Aims
Background Neonatal Hyperammonemia is a medical emergency requiring prompt management. The combination of neonatal hyperammonemia, lactic acidosis, ketonuria, and hypoglycemia is pathognomonic for carbonic anhydrase VA (CA-VA) deficiency (figure 1).

Methods
Objectives To present two siblings with CA-VA deficiency of East Asian ancestry and their clinical course.

Results
Clinical cases Parents are non-consanguineous from Punjab, India. The first patient is a full-term male who presented with hyperammonemic crisis on the second day of life. The highest ammonia level was 361umol/L (15-55). His metabolic investigations (plasma amino acids, acylcarnitine profile, and urine organic acids) had some overlapping features with a urea cycle disorder and organic academia. He was treated initially with nitrogen scavenger therapy and Carglumic acid but eventually needed hemodialysis. DNA analysis on an NGS Urea cycle panel identified two heterozygous variants in CA-VA: c.721G>A, p.Glu241Lys and c.619-?_774+?del. Both variants were considered probably pathogenic. Parental studies showed trans configuration. This confirmed the diagnosis of CA-VA deficiency (JIMD Reports 2020: 1-6).

His sibling, also a full-term male, was diagnosed antenatally with CA-VA deficiency based on molecular studies on amniocentesis. He was managed proactively for potential hyperammonemia at birth with IV fluids 10% Dextrose, intralipid 2 gm/kg, and Carbamyl 100 mg/kg. He did not require any further interventions. He was given regular formula and discharged on day five. Currently, the older brother is two years old and the younger brother is 11 months. Neither of them have had any further crisis and both are doing well without any treatment.

Conclusion CA-VA deficiency is a recently described rare autosomal recessive inborn error of metabolism which presents with neonatal hyperammonemia with good prognosis if managed appropriately. An isoform, CA-VB’s expression is likely upregulated in the absence of functional CA-VA. CA-VA deficiency should be considered in the differential diagnosis of neonatal hyperammonemia in patients of particularly Indian subcontinent origin as earlier patients have also been described from this region.
Introduction Cántú syndrome is a rare genetic disorder characterized by congenital hypertrichosis, osteochondrodysplasia, distinctive facial characteristics, and cardiac abnormalities. When initial genetic panel for mucopolysaccharidoses (MPS) is negative, genetic testing for Cántú syndrome should be included in the extended genetic panel, since these two clinical entities share certain phenotypic characteristics. We present a case of Cántú syndrome that was initially investigated as for MPS.

Methods Case Study A 4-year-old boy was referred for a paediatric assessment to rule out MPS since he had coarse facial characteristics.

He was born at 37 weeks of gestation with birth weight of 3.6 kg. He had undergone an umbilical hernia repair and adenoiectomy for sleep apnoea in the past. He had mild coarse facial features, bilateral epicanthic folds, a broad nasal bridge, a thick lower lip, and hypertrichosis. His weight and occipitofrontal circumference were above 99th centile. He did not show features of skeletal dysplasia clinically and he did not have mobility issues. A Grade 3 systolic murmur was identified. He did not have hepatosplenomegaly on clinical assessment. His neurodevelopment was age appropriate at the time of the assessment.

Discussion Cántú syndrome, also known as hypertrichotic osteochondrodysplasia is a rare clinical entity. 97% of reported cases are due to mutations in ABCC9 gene. The rest of the cases are mainly due to mutations in KCNJ8 gene, and one case has been reported due to monosomy 1p36. ABCC9 encodes a superfamily of transporter proteins known as ATP-binding cassette (ABC) Proteins which functions as potassium channels in cardiac, skeletal, and vascular smooth muscles. Mutations of this gene are described in association with Cántú syndrome, Intellectual disability and myopathy syndrome, Familial atrial fibrillation, and Familial dilated cardiomyopathy.

Both Cántú syndrome and MPS share similar clinical features including coarse facies, hypertrichosis, skeletal abnormalities, obstructive sleep apnoea, umbilical hernia, and cardiac abnormalities. Clinical differentiation between these two entities can be difficult, especially the milder phenotypes. Therefore, during evaluation of a child with MPS phenotype, it is important to extend the genetic testing towards Cántú syndrome, if MPS gene mutations are negative.