

# Partial Agenesis of Corpus Callosum in Sanjad-Sakati Syndrome (p-ACC)

Naif ALGhasab, A. Bruce Janati, Aslam Khan

Can J Neurol Sci. 2012; 39: 833-834

Sanjad-Sakati syndrome (SSS) was first described in the Middle-East in children of consanguineous parents<sup>1</sup>. It is a rare autosomal recessive disorder known also as Middle-East syndrome or Richadson-Kirk syndrome or hypoparathyroidism-retardation-dysmorphism (HRD) syndrome<sup>2</sup>. Children afflicted with this condition are born with intrauterine growth retardation, and present with hypocalcemic tetany or seizures due to hypoparathyroidism at an early stage in their lives<sup>3</sup>. In this paper we report, for the first time, the presence of partial agenesis of corpus callosum in SSS.

## CASE REPORT

A 13-year old Saudi male, a known case of SSS, came to the emergency room of King Khalid Hospital on Aug 11, 2011 with a chief complaint of persistent vomiting and fever of a two day duration. He had a history of oesophageal and urinary reflux, decreased appetite, and asthma.

Birth history revealed that he was born at King Khalid Hospital 13 years earlier by spontaneous vaginal delivery. He had a low birth weight (1.5kg) and had repeated convulsions shortly after delivery that prompted his admission to the intensive care unit where he was treated with calcium which was later switched to alfa calcidol, given on a regular basis. His weight increased to 2.51kg in two months.

Developmental milestones were delayed in that he was unable to sit until three years-of-age, walk until six years-of-age, and talk until ten years-of-age.

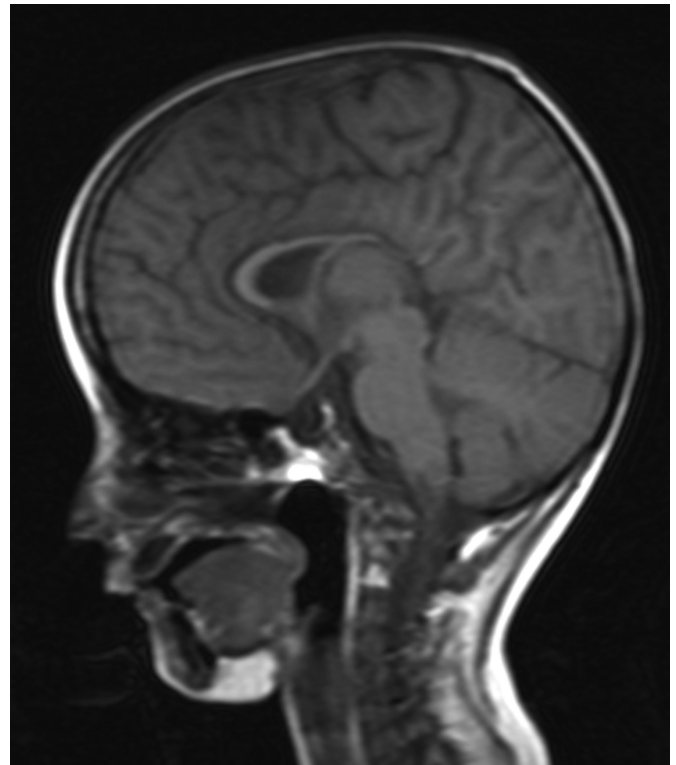
Family history revealed that parents were cousins. The patient has two siblings, a sister and a brother both of whom are in good health.

General physical examination showed the patient to be short-statured with facial dysmorphic features including a long narrow face, deep-set eyes, beaked nose, depressed nasal bridge, micrognathia, thin lips, low set and large floppy ears, small hands and feet. He also appeared dehydrated, restless and dyspneic. His weight was 9.8kg, height 80cm, and head circumference 40cm.

The patient had hypotonia, poor motor coordination, delayed developmental milestones, feeding difficulties caused by gastric reflux, impairment of chewing, and impaired swallowing, along with a low perception of pain. This symptom complex was consistent with (SSS).

The history was significant in that he was described as being aloof with a preference for socialization with adults rather than children.

A brain magnetic resonance image (MRI) showed absence of the splenium and part of the isthmus (Figure) with no abnormalities of anterior pituitary, the ventricular system, or the



**Figure:** Non-contrast MRI of the head (sagittal plane) shows partial agenesis of the corpus callosum. Note the absence of the splenium and part of the isthmus.

white matter. An electroencephalogram (EEG) showed moderate diffuse slowing of dominant background rhythms consistent with diffuse gray matter disease. There were no epileptiform discharges and no interhemispheric asynchrony.

## DISCUSSION

Sanjad-Sakati syndrome is an autosomal recessive disorder characterized by distinct clinical, biochemical, and genetic

From the Qassim University (NA), Buryidah; King Khaled Hospital (AK), Hail, Kingdom of Saudi Arabia; Center for Neurology (ABJ), Fairfax, Virginia, USA.

RECEIVED FEBRUARY 15, 2012. FINAL REVISIONS SUBMITTED MAY 15, 2012.

Correspondence to: Naif Saad Mohsen ALGhasab, P.O Box 6252, Hail City, ALHWAZIM area, Kingdom of Saudi Arabia, Postal code 81442.

Email: dr.legend@hotmail.com.

abnormalities, which typically present in the neonatal period with tetany, seizures or apnea due to hypocalcaemia. Patients have also been reported to have recurrent infections, probably due to immune system failure. Most of the cases reported have been associated with parental consanguinity and have come from the Arabian peninsula<sup>1</sup>. The corpus callosum is the largest midline structure of the brain. It begins to develop around the 10th to 11th week of pregnancy and consists of over 200 million nerve fibers that connect the two hemispheres of the brain. It transfers and integrates motor, sensory, and cognitive information between the cerebral hemispheres. It continues to mature throughout pregnancy and into childhood and adolescence. Absence of corpus callosum would be associated with physical, developmental, social/behavioural, and, cognitive/communication problems, a symptom-complex which existed in our patient<sup>4</sup>.

In a previous study of 65 individuals from 34 pedigrees of Middle Eastern origin, HRD syndrome was caused by a deletion of c.155-166del12 within the tubulin cofactor E (TBCE) gene that encodes a molecular chaperone that is required for heterodimerization of  $\alpha$ -tubulin with  $\beta$ -tubulin. Other mutations reported previously were a deletion of 2 bp in the first exon of the gene (c.66delAG, p.V23fs48X) and c.T1113A (p.C371X) in exon 12, identified in compound heterozygosity in a surviving Belgian child from a pedigree where two siblings manifested features of HRD syndrome<sup>5</sup>. The Sanjad-Sakati disorder had been mapped to the long arm of chromosome 1 (1q42-q43) and mutations in the gene coding for tubulin-specific chaperone E (TBCE) had been identified as the cause of the disease<sup>6</sup>. One study found another variant of SSS with no mutations in the TBCE gene<sup>6</sup>. In some studies of Sanjad-Sakati syndrome, MRI revealed different findings associated with the same TBCE gene mutation (c.155-166del12; p.del52–55) (Table)<sup>7</sup>, while others reporting different gene mutations lacked MRI data.

The diagnosis of our patient was made on clinical grounds only, due to unavailability of genetic studies in our institution.

The brain MRI in our patient showed partial agenesis of corpus callosum characterized by absence of splenium and part of the isthmus, a finding which has never been reported in SSS.

In conclusion, our patient showed partial agenesis of the corpus callosum which could explain the patient's motor, behavioral and developmental abnormalities, an association which has been documented in the literature<sup>4</sup>. Future studies of SSS should focus on a wide variety of MRI findings and their relationship to different genetic mutations in SSS.

---

**Table: Different MRI findings for TBCE gene mutation (c.155-166del12; p.del52–55)<sup>7</sup>**

---

- Reduced white matter mass
  - Delayed myelination
  - Hypoplastic anterior pituitary
  - Hypoplasia of the corpus callosum
  - Lateral ventricular dilation with prominent temporal horns
- 

#### REFERENCES

1. Sanjad S, Sakati N, Abu-Osba Y, et al. Congenital hypoparathyroidism with dysmorphic features: a new syndrome. *Pediat Res*. 1988; 23: 271A.
2. Richardson RJ, Kirk JMW. Short stature, mental retardation and hypoparathyroidism. *Arch Dis Child*. 1990; 65: 1113-17.
3. Bushra R, Saif Y. Sanjad-Sakati Syndrome in Omani children. *Oman Med J*. 2010 July; 25(3):227-9.
4. [umaine.edu](http://umaine.edu) [homepage on the Internet]. New England: Education and Human Development University of Maine; [about 2 screens], [Date accessed: 2012 Jan 7]. Available from: <http://umaine.edu/edhd/about/research/acc/what-is-agenesis-of-the-corpor-callosum-acc/>.
5. Parvari R, Hershkovitz E, Grossman N, et al. Mutation of TBCE causes hypoparathyroidism-retardation-dysmorphism and autosomal recessive Kenny-Caffey syndrome. *Nat Genet*. 2002; 32: 448–52.
6. Courtens W, Wuyts W, Poot M, et al. Hypoparathyroidism-retardation-dysmorphism syndrome in a girl: a new variant not caused by a TBCE mutation – clinical report and review. *Am J Med Genet*. 2006; 140: 611-17.
7. Raja P, Dan K, Martin P, et al. Mutation in the TBCE gene is associated with hypoparathyroidism-retardation-dysmorphism syndrome featuring pituitary hormone deficiencies and hypoplasia of the anterior pituitary and the corpus callosum. *J Clin Endocrinol Metab*. 2009; 94(8): 2686-91.