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Evolving role of genetic testing for the management of children with kidney disease: Clinical cases

Abstract:

Introduction: We are challenged to continue the momentum of the genomic era in pediatric nephrology by identifying novel disease-associated genetic variation and translating these discoveries into clinical applications. Here we present 2 clinical cases. The first was 5.5-year-old female child referred from for steroid resistant nephrotic syndrome (SRNS). Patient didn't respond to Cyclosporine nor to MMF. Therefore, all Immunosuppressants were stopped and patient was kept on conservative management. 3 years later, Genetic testing panel for SRNS was done for her as part of international study being conducted by Podo Net Consortium. It did show a mutation for the WT1 gene: Splice mutation consistent with the diagnosis of Frazier syndrome. WT1 mutation is related to increased risk of Wilms' tumor and gona do blastoma and can also cause urogenital malformations and sexual reversal. Therefore, a karyotype analysis revealed male genotype, therefore we were dealing with sexual reversal. Endocrine workup showed very high FSH & LH. Bilateral gonadectomy was performed in addition to psychiatric follow up. The 2nd case 2.5-month old male infant presented with a picture of acute onset of fever, watery diarrhea, frequent vomiting and excessive crying. After few hours, he developed cyanosis, respiratory distress and weak pulses, therefore, shifted to pediatric ICU, put on mechanical ventilation then he developed oliguric acute kidney injury with hemolytic anemia with fragmented RBCs and Increased LDH, Thrombocytopenia, Low C3 level with. The diagnosis of atypical Hemolytic Uremic syndrome (HUS) was clinically highly suspected. There was no reason to postpone eculizumab therapy. Over the next 2 days of eculizumab initial dose, the child started to stabilize with Improving urine output and renal function test, stabilizing hemoglobin and platelets and transferred back to pediatric ward before he was discharged home and kept on maintenance dose of eculizumab every 3 weeks until the patient reached 10 kg of weight when eculizumab dose became every 2 weeks. The genetic testing was done and did detect a heterozygous variant of the CFHR-1 gene. Software analysis indicate this variant is probably damaging. A genetic diagnosis of autosomal dominant CFHR1-related HUS is possible. Throughout the follow up period, the child did require to be hospitalized 3 times for chest and GI infections Otherwise, the child has always been in good clinical condition.

Conclusion: Genetic counselling is of the utmost importance, so all ethical and social concerns related to genetic testing are addressed in addition to patient satisfaction.

Biography

Council Member of the ISN 2023-2025 Member of the ISN Continuing Medical Education Committee (2022 – 2024) Representative of Syria in the ISN Middle East Regional Board. (2014 to date). Past president of the Middle East Society for Organ Transplantation (MESOT). Founder of the 1st Pediatric nephrology fellowship program in Syria in Nov. 2003 Founder of Pediatric Nephrology Department & Pediatric Dialysis Unit & pediatric Kidney transplant program at Surgical Kidney Hospital / Damascus / Syria / in February 2002 Member of the Declaration of Istanbul Custodian Group (DICG) Member of the Honorary Committee of the Advanced International Training Course in Transplant Procurement Management. TPM-DTI Foundation. Barcelona – Spain Founding member of the World Academy of Medical, Biomedical, and Ethical Sciences Country Liaison representing Syria in The Transplantation Society (TTS). Regional Representative of the Middle East/Africa region in the KDIGO Associate Editor of Experimental and Clinical Transplantation (ECT) Journal. Founder of the MESOT Fellowship Program Participant and Signatory to the final statement issued by the Pontifical Academy of Sciences (PAS) during the Vatican Summit on Organ Trafficking and Transplant Tourism held at the Vatican on February 7-8, 2017 Editorial Board member and reviewer in many journals