

CASE REPORT

Open Access

# Opitz trigonocephaly syndrome presenting with sudden unexplained death in the operating room: a case report

Laura Travan<sup>1\*</sup>, Vanna Pecile<sup>2</sup>, Mariacristina Fertz<sup>1</sup>, Antonella Fabretto<sup>2</sup>, Pierpaolo Brovedani<sup>1</sup>, Sergio Demarini<sup>1</sup> and John M Opitz<sup>3</sup>

## Abstract

**Introduction:** Opitz trigonocephaly C syndrome (OTCS) is a rare malformation syndrome with the following features: synostosis of metopic suture, craniofacial abnormalities, severe mental retardation and a multitude of pathological findings affecting almost every organ system. OTCS is associated with a high mortality rate.

**Case presentation:** We describe the case of a Caucasian male baby who died at five months of age during surgical correction of the craniofacial anomaly.

**Conclusion:** As previously reported, OTCS may have an increased mortality rate during craniofacial surgery. Careful evaluation of surgery risk-benefit ratio is warranted in such patients.

## Introduction

Opitz trigonocephaly C syndrome (OTCS) is a rare and heterogeneous genetic disorder characterized by synostosis of metopic suture, dysmorphic facial features, variable mental retardation and other congenital somatic and cerebral anomalies. Morbidity and mortality are very high. Fewer than 60 cases have been reported in the literature, mostly as single case reports or small series. We describe a white male baby who died at five months of age during surgery performed to correct the craniofacial anomaly.

## Case Presentation

Our patient was a Caucasian baby, born to nonconsanguineous parents at 39 weeks of gestational age. This was the first pregnancy of a 30-year-old mother with a bicornuate uterus. Pregnancy was complicated by early intrauterine growth retardation; antenatal ultrasound assessment was otherwise reported as normal.

Labor and delivery were spontaneous. The Apgar score was 9 and 10, respectively at one and five minutes. Birth weight was 2470 g (< 3rd percentile, small for

gestational age), length was 46.7 cm (3<sup>rd</sup> to 10th percentile), head circumference 33.1 cm (10th percentile).

At birth there was a marked trigonocephaly and other dysmorphic craniofacial features: micrognathia, upslanting eyelids, hypotelorism, depressed nasal bridge, low set ears. Cardiac and renal ultrasounds were normal. Computed tomography confirmed the early closure of metopic suture (Figure 1). Initially the baby was fed by nasogastric tube. At discharge after one week, he was fed completely by bottle.

At 40 wks post-conceptional age brain MRI showed a small area of hyper-intensity under the posterior horn of the left ventricle (interpreted as calcification of a periventricular hemorrhage) and a diffused alteration of white periventricular matter (Figure 2).

An auditory brain stem response (ABR) test performed at 44 weeks revealed an absent pattern on the left ear.

Clinical evaluation during the first four months of life did not show an evident psychomotor delay; however fidgety activity seemed absent.

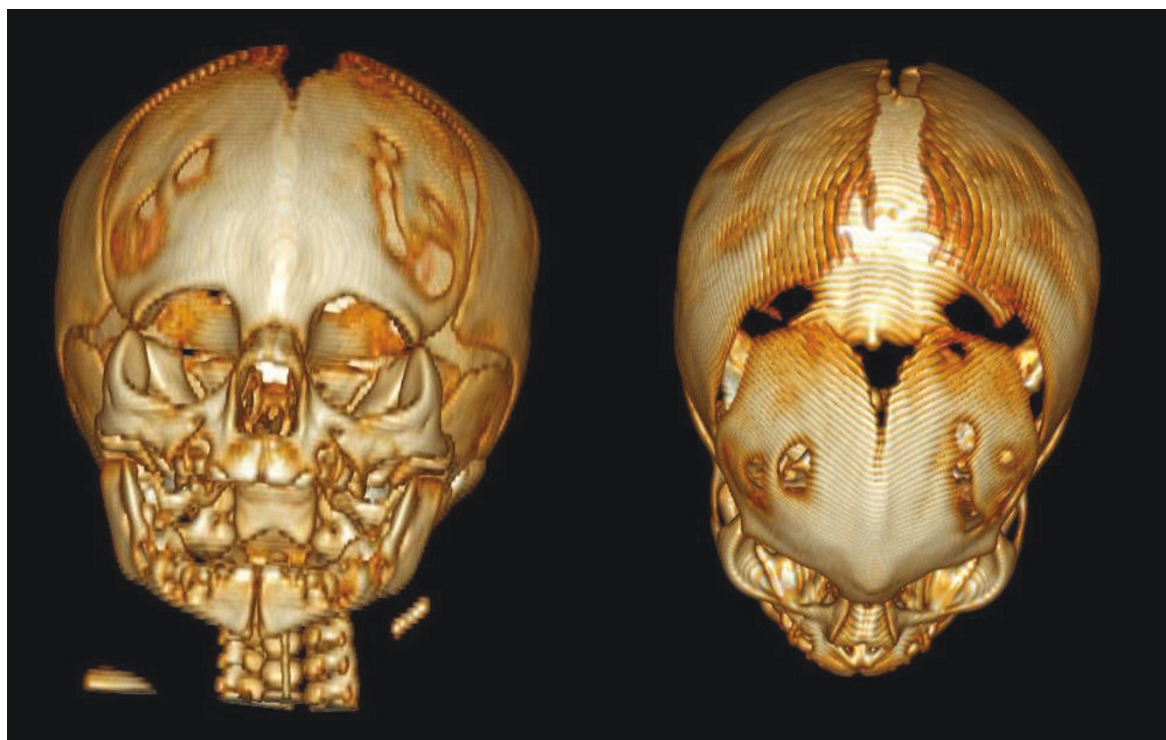
Chromosome analysis showed a normal 46 XY karyotype. We also performed single-nucleotide polymorphism (SNP) array without any significant finding.

The baby died unexpectedly at five months of age during surgery performed to correct the craniofacial anomaly.

\* Correspondence: ltravan@yahoo.it

<sup>1</sup>Neonatal Intensive Care Unit, Institute for Maternal and Child Health Burlo Garofolo, Via dell'Istria 65/1, 34100, Trieste, Italy

Full list of author information is available at the end of the article



**Figure 1** Three-dimensional computerized tomography. See the fusion of metopic suture.

Autopsy did not add anything to the clinical picture: specifically, there were no additional anomalies except for a double left renal artery. Some micro calcifications were found around brain vessels.

### Discussion

OTCS, first described in 1969 by Opitz [1] is characterized by trigonocephaly, mental retardation, short neck, typical facial appearance, joint and limb anomalies, up-slanting palpebral fissures, epicanthal folds, a broad depressed nasal bridge, small nose, abnormally low-set ears, and central nervous system and visceral anomalies, such as renal and heart anomalies.

OTCS is a heterogeneous genetic disorder which occurs sporadically, although familial cases have also been reported [2,3].

A very high mortality rate has been described: almost 50% of patients with OTCS die within the first year of life [3]. Some patients, however, may have a good quality of life: Patient 2 of Lalatta [4] has normal IQ. She underwent multiple craniotomies but she did well at the University and was also able to play the piano.

Our patient had many of the clinical and anatomic findings typical of OTCS: the dysmorphic face, white matter alteration, as described by Lalatta [4] and by Azimi [5], cerebral hemorrhage [3] and hearing loss as

reported by Nacarkucuk et al. [6] and Zampino et al. [7].

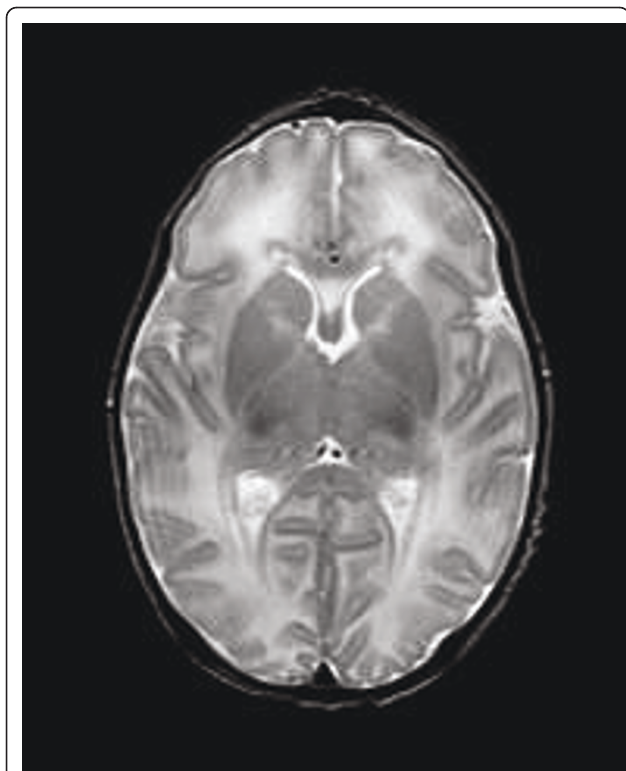
We did not find any genetic abnormality either in the karyotype or in the region of CD96 gene, as recently described by Kaname [8].

To the best of our knowledge this is the second case after patient 1 reported by Opitz [3] who died after surgery for craniotomies repair. That patient, after the skull reconstruction, developed hematuria, cardiac arrhythmia and severe acidosis requiring cardiopulmonary resuscitation. Twenty minutes later, he developed a severe intra-vascular coagulation. After the autopsy, experts in genetics, immunology and rheumatology concluded that patient 1 of Opitz had a possible connective tissue abnormality and increased vascular fragility that started the catastrophic cascade that led to death.

Our patient died under the same circumstances as patient 1 described by Opitz. Autopsy did not find vascular malformation or connective tissue anomalies that could have explained death during surgery. However, as in Opitz's patient 1 the cause of death was an unexpected massive bleeding.

### Conclusion

OTCS is a complex and heterogeneous condition that is still under-recognized and under-diagnosed. The fact that two children died as a consequence of craniofacial



**Figure 2** Cerebral MRI (whitened T2 sequences), showing diffuse white matter periventricular hyperintensity (hypointensity in T1 sequences).

surgery may have clinical implications: diagnosing OTCS in trigonocephalic patients before surgery, may allow a better evaluation of risks and benefits of craniostosis repair.

### Consent

Written informed consent was obtained from patient's next-of-kin for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### Author details

<sup>1</sup>Neonatal Intensive Care Unit, Institute for Maternal and Child Health Burlo Garofolo, Via dell'Istria 65/1, 34100, Trieste, Italy. <sup>2</sup>Department of Genetics, Institute for Maternal and Child Health Burlo Garofolo, Via dell'Istria 65/1, 34100, Trieste, Italy. <sup>3</sup>Departments of Pediatrics, Human Genetics, Obstetrics, and Gynecology, University of Utah, Salt Lake City, UT, USA.

### Authors' contributions

LT made the patient diagnosis confirmed by JMO; they and SD were major contributors in writing the manuscript. VP and FA performed and interpreted the genetic analysis. MF and PB performed clinical evaluations. All authors read and approved the final manuscript.

### Competing interests

The authors declare that they have no competing interests.

Received: 17 November 2010 Accepted: 21 June 2011  
Published: 21 June 2011

### References

1. Opitz JM, Johnson RC, Mc Creadie SR, Smith DW: **The C syndrome of multiple congenital anomalies.** In *Birth Defects, Original Article Series, Volume 2.* Edited by: Bergsma D. New York: The National Foundation; 1969:161-166.
2. Antley RM, Hwang DS, Theopold W: **Further delineation of the C (trigonocephaly) syndrome.** *Am J Med Genet* 1981, **9**:147-163.
3. Opitz JM, Putnam AR, Comstock JM, Chin S, Byrne JL, Kennedy A, Frikke MJ, Bernard C, Albrecht S, Der Kaloustian V, Szakacs JG: **Mortality and pathological findings in C (Opitz trigonocephaly) syndrome.** *Fetal Pediatr Pathol* 2006, **25**:211-231.
4. Lalatta F, Clerici Bagozzi D, Salmoiraghi MG, Tagliabue P, Tischer C, Zollino M, Di Rocco C, Neri G, Opitz JM: **"C" trigonocephaly syndrome: clinical variability and possibility of surgical treatment.** *Am J Med Genet* 1990, **37**:451-456.
5. Azimi C, Kennedy SJ, Chitayat D, Chakraborty P, Clarke JT, Forrest C, Teebi AS: **Clinical and genetic aspects of trigonocephaly: a study of 25 cases.** *Am J Med Genet A* 2003, **117A**:127-135.
6. Nacarküçük E, Okan M, Sarimehmet H, Ozer T: **Opitz trigonocephaly C syndrome associated with hearing loss.** *Pediatr Int* 2003, **45**:731-733.
7. Zampino G, Di Rocco C, Butera G: **Opitz C trigonocephaly syndrome and midline brain anomalies.** *Am J Med Genet* 1997, **73**:484-488.
8. Kaname T, Yanagi K, Chinen Y, Makita Y, Okamoto N, Maehara H, Owana I, Kanaya F, Kubota Y, Oike Y, Yamamoto T, Kurosawa K, Fukushima Y, Bohring A, Opitz JM, Yoshiura K, Niikawa N, Naritomi K: **Mutations in CD96, a Member of the Immunoglobulin Superfamily, Cause a Form of the C (Opitz Trigonocephaly) Syndrome.** *Am J Med Genet A* 2007, **81**:835-841.

doi:10.1186/1752-1947-5-222

**Cite this article as:** Travan et al.: Opitz trigonocephaly syndrome presenting with sudden unexplained death in the operating room: a case report. *Journal of Medical Case Reports* 2011 **5**:222.

**Submit your next manuscript to BioMed Central and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
www.biomedcentral.com/submit

