A Rare Case of 2q37 Deletion Syndrome Presented with Patent Foramen Ovale

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Abstract

Here we report a patient with 2q37 deletion syndrome confirmed by comparative genomic hybridization (CGH) plus single nucleotide polymorphism (SNP), who does not suffer from mental developmental abnormalities. The patient, however, does suffer from fatigue and gross motor delay, and the presence of a patent foramen ovale.

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Informed Consent

Written informed consent was obtained from the patient's legal guardian to publish this report in accordance with the journal's patient consent policy.

Abstract

Here we report a patient with 2q37 deletion syndrome confirmed by comparative genomic hybridization (CGH) plus single nucleotide polymorphism (SNP), who does not suffer from mental developmental abnormalities. The patient, however, does suffer from fatigue and gross motor delay, and the presence of a patent foramen ovale.

Key Clinical Message

2q37 deletion syndrome is associated with mild to severe intellectual disability, delayed motor skills such as sitting and walking, and behavioral problems. However, cardiac anomalies are up to 20% in this syndrome.

Keywords: 2q37 deletion syndrome; patent foramen ovale; cardiac Anomalies; chromosome 2; comparative genomic hybridization; single nucleotide polymorphism

Introduction

2q37 deletion syndrome is a chromosomal condition in which the patient has lost a small portion of genetic material. The deletion of the 2q37 gene can result in chromosomal breaks in three different bands: 2q37.1, 2q37.2, and 2q37.3. The 2q37 region in the long q arm of chromosome 2 is divided into three cytogenic areas with a subsequent 179 genes inside them. However, only 11 genes are related to the 2q37 deletion syndrome. The lost material is variable and found in one of the patient's 2 chromosome 2s [1]. The majority of patients with the 2q37 microdeletion syndrome are isolated cases with normal parenteral phenotype-karyotype [2]. The patient's development is affected, but how the patient is affected, or the affection rate varies widely and even differs for people who lost the same DNA. The usual characteristics found in babies include low muscle tone and feeding difficulties. Later, the patient suffers from developmental delay, learning disabilities, changes in appearance, and low muscle tone. Asthma and ear and chest infections are common. Seizures occur in some patients. Patients mostly presented with brachycephaly, obesity, hypotonia, failure to thrive, seizures, digit abnormalities, and autism. Facial dysmorphia differs from one to another; any of these features may be present (prominent forehead, sparse, flared medial eyebrows, depressed nasal bridge, V-shaped nasal tip, high-arched palate, alopecia totalis, boxy skull with prominent forehead, up-slanting palpebrae [3-4]. The 2q37 deletion syndrome can also cause gastrointestinal anomalies, such as pyloric stenosis [5], and central nervous system (CNS) anomalies, such as holoprosencephaly [6]. In this case, the cardiological malformation associated with the 2q37 deletions is apparent. Nearly 20% of patients have cardiac anomalies such as ventricular septal defects and aortic coarctation [7]. Following an exhausting (English) literature search, this is the first case with 2q37 deletion syndrome presented with cardiac anomalies being reported.

Case Presentation

A 3-year-old female child was presented to the clinic with easy fatigability, gross motor delay, low muscle tone, and flexible pes planus. The parents have had concerns that she appears to have difficulty keeping up with kids her age. The patient is otherwise healthy, growing, and developing normally. The examination was performed and revealed the following; on general examination, the patient was pleasant and cooperative. The head was normocephalic with no dysmorphic features. On the HEENT (head, eyes, ears, nose, and throat) exam, the oropharynx was clear with moist mucous membranes. The neck was supple. A cardiovascular exam revealed strong peripheral pulses with a brisk capillary refill and normal breathing. The abdomen was soft with no palpable masses. Extremities were warm and well perfused. Observational gait analysis showed a heel-toe reciprocating gait with no deviations noted and normal bulk. The tone was mildly reduced throughout. No tremors or other abnormal movements were noted (Tables 1 &2).

An echocardiogram was done and revealed a patent foramen ovale (PFO) with left-to-right shunting (Figure 1). Also, comparative genomic hybridization (CGH) plus single nucleotide polymorphism (SNP) was ordered, and the results demonstrated chromosome 2q37 deletion syndrome. The patient was advised to have 2 sessions and a follow-up echocardiogram for her abnormal motor delay. After one year of physical therapy per week, which improved her hypotonia and gross motor delay.

Discussion

2q37 deletion syndrome first appeared in the literature in 1989. Since then, approximately 74 children and adults have been presented in the medical literature with 2q37 gene deletion with no additional chromosomal involvement [8]. In 2004, US geneticist Dr. Kari Casas described 66 cases in addition to describing 6 case reports [8].

2q37 deletion syndrome is a rare disease that has affected around 100 reported cases worldwide [9]. The deletion results in developmental delay, brachydactyly of the third to fifth digits and/or toes, obesity, short stature, change of facial appearance, and an autism spectrum disorder [3]. Patients with deletion syndrome also have some form of mental retardation [10].

We report an American female patient with a 2q37.3 deletion that was confirmed by comparative genomic hybridization (CGH) plus single nucleotide polymorphism (SNP). Although clinical presentation is variable, almost all patients have some degree of mental retardation and facial dysmorphism. The patient presented with easy fatigability, gross motor delay, and low muscle tone. An echo was performed, which revealed a patent foramen ovale with a left-to-right shunt. A cardiovascular exam found that the heart experienced strong peripheral pulses with a brisk capillary refill. The patient is otherwise healthy with no dysmorphic features. The HEENT exam revealed a clear oropharynx with moist mucous membranes.

Congenital heart defects have been found in around 20% of patients with 2q37 deletion syndrome. Both septal defects and aortic coarctation have been described in patients with 2q37 deletion syndrome [3]. The patient presented does not have aortic coarctation but does suffer from the presence of a patent foramen ovale in the atrial septum, which was confirmed using an echo. The ascending aorta, transverse arch, and descending aorta were also found to be wide open and not blocking blood flow.

The patient is growing and developing normally, both physically and mentally. Growth hormone deficiency has been found in 4 patients with 2q37 gene mutations, which led to short stature. All 4 patients experienced improved growth following growth hormone administration [11-13].

The better status of the patient who presented with no mental or physical developmental abnormalities or delays can be attributed to the size of the deletion. The patient had a gene deletion size of 2.63 MB. The largest deletion is 10 MB; most are usually greater than 3 MB [14]. Almost 30% of patients with 2q37 deletion syndrome have major malformations. These generally include the gastrointestinal, nervous system, and cardiac abnormalities [3].

Conclusions

2q37 deletion syndrome is a rare disease that has affected around 100 reported cases worldwide. The deletion results in developmental delay, brachydactyly of the third to fifth digits and/or toes, obesity, short stature, change of facial appearance, and an autism spectrum disorder. In our report, we have reported a very rare case with 2q37 deletion syndrome confirmed by comparative genomic hybridization (CGH) plus single nucleotide polymorphism (SNP) that presented with unusual cardiac anomalies (patent foramen ovale with a left to right shunting). However, on follow-up, the patient showed improvement with the physical therapy.

Declarations

Ethics approval and consent to participate

The article describes a case report. Therefore, no additional permission from our Ethics Committee was required.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Ahmed Zaki, Nour Shaheen, Mohamed Hosny, Abdelraouf Ramadan, Abdulqadir J. Nashwan: Data Collection, Literature Search, Manuscript Preparation

All authors read and approved the final manuscript

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Tables & Figures:

Figure 1: Echocardiography shows patent PFO

Levocardia, Situs solitus, normal intracardiac anatomy, patent foramen ovale (PFO) 3 mm with a left to

right shunting, Qualitatively Normal right ventricular size and systolic function, Normal left ventricular size and systolic function, and no evidence of significant pericardial effusion.

Vital signs	Value
Temperature	36.4 C
Height	38.1 inches (96.8 cm)
Weight	15.3 kg
BMI	16.37 kg/m^2

Table 1: Vital signs of the presented case

BMI: Body Mass Index

Lab results	Value	Reference Range
TSH	1.4	0.7 - 6.6 m(iu)/L
CK	69	$<$ 250U/L
Calcium	10.7	8.8-10.8 mg/dL
Potassium	4.5	3.5 -5 mmol/L
Creatinine	0.31	0.20 -0.43 mg/dl

Table 2: Laboratory results of the presented case

TSH: Thyroid Stimulating Hormone; CK: Creatine Kinase