2q24 deletion in a 9-month old girl with anal atresia, hearing impairment, and hypotonia

Peiwei Zhao\textsuperscript{a,1}, Bing Mao\textsuperscript{b,d,1}, Xiaonan Cai\textsuperscript{a}, Jun Jiang\textsuperscript{c,e}, Zhisheng Liu\textsuperscript{b,d,***}, Jun Lin\textsuperscript{f,**}, Xuelian He\textsuperscript{a,*}

\textsuperscript{a} Clinical Research Center, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, China
\textsuperscript{b} Department of Neurology, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, China
\textsuperscript{c} Department of Rehabilitation, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, China
\textsuperscript{d} Department of Neurology, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science & Technology, 430016, China
\textsuperscript{e} Department of Rehabilitation, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science & Technology, 430016, China
\textsuperscript{f} EEG Room, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science & Technology, 430016, China

\textsuperscript{1} Equally contributed.

\textsuperscript{*} Corresponding author. Clinical Research Center, Wuhan Children's Hospital, China.
\textsuperscript{**} Corresponding author. Department of Rehabilitation, Wuhan Children's Hospital, China
\textsuperscript{***} Corresponding author. Department of Neurology, Wuhan Children's Hospital, China
E-mail addresses: liuzsc@126.com (Z. Liu), setyykf@163.com (J. Lin), hexuelian2013@hotmail.com (X. He).

\textbf{ARTICLE INFO}

\textbf{Keywords:}
Intellectual disability
Developmental delay
TBR1
Pathogenic genes
Phenotype

\textbf{ABSTRACT}

Deletion of 2q24.2 is a rare cytogenetic aberration in patients, exhibiting heterogeneous clinical features, and common phenotypes included developmental delay, intellectual disability, hypotonia, and mild dysmorphic features. Hearing impairment and anal atresia are rarely described. Here we described a 9-month-old female patient with hypotonia in all four limbs, developmental delay, and intellectual disability. In addition, congenital anal atresia was diagnosed and treated after birth, and hearing impairment was found in right ear. Single nucleotide polymorphisms (SNP) array detected a 5.2 Mb deletion on 2q24.2q24.3, including 19 genes (ITGB6; TBR1; SLC4A10; KCNH7 SCN3A; SCN2A et al.). Among these genes, it is affirmative that TBR1 is a causative gene for intellectual disability; however, the pathogenic genes of other phenotypes remain unclear. We briefly review the knowledge of genes likely involved in these clinical features, including hearing impairment, anal atresia, and developmental delay.

1. Introduction

Since Takatsuki et al. firstly reported a patient with 2q24.2q24.3 with low-birth weight, hypotonia, seizure, and dysmorphic features \cite{1}, a few cases with different clinical features were reported \cite{2,3}; The clinical features of 2q24 microdeletion syndrome include developmental delay, intellectual disability, hypotonia, joint laxity, seizure, dysmorphic features, and pulmonary emphysema \cite{4}. The heterogeneous phenotypes are due to the different deletion size, deleted genes, and genetic variations in the remaining allele, and the influence of the rest of the genome. To our knowledge, studies reporting 2q24.2q24.3 deletion with hearing impairment are very rare, and only Ono et al. reported that a patient with a deletion of q24.1q24.3 with hearing impairment.

Here we report a patient with a 5.2 Mb deletion in 2q24.2q24.3 with hearing impairment and anal atresia, and we also discussed the possible pathogenic genes by comparing the phenotypes presented in these patients with 2q24.2q24.3 reported in the literature.

2. Materials and methods

2.1. Subject

The girl is the first child from nonconsanguineous healthy parents. Her mother reported that they had taken drugs for gynecological inflammation and became pregnant during medication duration. The parents denied family history of congenital abnormality, developmental delay, seizure, and recurrent pregnancy loss. Pregnancy was complicated by intrauterine growth retardation. The baby was born at 38 weeks of gestation by cesarean delivery. The birth weight was 2,850 g.
the length of the baby was 46 cm, and the head circumference was 30 cm. After delivery, initial physical examination showed congenital anal atresia and hypotonia, and immediate surgical treatment was performed. The baby failed in neonatal hearing screening and showed no response in her right ear to diagnostic auditory brainstem response (ABR) testing.

At 4 months, she was able to raise head. At 9 months, she was referred to our hospital because she was unable to stand alone. Clinical examination show short stature, inverted-V-shaped upper lip, joint laxity, hypotonia in all four limbs, and absence of knee jerks. Speech development was delayed, and was not able to call “ma” or “ba”. She also showed moderate to severe intellectual disability. Brain MRI and EEG examinations were normal.

2.2. Cytogenetic analysis

Culturing, harvesting of peripheral blood cells and chromosome banding were performed according to standard methods. GTG-banded chromosomes were studied and the karyotype was interpreted according to the International System for Human Cytogenetic Nomenclature (ISCN 2009).

2.3. Whole-genome SNP array analysis

Genomic DNA was extracted from peripheral blood lymphocytes of the patient using phenol–chloroform method. Genomewide copy number analysis was performed using Illumina Human Cyto-SNP12 BeadChip (Illumina, San Diego, CA). The data from the images were analyzed using KaryoStudio v1.4.

2.4. Quantitative PCR(qPCR)

Semi-quantitative qPCR was performed to confirm the presence of the deletion and its boundary by detecting the copies of DNA fragments within inside and outside the proximal and distal boundary, respectively, on both the patient and her parents, as well healthy control (shown in Fig. 2). The primers for these genes were designed by referring the SNPs near the boundaries according to whole-genome SNP array analysis results. The primers for these DNA fragments are as followings: P1 (forward primer: 5’-CCA GAC CAG AAG TCC TAA ACC AG-3’, reverse primer: 5’-GAA GCA GCT GTG AAT GTG CTC-3’), P2 (forward primer: 5’-GAA GGA ACT AGG AGC TCT GCC-3’, reverse primer: 5’-GTC AGA ACT GTA GAG CTT TCC TG-3’), P3 (forward...
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات