Author’s response to reviews

Title: 4q27 deletion and 7q36.1 microduplication in a patient with multiple malformations and hearing loss: a case report

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Version: 1 Date: 30 Dec 2019

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Replies to Annamaria Franze (Reviewer 1)

1. The manuscript could be interesting, but it is written in a very unclear way. It must therefore be rewritten from the beginning.

Response: We have rewritten our manuscript and have it edited and proofread by Shanghai Meisi Medical Technology Co.Ltd.

Replies to Yoshihiro Noguchi, M.D., Ph.D. (Reviewer 2)

1: p5. Brainstem auditory evoked potential showed the left auditory pathway disorder. Authors should mention acoustic stimulus (click?) and sound intensities used for measuring BAEP, and BAEP thresholds for both ears. Otherwise, severity of hearing loss is unclear.

Response: The detail outcome of Brainstem auditory evoked potential has been described in the revised version (p4). The left auditory pathway disorder showing no reaction to clicking sounds ranging from 30 to 120dB. However, the right auditory pathway reaction was well with a BAEP threshold of 30dB.

2: In general, hearing impairment is divided into conductive (external and/or middle ear impairments) and sensorineural (inner ear, cochlear nerve and/or central auditory pathway impairments) hearing loss. This patient had low-set ears, which was a kind of external ear anomaly, and was frequently combined with middle ear anomaly including malformation of auditory ossicles. These anomalies cause conductive hearing loss. Besides, a patient with diploegenesis is easily suffered from middle ear infection (otitis media with effusion etc.), which can cause conductive hearing loss. Therefore, authors should show otoscopic (eardrum and external auditory canal) finding and CT images of temporal bones of this patient.
Response: Unilateral hearing loss is more common than bilateral, and it was previously reported that more than one out of ten children initially diagnosed with unilateral hearing loss will progress to bilateral hearing loss. According to a literature search, all patients of 4q deletions or 7q duplications with hearing impairment had low-set ears, almost of who were sensorineural. This boy had several times hospitalizations from birth to death, none of pediatricians found any signs of middle ear infection. Due to low-body weight and consideration of cumulative radiation dose of several chest CT required by frequent pneumonia, he did not get CT examination for his temporal bones.

3: Authors make mention on GAB1 gene, which is located on the deletion area of 4q. GAB1 is the causative gene for autosomal recessive non-syndromic hereditary hearing loss (DFNB26) and its variants can cause bilateral profound sensorineural hearing loss. However, hearing impairment recognized in this patient seems to be unilateral. Besides, it is unknown whether the hearing impairment is sensorineural hearing loss or not. I think that GAB1 gene is not associated with left hearing impairment of this patient.

Response: We are very sorry for our negligence of detail information of GAB1. We removed discussion about GAB1 in the revised version. After searching the deletion and duplication regions more carefully, we found the deletion of FGF2 highly likely to exhibit haploinsufficiency which could reduce the proliferation and survival of auditory neuroblasts in murine (p7).

4: All gene symbols should be italicized.

Response: We corrected the format of gene symbols in the revised version.