Author's response to reviews

Title: Opitz trigonocephaly syndrome died during surgery: a case report

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Author's response to reviews: see over
Answers to Editorial Team comments
1. We obtained the consent from the parents’ patient and not from the patient himself: we modified the consent statement on our manuscript.
2. We sent a copy of parent consent for image publication to jmcreditorial@biomedcentral.com. The consent is in Italian. Parents did not understand English. If it is strictly necessary having an English consent, we will see parents again on 24 February.

Comments to reviewers’ reports

Referee 1:
The referee 1 wrote: “May be much better - especially if you are 7 - to have more than one case of the same diagnosis, especially if the diagnosis is not very rare”.

Unfortunately at this time this is the only case of Opitz C syndrome, after that reported by Opitz in 2006, who died as a consequence of surgery for craniostenosis repair. The disease is not so common to allow us to collect more cases in short time. We think that the message of balancing advantages and risks of surgery in this delicate type of patients is too important for waiting other cases to publish.

Referee 2:

1) the Referee asks: “what is the impact to produce the syndrome and how they assess the degree of the intrauterine growth retardation as no further signs reported?” The intra uterine growth retardation (IUGR) is an Obstetric evaluation (abdomen < 10° percentile) found sometimes in syndromic foetuses, IUGR is only one of the possible signs of Opitz C syndrome, but not cause/effect related to it. Moreover IUGR foetuses often have no pathology after birth: almost 85% are constitutional IUGR, 14% are due to uterus-placental insufficiency, only 1% to syndromes.

2) The Referee wrote: “The patient description showed that at 44 weeks there is brain stem cerebral lesion producing the hearing loss despite that no psycho motor delay was evident till age of 4 months which is confirmed by the SNPS array of no significant findings: the records of the patient should be revised carefully as no speculation
from reporting the case with no positive findings at clinical or histopathological or chromosomal or autopsy study …”.

We delete the sentence in page 4, line 7 “…, initially attributed to the cerebral lesion” avoiding any speculation.

The fact that SNPS array was normal does not exclude psycho motor delay: there are a lot of syndromic infants and infant with mental impairments without any revealed genetic alteration.

3) “at surgery where the mishap occurs a number of questions has to be answered:

a) what is the level of the surgeon performing the surgery and experience as the center load could be different from that of center with high load which will sure affect outcome as compared to papers like Azimi et al (ref 5 with 25 cases) or Optiz et al. Supporting this notion that no findings and as compared to discussion in Case 3 of Opitz et al (re 3) with connective tissue disorder which is not the same.”

The level of surgeon and of the team performing the craniostenosis repair was “level 3”, that is the highest level in our country (Italy). This kind of surgery is performed only by expert teams.

Surgeon and anaesthetist claimed that the little patient “was bleeding like a fountain”. But there was not clotting disorders. The autopsy was a mutual one and after that parents wanted the little body to go back to Albania, their native nation. There was no time and no consent for further medical investigations.

b) “what is the cause of bradycardia, could be iatrogenic from brain insult”.

The autopsy and the judges claimed it was not an iatrogenic brain insult, but that death was probably due to excessive bleeding, causing bradycardia and then death.

c) Haw the mylenization problem is excluded in your case with possibility in producing the hearing loss.

The myelinization is not the cause of hearing loss but it is only associated to cerebral lesions in Opitz C syndrome patients (Antley RM, 1981, 2; e Opitz JM 2006, 3).

In page 5 line 10 we delete “…the suggestion of”.

4) “Death in this case need to be explained better”
At page 5 line 22 we added the sentence “…realistically death was due to excessive bleeding, causing extreme bradycardia and then death. Unfortunately parents wanted the little body to go back to their native nation (they were not Italians) and there was no time and no consent for further medical investigations”.
We deleted in page four line 14 “due to cardiac arrest probably following extreme bradycardia”.

Referee 2 wrote: “…the authors could not provide new data in the syndrome…”. Our intent with this manuscript was not to add new data, but to recommend a mandatory careful evaluation of surgery risks in craniofacial or even in other not strictly necessary kind of surgery in children affected by Opitz trigonocephaly C syndrome, because the outcome could be death. We think this is strongly important for Paediatricians and Surgeons who diagnose and manage Opitz C little patients, avoiding predictable deaths.