. We highlighted their initial clinical presentations, hematological and biochemical abnormalities, course of their diseases, as well as the satisfactory and immediate responses to both induction and maintenance dosages of anti-C5 monoclonal antibody.

Results: Patient 1 is a Saudi girl who is a product of uneventful pregnancy for a first-degree cousin. She was admitted at the age of four-month with sepsis picture, and was found to have a picture of hemolytic uremic episode with low hemoglobin and platelets and high creatinine and Lactate dehydrogenase (LDH). She was transferred to our center and immediately started on induction doses of anti-C5 monoclonal antibody (Eculizumab). As she was not vaccinated, she was maintained on prophylactic antibiotic. Her initial complement C3 was low. She showed a dramatic response with normalization of her serum creatinine, Platelets count, Hemoglobin, and LDH. and maintained on regular maintenance doses every two week. She is monitored regularly, and she continues to have low level of Complement CH50 as indicator of proper suppression of complement system. Genetic testing shows homozygous mutation at Complement C3 gene with variant c.3326T>G p. (Leu1109Arg). Patient 2 & 3 have more or less similar presentation before their first birthdays with chest infection that precipitate a hemolytic uremic syndrome episode. Both were transferred to our center and their laboratory parameters respond dramatically to the first dose of Eculizumab, and maintained on it after that every two weeks. Genetic testing's show exact mutation as patient 1. Interestingly, all the three infants have a persistently low complement C3 during both flaring up and remission of their diseases.

Conclusions: Homozygous C3 gene mutation resulting in atypical hemolytic syndrome can have an early and devastating course, but fortunately its response to Anti-C monoclonal antibody is excellent. Larger sample size study with prospective design will definitely needed for better characterization of the course of the disease as well as potential complication of prolonged Complement C5 inhibition.

No conflict of interest

GENOTYPE-PHENOTYPE CORRELATIONS OF PREDICTED LOSS OF FUNCTION MUTATIONS IN ATYPICAL ADPKD GENES

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Introduction: Autosomal dominant polycystic kidney disease (ADPKD) are mostly caused by mutations in PKD1 and PKD2, but could also be a result of mutations in ALG8, ALG9, GANAB, LRPS, PKHD1, PRKCSH, and SEC63. However, the penetrance and expressivity of mutations in these atypical ADPKD genes has been largely unexplored. To better understand their impact, we used whole exome sequencing (WES) data in an electronic health record (EHR)-based research cohort to evaluate the phenotypic spectrum of rare predicted loss of function (pLOF) mutations in atypical ADPKD genes.

POSTER SESSION: GENETICS AND EPIGENETICS (INCLUDING COMMON AND RARE GENETIC DISEASES)

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