**Abstract ID:-** 170

**Abstract Topic:-** Clinical Genetics

**Abstract Title:-** A unique confluence of genetic anomalies: coexisting gene mutation, pseudogene, and microdeletion.

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**Aims:-**To understand the genetic interactions of a microdeletion and pseudogene coexisting with an ultra-rare variant and its clinical relevance in genetic diagnosis.

**Methods:-** Whole mitochondrial genome sequencing and Whole exome sequencing (WES) was performed for a patient. Variant validation and familial segregation for patient and parent samples were done by Sanger sequencing. Multiple sequence alignment of CA5A with pseudogenes was performed using clustal omega. Microdeletion on proband and father was identified and quantified by qPCR. Microdeletion size was identified by long range PCR.

**Results:-** A 4-day old baby girl born to non-consanguineous parents was presented with respiratory distress post feeding and clonic seizures. Baby was found to have metabolic acidosis, respiratory alkalosis, elevated ammonia and lactate levels on clinical examination and was suspected of Inborn Errors of Metabolism (IEM). No pathogenic or likely pathogenic variants were identified in mitochondrial genome sequencing; WES analysis revealed a pathogenic homozygous missense variant in gene CA5A (NM_001739.2:exon6: c.721G>A:p.Glu241Lys) known to cause Hyperammonemia due to carbonic anhydrase VA deficiency. Familial segregation analysis revealed the likelihood of the proband inheriting a microdeletion and being hemizygous for the variant. Copy number analysis of the allele showed the presence of a microdeletion in both proband and father. Long range PCR identified the deletion to be 4KB long and present in a highly repetitive region.

**Conclusions:-** We identified a combination of an ultra-rare variant in CA5A co-occurring with a microdeletion in the other allele, manifesting as a case of Hyperammonemia due to CA5A deficiency, a rare paediatric mitochondrial disorder. Hence, the complex genetic landscape of the variant, paired with a structural genomic alteration, becomes more intricate due to the existence of pseudogenes.

**Keywords:-** rare genetic disorder, mitochondrial disorder