**Author's response to reviews**

**Title:** Seizures as the first manifestation of chromosome 22q11.2 deletion syndrome in a 40-year-old man: case report.

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**Author's response to reviews:**

8/20/2007

Dear Dr Syed M Jalal:

I would like to thank you for the time and dedication invested in reviewing our manuscript. I agree and appreciate your suggestions. I made the necessary changes in the body of the manuscript in response to your suggestions:

**Major concern:**

1. To prove the point that seizures are the first manifestations of the syndrome, especially in adults

   (1) It should be clarified when seizures were first observed in this patient. In the case presentation the point is unclear.

   The patient presented with his first seizure event at the age of 40. He never had seizure before. I clarified this in the case presentation.

   (2) A careful literature search needs to be done to clarify if seizures are indeed one of the first indications of the disease. There are some 10 publications on the topic that are not cited in this paper. A few are: Karr et al. J Clin Pathol 2005;58:655-657; Bosch et al. Am J Med 2001;112:161-162. Would it not be more appropriate to suggest both seizures and hypocalcemia as the major features in adults?

   Seizures are not one of the first indications of the disease, but one of the 180 clinical features that patients might present with. I agree that both seizures and hypocalcemia are major features, and for this reason I added a new paragraph in the discussion. Usually the seizures are related to hypocalcemia but other explanations are also possible (stroke, cerebral atrophy, etc).

2. Appropriate changes in the abstract and discussion should be made in response to item 1.
Minor concerns:
1. Change 22Q11.2 to 22q11.2 in the title
   Done
2. In figure 1, normal and abnormal brain tomography should be so labeled.
   In figure 1 both brain computer tomography cuts are from the patient and abnormal. I clarify this on the figure legend.
3. Del22q11.2 is not an acceptable cytogenetic expression. Change it to del(22)(q11.2) or microdeletion of 22q11.2. Technically, the deletion is del(22)(q11.2q11.2).
   I changed it to the appropriate expression.

Sincerely,
Adriano Tonelli, MD.
8/20/2007
Dear Dr Renzo Guerrini

We are grateful for the time you devoted to review our manuscript. We appreciated your observations and we improve the manuscript accordingly. In response to your suggestions:

This paper describes a 40 year old man in whom chromosome 22q11.2 deletion was detected following investigations for a hypocalcemic seizure.
The notion that adult-onset seizure may be the presenting symptom of hypocalcemic hypoparathyroidism is nothing new.
One similar case was reported by Kar et al. [2005] (not quoted by the authors).
Therefore the report by Tonelli et al. is not entirely original.

Tough our case is not the first one reported in the literature, we believe that is relevant as 22q11.2 deletion syndrome should be part of the differential diagnosis in patients with idiopathic hypoparathyroidism, even in adulthood. It has variable phenotypical manifestations and on occasions it can present in a subtle way, like in our patient. Its identification is relevant as it can be treated with calcium without the need of antiepileptic agents, medications that can make the condition worse as some may aggravate the hypocalcemia.

The statement that Maalouf¿s case presented with new onset seizures in adulthood is not true in that that patient had a first seizure at age 14.
You are right, the syndrome was diagnosed at the age of 32, but the patient had his first episode of seizure at the age of 14. I corrected the text in agreement with
your observation.

The patient’s phenotype does not seem to be particularly suggestive of Chromosome 22q11.2 deletion. The authors should explain why they performed a FISH study for Chromosome 22q11.2 Deletion Syndrome.

A FISH study was done because of the subtle physical characteristics and the presence of hypoparathyroidism with any obvious explanation. I improved his physical description and added why we order the test.

It should be mentioned whether any psychiatric condition or cognitive impairment was present in the patient.

The patient did not have any psychiatric disorder or obvious cognitive impairment. This was added in the case presentation.

Sincerely,

Adriano Tonelli, MD.