Original Article

Sanjad-Sakati Syndrome in Sudanese children

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ABSTRACT

We report on the first 4 cases (3 girls and one boy belonging to 4 families) of Sanjad-Sakati syndrome from Sudan. They presented within the first 2 months of life with repeated hypocalcaemic convulsions, severe growth retardation and dysmorphic features. They all had low parathyroid hormone levels. All patients came from consanguineous families who are of Arab descent, and 8 of their siblings had similar condition and died without being diagnosed.

Key words: Sanjad-Sakati syndrome; Hypoparathyroidism; Retardation; Dysmorphism; Child; Sudan.

INTRODUCTION

Sanjad-Sakati syndrome (SSS) or hypoparathyroidism-retardation-dysmorphism has mainly been described from the Middle East and Arabian Peninsula. Children affected with this condition are typically born with features of intrauterine growth retardation (IUGR) and present early with hypocalcaemic convulsions, typical facial dysmorphic features, growth retardation, developmental delay and hypoparathyroidism [1-4].

In this article we report on the first 4 cases of SSS from Sudan, and highlight the disease since the families of our patients lost 8 siblings with similar clinical presentation without being diagnosed. We also review the literature on SSS.

CASE REPORTS

The proband, a 50-day-old girl, was referred to Gaafar Ibn Oaf Children's Specialist Hospital in Khartoum with repeated generalized tonic-clonic convulsions and vomiting. She was an outcome of full term normal pregnancy and spontaneous vaginal delivery in hospital, and started to have recurrent attacks of generalized tonic and clonic convulsions since the age of one month. Convulsions were not associated with fever. The baby was on exclusive breast feeding and without any vitamin supplementation. Her parents are first degree relatives from Arakieen tribe, originally from Al Kamleen in Al Gazeera State. There is positive family history of similar condition: 3 siblings, 2 girls and a boy, had repeated convulsions between age one and two months and all died. They were described by their parents as being small and looked like our index patient. On examination, the patient looked ill, pale, not jaundiced or cyanosed. She had growth retardation: weight: 3 kg (-3SD), length:50 cm (-3SD), head circumference: 34 cm (-3SD), associated with dysmorphic features including small hands and

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feet, prominent forehead, deep-set eyes, large low set big ears, beaked nose, depressed nasal bridge, and long philtrum. She had no social smile yet.

Investigations showed severe hypocalcaemia: 1.6 mmol/L (N= 2.3-2.8), hyperphosphatemia: 1.79 mmol/L (N= 1.45-2.16), and low parathormone (PTH): 2.4 pg/ml (N= 10-60). Echocardiography was normal. The family was counseled and the baby received calcidiol drops (0.1 µg/kg/day) and calcium supplementation (I mmol/kg/day). At the age of 6 months her weight was 4 kg (- 4 SD), length was 54 cm(- 4SD), with global developmental delay.

Tables 1, 2, and 3 show the history, clinical findings and results of investigations for the 4 patients. Three of the cases were females and the fourth was a male. All were full term and born very small. Unfortunately, in none of the cases was the exact birth weight available. The disease manifested in all of them within the first month of life. The commonest symptoms were repeated tonic-clonic convulsions, growth failure and developmental delay. All affected families were from tribes of Arab origin and parents were first degree cousins. The 4 families lost 8 siblings with similar symptoms and most died between 2-3 months without being diagnosed.

All had the typical reported clinical findings of Sanjad-Sakati syndrome as shown in Table 2, including the facial dysmorphism, severe growth failure, and developmental delay (Figure). Brain MRI and CT, done on 2 patients, were normal.

The laboratory findings of hypocalcaemia, hyperphosphataemia with low parathyroid hormone level supported the diagnosis of hypoparathyroidism. Parathyroid hormone assay was done by Bioscientia Laboratories, Germany. Molecular genetic studies were not done due to logistic reasons.

The patients were treated with calcidiol drops (0.1 µg/kg/day) plus oral calcium (1 mmol/kg/day) and titrated according to laboratory results.

Cases 1, 2, 3 and 4 were alive at ages of 6,10,18 and 11 months, respectively; but all had significant growth failure and developmental delay. Two patients (case 2 and 3) had recurrent chest infections.

Table 1 - History of the 4 patients with Sanjad-Sakati syndrome

	Case 1	Case 2	Case 3	Case 4
Sex	F	F	F	M
Gestational age	Full term	Full term	Full term	Full term
Birth weight	low	low	low	low
Age at onset of symptoms	1 month	3 weeks	First week	37 days
Age at diagnosis	50 days	2 months	10 months	2 months
Developmental history	delayed	delayed	Severe delay	delayed
Failure to grow	+	+	+	+
Consanguinity	+	+	+	+
Tribe	Arakieen	Gaalyeen	Dar Hamid	Hassaniah
State	Gazeera	Gazeera	Kordofan	White Nile
Family history	3 siblings died with similar symptoms	One sibling died with similar symptoms	2 siblings died with similar symptoms	2 siblings died with similar symptoms

Abbreviations: F- female, M - male

Table 2 - Clinical findings of the 4 patients with Sanjad-Sakati syndrome

Reported features	Case 1	Case 2	Case 3	Case 4
Microcephaly	HC=34 cm (-3SD)	HC=33 cm (-4SD)	HC=35 cm (-3SD)	HC=33 cm (-4SD)
Deep-set eyes	+	+	+	+
Thin lips	+	+	+	+
Beaked nose tip	+	+	+	+
Low set ears	+	+	+	+
Big rotated ears	+	+	+	+
Micrognathia	+	+	+	+
Prominent forehead	+	+	+	+
Depressed nasal bridge	+	+	+	+
Small hands and feet	+	+	+	+
Esotropia	+	+	-	+
Micropenis	N/A	N/A	N/A	+
Cryptorchidism	N/A	N/A	N/A	-
Weight	3 kg (-3SD)	3.5 kg (-3SD)	3.5 kg (-2SD)	2.6 kg (-4SD)
Length	50 cm (-3SD)	46 cm (-4.5SD)	43 cm (-6SD)	46 cm (-4SD)
Echocardiography	Normal	Normal	Normal	Normal
Brain CT	-	-	Normal	Normal
MRI brain	-	-	-	-

+ : Present; - : Absent

Abbreviations: CT – computed tomography; HC – head circumference; MRI – magnetic resonance imaging; N/A- not applicable; ND – not done; SD – standard deviation

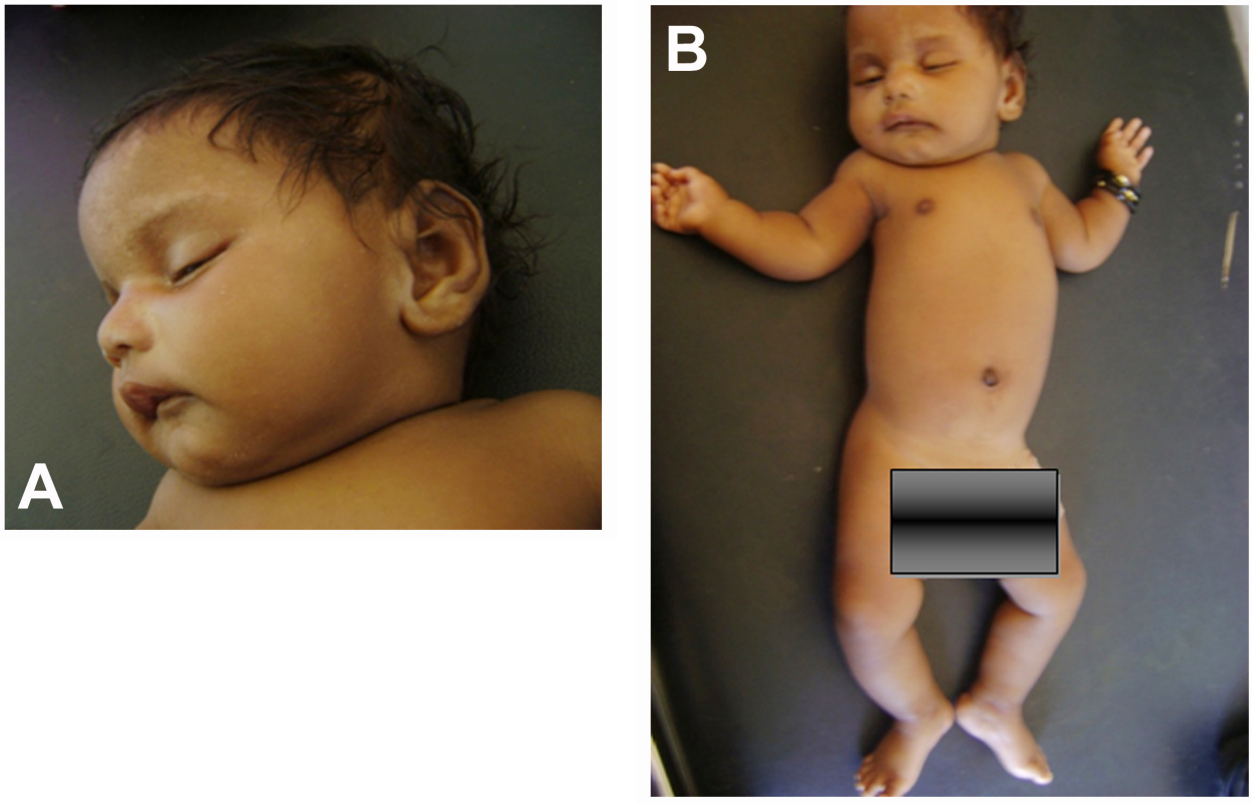
Table 3 - Results of biochemical and hormonal analyses

	Case 1	Case 2	Case 3	Case 4
Calcium (N= 2.3-2.8 mmol/L)	1.6	-	-	-
Phosphate (N=1.45-2.16 mmol/L)	1.8	-	-	-
Parathyroid hormone (N=10 - 60 pg/ml)	2.4	4	Less than 1	Less than 1
Creatinine (µmol/L)	26	28	30	-

- : Not available/ascertained

Abbreviations: N - normal level

Figure: Features of Sanjad-Sakati syndrome in Case 2. (A) Deep-set eyes, beaked nose and microcephaly. (B) Small hands and feet.



DISCUSSION

Hypocalcaemia should be considered in the differential diagnosis of any child presenting with afebrile convulsions. Hypocalcaemic convulsions may be clonic, focal clonic, multifocal, jacksonian, or apnoeic. Affected babies may also develop opisthotonous posture, irritability, high pitched cry or jitteriness. Full clinical picture of tetany, including carpopedal spasm, laryngospasm, muscle cramps, paraesthesia, Chvostek sign,Trousea's sign, bulging anterior fontanele, bradycardia, heart failure and generalized oedema, are some of the less common signs [5].

The patient should be considered to have hypocalcaemia if the total serum calcium is below 2 mmol/L (8 mg/dl) in term infants and young children; and below 1.75 mmol/l (7mg/dl) in preterm infants, or if the ionized calcium is below 1 mmol/L [5]. In all hypocalcaemic patients, blood samples should be taken for calcium, phosphate, alkaline phosphatase, serum albumin and magnesium levels. It is also preferable to draw a blood sample for parathyroid hormone (PTH) level and separate the serum and freeze it for further assay if needed. Combination of low calcium and high phosphate level is highly suggestive of hypoparathyroidism provided that the renal function tests are normal. The diagnosis is confirmed by measuring PTH. All our patients had significantly low PTH levels.

There are many causes of congenital hypoparathyroidism. Some are transient, others are permanent [5]. Permanenet causes include: Di George syndrome, Kenny-Caffey syndrome, Sanjad-Sakati syndrome and others [5].

Sanjad-Sakati syndrome (SSS) is characterized by microcephaly, deep-set eyes, beaked nose, depressed

nasal bridge, difficulty of feeding in infancy, long philtrum, thin lips, micrognathia, small hands and feet, prenatal and postnatal severe growth retardation, teeth anomalies, thick large floppy ear lobes, mental retardation and occasionally cellular immune defect [1-4].

The craniofacial features and growth retardation with small hands and feet impart such a characteristic appearance on these patients that makes the diagnosis easy once one had seen a case previously [3]. Most of these features are present in our patients and the diagnosis was suspected as one of the Authors had seen many cases in Saudi Arabia (MAA). Other features that had recently been reported include pyloric stenosis, atrial septal defect, craniosynostosis, congenital volvulous, retinal vessles tortousity and cataracts [6], and multiple pathological fractures. Most studies showed normal brain imaging as in our cases [2-4].

Sanjad-Sakati syndrome is an autosomal recessive disease. All of our cases were the outcome of consanguineous marriages which are common in Sudan as in many other Middle Eastern countries. Parvari et al [7] reported the causative gene encoding tubulin-specific chaperone E (TBCE) located at 1q42-43. No molecular genetic study was done in our cases. This syndrome has to be differentiated from Kenny-Caffey syndrome which often shows cortical thickening of long bones with medullary stenosis, macrocephaly or normocephaly, normal mentality and immune deficiency. Kenny-Caffey syndrome type 1 may show the same mutation in the tubulin-specific chaperone E gene [8].

SSS was first reported by Sanjad et al in 1988 [1], who further published other series [3] later on. The syndrome was also described by Richardson and Kirk in 1990 [2], and in 1992 by Kalam and Hafeez [4]. Thereafter the disease was reported from Qatar, Bedouin Arabs living in Israel, Kuwait and Oman [9], i.e. mostly from the Arabian Peninsula [1-4]. To the best of our knowledge this is the first report of SSS from Sudan. It is very interesting that all our patients came from tribes of Arab ancestry. Many Arab tribes immigrated to Sudan in both pre and post Islamic era [10]. It is interesting to mention that most published Saudi cases originated from Central and Western Saudi Arabia [3], i.e. just across the Red Sea where similar recessive diseases has been described from Sudan and Saudi Arabia [10].

Patients' hypocalcaemia is usually treated with calcium and calcidiol as we treated our patients. However they tend to continue having poor growth. Attempts to use growth hormone in some of the cases proved unsuccessful [9]. Most patients tend to die early with recurrent infections [1-4], but rare cases have survived up to the age of 18 years [11]. An interesting problem observed by one of the Authors (MAA) in older children is severe constipation with gut dilatation.

Prevention of the recurrence of SSS in index families could be achieved by preimplantation genetic diagnosis (PGD) and carrier detection [12].

In conclusion, we have reported the first case series of Sanjad-Sakati syndrome (SSS) from Sudan. Paediatricians should consider this condition in the differential diagnosis of any dysmorphic hypocalcaemic children especially newborns and young infants. All of our cases belonged to Sudanese tribes of Arab descent. It would be interesting to see if SSS exists among other African tribes or admixture of Arab-African population, and further identify its molecular genetics.

REFERENCES

1. Sanjad S, Sakati N, Abu Osba Y. Congenital hypoparathyroidism with dysmorphic features: a new syndrome . Pediat. res.1988, 23:271 A
2. Richardson RJ, Kirk JMW. Short stature, mental retardation, and hypoparathyroidism: a new syndrome. Arch Dis Childhood London 1990;65:1113- 117
3. Sanjad S, Sakati N, Abu-Osba YK, kaddora R, Milner RDG. A new syndrome of congenital hypopatathyroidism,seizure, growth failure and dysmorphic features. Arch Dis Childhood London 1991; 66: 193-196
4. Kalam MA, Hafeez W. Congenital hypoparathyroidism, seizure, extreme growth failiure with developmental delay and dysmorphic features-another case of this syndrome. Clin Genet 1992;42:110-13.
5. Kelly A and Levine MA. Disorders of bone metabolism in : kappy MS, Allen OB, Geffrey ME eds: Pediatric Practice Endocrinology, 1st edition Mc Grow Hill Medical. New York 2010; 191-256.
6. Al Dhoyan N, Al Hemidan A, Ozand PT.Ophthalmic manifestations of Sanjad-Sakati Syndrome. Oph Gen 2006;27 (3):83-87.
7. Parvari R, Hershkovitz E, Grossman N, Gorodischer R, Loeys B, et al. Mutation of TBCE causes hypoparathyroidism-retardation-dysmorphism and autosomal recessive Kenny-Caffey syndrome. Nature Gen 2002; 32: 44m-52.
8. Naguib KK, Gouda SA, Elshafey A, mohammed F, Bastaki L, Azab AS, et al.Sanjad –Sakati syndrome/kenny-Caffey syndrome type 1: a study of 21 cases in Kuwait.Eastern Mediterranean health Journal 2009,15 (2):345-352.
9. Rafique B, Al-Yaarubi S. Sanjad-Sakati Syndrome in Omani children. OMJ 2010; 25:227-229.
10. Salih MAM. Genetic disorders in Sudan. In: Teebi AS, ed. Genetic Disorders among Arab Populations (2nd ed). Berlin Heidelberg: Springer-Verlag, 2010:575-612.
11. Tanna N, Preciado DA, Brian N. The otolaryngologic features of Sanjad Sakati syndrome.Arch otolaryngol Head Neck Surg. 2009; 135:7.
12. Hellani A, Aqueel A, Jaroudi K, Ozand P, Coskun S.Pregnancy after preimplantation diagnosis for Sanjad-sakati syndrome.Prenatal Diagnosis 2004;4:302-306