Sanjad Sakati Syndrome

Husain Y. Ahmed, MBBCh* Fatema M. Almeshkhas, MBBCh**
Zahra A. Hasan, MD*** Hasan M. Isa, MBBCh, CABP****

Sanjad Sakati Syndrome (SSS) is a rare autosomal recessive congenital disorder. It was reported exclusively in people of Arabian origin. SSS comprises of congenital hypoparathyroidism, severe growth retardation, mental retardation and dysmorphic facial features. The typical metabolic derangements lead to several morbid manifestations. SSS is also known as hypoparathyroidism-retardation-dysmorphism (HRD) which was listed in Online Mendelian Inheritance in Mean (OMIM) #241410.

We present the first case of SSS in Bahrain in a 40-days-old female. She was thin and lean. She had a narrow face, deep-seated eyes, peaked nose, long philtrum, thin lips, and micrognathia. She had short stature, small hands and feet, long tapering fingers and clinodactyly.

Parathyroid hormone was 0.3 pmol/L (normal range 0.99-6.05) and and 25-Hydroxy vitamin D was 7 nmol/L (normal range 53-150). The infant is the 4th child of consanguineous parents. The elder male brother who had features suggestive of SSS died at the age of 7 years.

The patient was treated with calcium and vitamin D therapy. Her convulsions were controlled. However, her anthropometric measure did not improve despite aggressive nutritional support via gastrostomy tube feeding. The patient is still alive at the age of 14 years and eight months.

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Sanjad-Sakati syndrome (SSS), is an autosomal recessive disorder (OMIM #241410) and represents a rare type of hypoparathyroidism mainly reported in the Arabian Peninsula[1,2,3]. This syndrome presents with dysmorphic features, seizures and severe failure to thrive[4]. The dysmorphic features include deep-seated eyes, microcephaly, micrognathia, thin lips, beaked nose, depressed nasal bridge, external ear anomalies, small hands and feet, short stature and learning difficulties[5]. In addition, it presents with mental retardation, metabolic derangements and immune deficiency which causes seizures and nephrocalcinosis[1,2,6].

The aim of this report is to present the first case of SSS in Bahrain.

THE CASE

A Bahraini female infant, product of full-term normal vaginal delivery with a birthweight of 2.600 kg, presented at the age of 40 days with a history of tonic-clonic seizures.

The patient had characteristic features of SSS. She was thin and lean. She had a narrow face, deep-seated eyes, peaked nose, long philtrum, thin lips, and micrognathia. She also had short stature, small hands and feet, long tapering fingers and clinodactyly.

Serum calcium level was 1.36 mmol/L (normal range 2.13-2.63) and magnesium level of 0.70 mmol/L (normal range 0.8-1.4); phosphorus level was 2.30 mmol/L (normal range 0.8-1.4). Alkaline phosphtase was 412 u/L (normal range 150-420). Parathyroid hormone was 0.3 pmol/L (normal range 0.99-6.05) and 25-Hydroxy vitamin D was 7 nmol/L (normal range 53-150). However, 1,25 hydroxy vitamin D was normal at 100pmol/L (normal range 13-140).

The infant is the 4th child of consanguineous parents. The patient was suspected to have SSS based on classical biochemical abnormalities with a family history of an elder male brother who had features suggestive of SSS and passed away at age of 7 years, and a diseased cousin ho shared the same features, see figure 1.

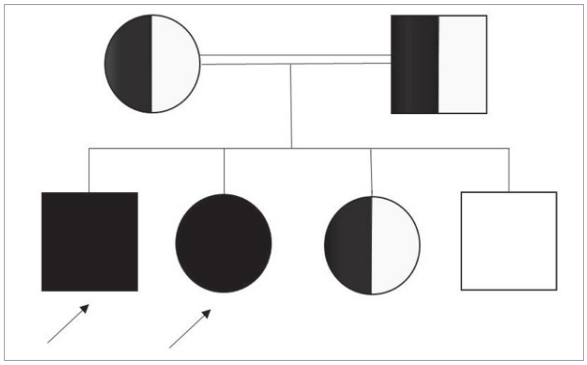

Figure 1: Family Pedigree Showing Two Siblings with Sanjad-Sakati Syndrome (Arrows). Carriers Are Indicated by Half-Shaded Symbols, Unshaded Symbol Indicates Healthy Siblings

Follow-up of the patient revealed severe growth retardation. Anthropometric measurements at 23 months showed a weight of 5.7 kg (<1 percentile) and a height of 67 cm (<1 percentile).

* Intern
** Intern
*** Intern
**** Assistant Professor, Arabian Gulf University
Consultant Pediatric Gastroenterology
Pediatric Department
Salmaniya Medical Complex
Kingdom of Bahrain
E-mail: Hyusuff93@gmail.com, Fatema.m.636@gmail, Zahraaabdulla1994 @gmail, halfaraj@hotmail.com

Abdominal and chest ultrasound revealed no features of pyloric stenosis and normal thymus gland. Ultrasound showed early changes of nephrocalcinosis, see figure 2. Brain MRI showed bilateral symmetrical posterior periventricular hyperintensities, which could be either due to terminal zones of myelination or delayed myelination. Focal dilatation of the temporal horn of the left lateral ventricle was also noted. Besides, evidence of empty sella syndrome (ESS) was found, see figure 3.

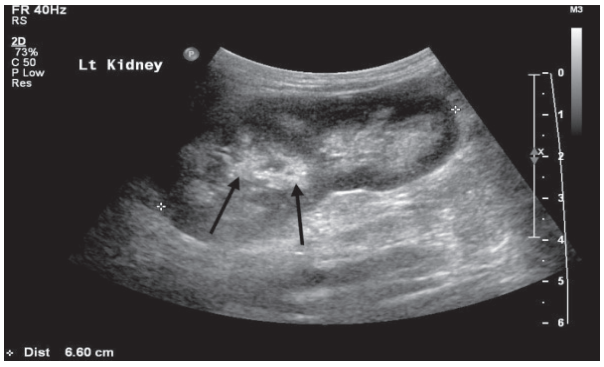

Figure 2: Left Renal Ultrasound Showing Early Changes of Nephrocalcinosis

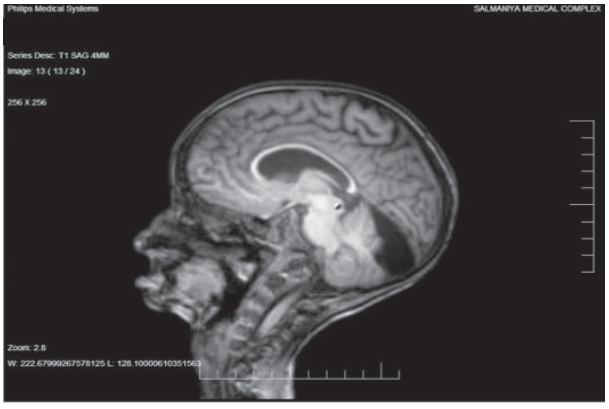

Figure 3: Brain MRI Showing Evidence of Empty Sella Syndrome

Wrist joint X-ray showed no evidence of bone injuries. However, it showed a slight reduction in bone density. Besides, there was a patchy area of increased density within the soft tissue at the medial aspect of the distal forearms just medial and above the distal end of the ulna. These findings are suggestive of soft tissue calcification because of the patient's known history of hypoparathyroidism, see figure 4.

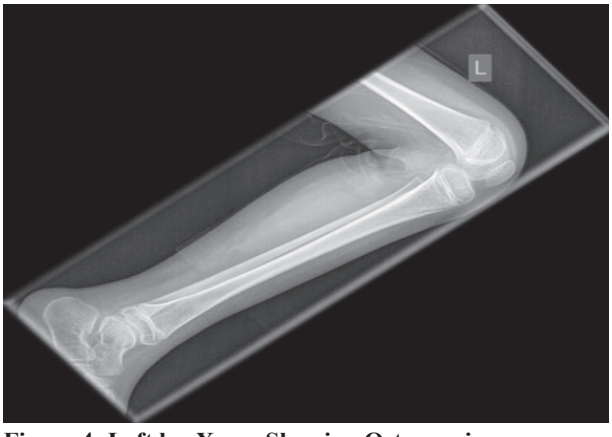

Figure 4: Left leg X-ray Showing Osteopenia

Repeat renal ultrasound confirmed persistent nephrocalcinosis. Electrocardiography (ECG) was normal.

Hearing assessment was unremarkable. Preschool intellectual examination and interviews at the age of five years and two months at the psychiatric hospital revealed evidence of developmental delay and cognitive abilities of four and a half years, self-reliance of four years, kinetic abilities of three and a half years, language capabilities of four years, and socialization of four years.

The patient was treated with calcium and vitamin D therapy. She showed excellent response and controlled convulsions. However, her anthropometric measure did not improve despite aggressive nutritional support via gastrostomy tube feeding. She also had multiple episodes of aspiration pneumonia that required home mechanical ventilation. The patient is still alive at the age of 14 years and eight months.

DISCUSSION

This is the first case to be reported in Bahrain of a rare condition called Sanjad-Sakati syndrome or hypoparathyroidism-retardation-dysmorphism (HRD)[7]. Sanjad syndrome is an autosomal recessive disorder (OMIM #241410) and represents a rare type of hypoparathyroidism[1,2,3]. It was first reported by Sanjad et al[5].

SSS or HRD is caused by a gene-encoding tubulin-specific chaperone E mutation (TBCE; 604934), on chromosome 1q42.3.3[8,9].

Most hypoparathyroidism syndromes have underlying embryogenic structural defects, mainly from the third and fourth pharyngeal pouches and fourth branchial arch[4]. The main features of these syndromes are parathyroid hormone deficiency, hypocalcemia and hyperphosphatemia[4].

Congenital hypoparathyroidism can be due to transient or permanent causes which include DiGeorge syndrome, Kenny-Caffey syndrome and Sanjad-Sakati syndrome[7]. Some of the features are similar to DiGeorge syndrome and Kenny-Caffey syndrome[10]. However, features of SSS are quite distinctive from those of DiGeorge syndrome[4]. SSS can be distinguished from DiGeorge syndrome by the absence of cardiac lesions, lymphopenia or skeletal abnormalities[10]. Also, Kenny-Caffey syndrome presents with ocular diseases, thickening of long bones, normal mentality and immunodeficiency[10,11].

SSS has been reported from the Middle East and Arabian Peninsula[7]. Patients with SSS have been reported from Qatar, Kuwait, Oman, Saudi Arabia, Sudan, Egypt and others[2,3,10]. This case is the first reported in Bahrain.

Sanjad-Sakati syndrome is usually a result of consanguineous marriages[8]. Therefore, the prevention of SSS can be achieved by pre-marital genetic counseling and preimplantation genetic diagnosis[12].

Treatment of SSS is challenging due to electrolyte imbalance[10]. Although children with SSS are usually treated with vitamin D drops and oral calcium, they continue to have a failure to thrive, similar to our patient[10]. There were some attempts to use growth hormones which were mostly unsuccessful except in one reported case in which the height has improved[10].

CONCLUSION

This is the first reported case of SSS in Bahrain. Genetic testing can help in confirming the diagnosis of SSS patients. Early management may prevent complications and minimize consequences. Furthermore, pre-marital counseling program is important for early detection of siblings at risk. Pediatricians should consider SSS in any child who presents with hypocalcemia and dysmorphic features.

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REFERENCES

1. Pal K, Moammar H, Mitra D. Visceral Myopathy Causing Chronic Intestinal Pseudo Obstruction and Intestinal Failure in a Child with Sanjad-Sakati Syndrome. J Pediatr Surg 2010;45: 430-434.
2. Pal K. Sanjad - Sakati Syndrome in a Neonate. Indian Pediatrics 2010; 47: 443-444.
3. Arabi W, Basheer A, Abdullah M. Sanjad-Sakati Syndrome in Sudanese Children. Sudan J Paediatr 2011;11(1): 43-47.
4. Sanjad SA, Sakati NA, Abu-Osba YK, et al. A New Syndrome of Congenital Hypoparathyroidism, Severe Growth Failure, and Dysmorphic Features. Arch Dis Child 1991; 66: 193-196.
5. Al-Malik M. The Dentofacial Features of Sanjad–Sakati Syndrome: A Case Report. Int J Paediatr Dent 2004; 14: 136–140.
6. AlAyed O. Sanjad-Sakati Syndrome and Its Association with Superior Mesenteric Artery Syndrome. Case Rep Pediatr 2014; 2014:108051.
7. Kelly A, Levine MA. Disorders of Bone Metabolism. In: Kappy MS, Allen OB, Geffrey ME, eds. Pediatric Practice Endocrinology. 1st edition. New York: Mc Grow Hill Medical, 2010. 191-256.
8. Sanjad SA, Sakati NA, Abu-Osba YK. Congenital Hypoparathyroidism with Dysmorphic Features: A New Syndrome. Pediat Res 1988; 23:271A.
9. Parvari R, Hershkovitz E, Kanis A, et al. Homozygosity and Linkage- Disequilibrium Mapping of the Syndrome of Congenital Hypoparathyroidism, Growth and Mental Retardation, and Dysmorphism to a 1-cM Interval on Chromosome 1q42-43. Am J Hum Genet 1998; 63:163–169.
10. Rafique B, Al-Yaarubi S. Sanjad-Sakati Syndrome in Omani Children. Oman Med J 2010; 2010(25):227–229.
11. Khan AO, Al-Assiri A, Al-Mesfer S. Ophthalmic Features of Hypoparathyroidism- Retardation-Dysmorphism. J AAPOS 2007; 11:288–290.
12. Hellani A, Aqueel A, Jaroudi K, et al. Pregnancy after Preimplantation Diagnosis for Sanjad-Sakati Syndrome. Prenat Diagn 2004; 4:302-306.