

## Hypoparathyroidism-retardation-dysmorphism syndrome

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Congenital hypoparathyroidism, growth retardation and facial dysmorphism is a rare autosomal recessive disorder seen among children born to consanguineous couple of Arab ethnicity. This syndrome is commonly known as Sanjad-Sakati or hypoparathyroidism-retardation-dysmorphism syndrome (HRD). We report 13-year-old Hindu boy with hypoparathyroidism, tetany, facial dysmorphism and developmental delay, compatible with HRD syndrome.

**Key words:** Hindu, hypoparathyroidism-retardation-dysmorphism syndrome, Sanjad-Sakati syndrome

### Introduction

Hypoparathyroidism-retardation-dysmorphism (HRD) syndrome also known as Sanjad-Sakati syndrome is characterized by permanent parathyroid hormone (PTH) deficiency, hypocalcemia, hyperphosphatemia, facial anomalies, and psychomotor retardation.<sup>[1]</sup> Most of the cases reported have been associated with parental consanguinity and have come from the Arabian peninsula.<sup>[1,2]</sup> We report hypoparathyroidism, tetany, short stature, facial dysmorphism and growth retardation suggestive of HRD in a Hindu child born to consanguineous couple.

### Case Report

A 13-year-old Hindu male child 4<sup>th</sup> born to a

consanguineously married couple with uneventful perinatal event, having delayed social and personal development was brought with spasms of the upper and lower limbs. He has been suffering from similar episodes of spasms frequently since the age of 5 years. He also had developmental bilateral cataract for which he was operated at the age of 6 years. At admission, he had carpopedal spasm and his vitals were normal. His weight was 29 kg (<5<sup>th</sup> centile), height 132 cm (<5<sup>th</sup> centile) and head circumference 49 cm (<3<sup>rd</sup> centile). On examination, he had facial dysmorphism features like long face, prominent forehead, bilateral dropping of eyelids, preauricular tag on the right side, bilateral pseudophakia with posterior capsular opacification (secondary), beaked nose, depressed nasal bridge, long philtrum, high arched palate, maloccluded teeth, micrognathia and microcephaly [Figure 1]. Latent tetany signs Trousseau sign and Chvostek sign were positive. Intelligent quotient assessment revealed mild mental retardation. Other systems examinations were normal. One of his sisters also had operated for developmental cataract at the age of 4 years, having delayed social and personal development, similar facial dysmorphism [Figure 1] but no tetany or latent tetany signs. Both parents and other two sibs were phenotypically normal.

His investigations revealed normal blood counts and peripheral smear. His serum calcium was 6.8 mg/dl, serum phosphorus 7.1 mg/dl, serum magnesium 2.2 mg/dl, serum albumin 3.2 g/dl, alkaline phosphatase 124 U/L and intact PTH was 5.46 pg/ml (N = 15-65 pg/ml). Blood urea, blood sugar, serum creatinine and electrolytes were normal. Urine chromatography was normal and urinary pH 8. His urine for sugar and ketones was absent. Chest X-ray, humerus X-ray and ultrasound abdomen

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**Figure 1: Facial dysmorphism features like long face, prominent forehead, bilateral drooping of eyelids, preauricular tag on the right side, beaked nose, depressed nasal bridge, long philtrum, maloccluded teeth, micrognathia and microcephaly**

was normal. Computerized tomographic (CT) scan of the head showed bilateral globus pallidus calcification. Audiogram showed mild hearing loss on the left side with normal hearing on the right side. He was started on intravenous calcium gluconate slow infusion for 2 days followed by calcium tablets. His facial dysmorphic sister serum calcium, phosphorus, magnesium, albumin, alkaline phosphatase, intact PTH and CT head were normal.

## Discussion

Hypoparathyroidism is an uncommon metabolic disorder characterized by hypocalcemia, hyperphosphatemia with absent or low levels of PTH.<sup>[1]</sup> Congenital hypoparathyroidism may be isolated or associated with syndromes. Familial occurrence of hypoparathyroidism with autosomal dominance, autosomal recessive or X-linked recessive have been well-established.<sup>[1,3]</sup> HRD or Sanjad-Sakati syndrome (Online Mendelian Inheritance in Man [OMIM] #241410) is a rare autosomal recessive syndrome predominantly seen patients of Arab origin.<sup>[1,2]</sup> It is characterized by hypoparathyroidism, hypocalcemia, hyperphosphatemia, facial anomalies, and psychomotor retardation.<sup>[1]</sup> It was first reported in 1988 and confirmed by definitive report in 1991.<sup>[2]</sup> Clinically, the syndrome has typical facial dysmorphism features like long narrow face, deep set eyes, microcephaly, micrognathia, thin lips, long philtrum, beaked nose, depressed nasal bridge, ear anomalies.<sup>[1,2,4,5]</sup> Microcephaly with various

degrees of mental retardation ranging from mild to severe degree is usual.<sup>[4]</sup> Short stature, small hands and feet are very frequently seen. Tapering of the mandible towards the chin is a unique feature of this syndrome.<sup>[5]</sup> Our child facial dysmorphism findings are consistent to which are described in the literature. Even his sister has similar facial dysmorphism. However, her biochemical parameters and CT scan head were normal. This could be due to variable expression of the gene. The molecular pathology of this syndrome was shown to be due to mutations in the tubulin-specific chaperone E (TBCE) gene in chromosomal area 1q42-q43 and encoding a TBCE.<sup>[6,7]</sup> TBCE mutations also cause Kenny-Caffey syndrome (KCS; OMIM 244460) similar to HRD syndrome with permanent hypoparathyroidism. Both syndromes commonly occur in children born to consanguineous couple of Arab ethnicity.<sup>[1,6,7]</sup> They share the same gene locus, but clinically Kenny-Caffey is characterized by normal intelligence, late closure of anterior fontanel, microcephaly, postnatal growth retardation along with cortical thickening and medullary stenosis of the bones.<sup>[2,5,8,9]</sup> Ophthalmic examination help to differentiate the two syndromes.<sup>[4]</sup> Nanophthalmos and corneal opacity have been documented in KCS patients, but ocular disease has not been well-described in HRD apart from the external ophthalmic features.<sup>[4,10]</sup> Parvari *et al.* demonstrated that both maps to the same region and suggested that these were likely to be allelic disorders, if not the same condition.<sup>[2,6,7]</sup> Usually they manifest in the new born period with complications of hypocalcaemia

as seizures or tetany.<sup>[2,5]</sup> However, the age at the diagnosis of the previously reported cases ranged from 4 months to 12 years.<sup>[2,7,8]</sup> Our child also had symptoms of hypoparathyroidism as tetany at the age of 5 years along with cataract. Estimated incidence of HRD varies from 1:40,000 to 1:100,000 live births in Saudi Arabia.<sup>[2]</sup> Affected siblings, mainly as products of phenotypically normal consanguineous parents, have been reported.<sup>[2]</sup> Until now more than 26 patients have been reported, of whom more than half were familial and affected siblings were reported in five non-consanguineous families also.<sup>[2]</sup> The therapeutic options are limited to correct hypocalcaemia and treatment of infections.<sup>[2]</sup> However, prevention could be achieved through pre-implantation genetic diagnosis and carrier detection.<sup>[2]</sup> To conclude, it is better to do molecular study for TBCE gene, which confirm our clinical evaluation and help much in genetic counseling for the family.

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