Somato Publications ISSN: 2688-1071

Archives of Clinical Case Reports

Case Report

Tetralogy of Fallot Associated with del (1q) (q42.1-qter): A Rare Association

Muhlike Güler[1*], Naci Ceviz[2] and Çiğdem Yüce Kahraman[3]

[1]Pediatric Cardiologist, Atatürk City Hospital, Balıkesir, Turkey

[2]Professor in Pediatric Cardiology, Atatürk University School of Medicine, Division of Pediatric Cardiology, Erzurum, Turkey

[3]Atatürk University School of Medicine, Department Medical Genetics, Erzurum, Turkey

*Address for Correspondence: Muhlike Güler, Pediatric Cardiologist, Atatürk City Hospital, Balıkesir, Turkey, E-mail: muhlikeguler@gmail.com

Received: 08 December 2019; Accepted: 20 March 2020; Published: 24 March 2020

Citation of this article: Güler, M., Ceviz, N., Kahraman, CY. (2020) Tetralogy of Fallot Associated with del (1q) (q42.1-qter): A Rare Association. Arch Clin Case Rep, 3(2): 05-09.

Abstract

The terminal deletion of chromosome 1q is a rare disease. Phenotypic features of the disease have a wide spectrum including growth retardation, psychomotor retardation, craniofacial and extremity anomalies and cardiac and urogenital malformations. The patient had dysmorphic phenotypic features, Tetralogy of Fallot, renal agenesis, and corpus callosum agenesis. Chromosome analysis revealed del (1q) (q42.1-qter). Our case has a rare togetherness.

Keywords: del (1q) (q42.1-qter), Dysmorphic phenotype, Tetralogy of fallot

Introduction

The terminal deletion of chromosome 1q is a rare disease [1]. It is first reported in 1978 as a case report, however, with the advance of genetic, the large series reported after 2000 [2]. Phenotypic features of the disease has a wide spectrum including growth retardation, psychomotor retardation, craniofacial and extremity anomalies and cardiac and urogenital malformations [3].

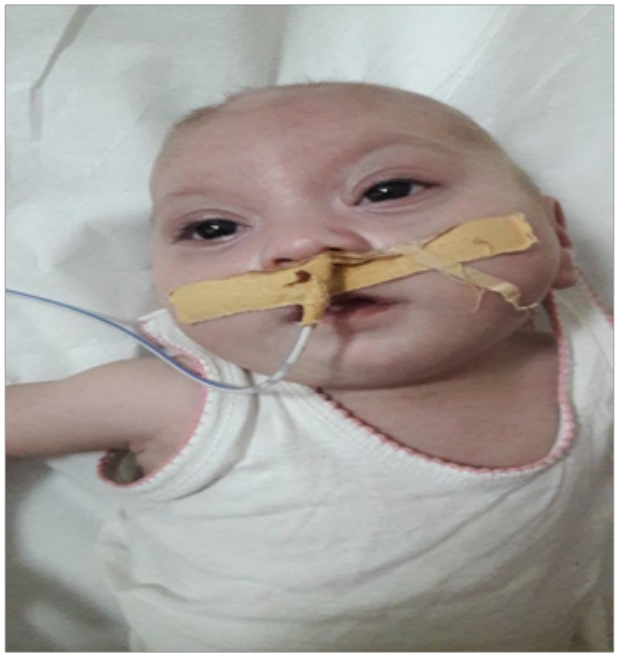
With a clear definition of phenotypic abnormalities by fetal ultrasonography, its prenatal diagnosis is now possible by chorion villus sampling [1,3]. Although, it is said that congenital heart defect (CHD) can be associated with del (1q) (q42.1-qter), there are few reports about their association [1-5]. But a relationship with a specific CHD has not been reported.

In the present study, we report a case of tetralogy of Fallot with multiple dysmorphic features, who was diagnosed as having (1q) (q42.1-qter) deletion.

Case Report

The patient was the second gestation of a mother of 22 years of age. She was a term baby and birth weight was 2000 gr (<3P). The first pregnancy had resulted in spontaneous abort at 12th gestational weeks. The patient admitted to the Pediatric Cardiology outpatient clinic in the first postnatal week due to a murmur heard during evaluation for hematuria. Weight, height and head circumference were under 3P. Physical examination revealed hypotonia, microcephaly, brachycephalic, sparse hair, high palate, long philtrum, micrognathia, hypertelorism, broad nasal bridge, short neck, flat and round face, smooth occiput, low ear, accesso-

Figure 1: Dysmorphic head structure of the case.



ry finger (Figure 1).

She was mentally retarded. A 3/6 systolic murmur was heard at the left upper sternal border. Femoral artery pulsations were normal. External genital structures were normal for the female gender.

Echocardiographic examination revealed a large perimembranous ventricular septal defect, an overriding aorta (approximately 40%), valvular pulmonary stenosis with 60 mmHg systolic gradient, patent ductus arteriosus and atrial septal defect (tetralogy of Fallot with Patent ductus arteriosus and atrial septal defect). Ductus arteriosus closed spontaneously during follow-up (During the month of first).

Urinary tract infection was found as the cause of hematuria. E. coli reproduced in urine culture. The infection did not repeat during the follow-up. Ultrasonography revealed the right renal agenesis. Cranial MR showed the corpus callosum agenesis. She developed epileptic seizures in the 9th month and controlled by

Figure 2: Karyotype analysis of the patient

two antiepileptic drugs (Levetiracetam and phenobarbital). She did not have seizures.

Chromosome analysis and also FISH analysis for 22q11 deletion to exclude Di George's disease were studied in the department of medical genetics. Chromosome analysis that evaluates the number and structure of a person's chromosomes to detect abnormalities is the first step of screening genetic conditions. Our patient's chromosomal analysis revealed 46, XX, del(1) (q42-qter). It demonstrates a deletion in the q arm of chromosome 1 and the bands between q42 and q terminal have been deleted. FISH analysis for 22q11 deletion was negative (Figure 2). Chromosomal analysis of parents was studied to exclude a familial genetic aberration and results were normal.

During follow up, the patient was hospitalized for repeated gastroenteritis, lower respiratory tract infections, and aspiration pneumonia. After feeding by nasogastric catheter, the number of hospitalizations decreased significantly.

Discussion

Submicroscopic deletions involving the distal region of chromosome 1q results in severe phenotypic features like growth retardation, psychomotor retardation, anomalies (agenesis/thin corpus callosum, hydrocephalus, Arnold-Chiari type 1 malformation), hypotonia, seizures, autonomic dysfunction, dysphagia, feeding difficulties, craniofacial anomalies (microcephaly, fine hair, round face, epicanthic folds, an impression of hypertelorism, strabismus, short-broad nose/flat nasal bridge, smooth-long philtrum, thin vermillion borders, well-formed micro/retrognathia, abnormal palate, low set/dysplastic eye, short/webbed neck), abnormal hands (clinodactyly of 5th fingers, small hands, tapering), abnormal feet, urogenital and cardiac anomalies, skeletal anomalies (dyspondylism) [2,4,6,7]. It can be easily diagnosed by chromosomal analysis. Clinical Findings of del(1q) Syndrome are also given in Table 1.

In our patient a chromosomal analysis was done due to her phenotypic features and (1q) (q42.1-qter) deletion was determined.

In patients with distal region deletions in chromosome 1q associated CHD's had been reported. In 3 of 15 patients with 1q42 deletion and in 1 of 7 patients with 1q43 deletion any type of CHD had been detected, nevertheless, the type of the CHD had

Table 1: Clinical Findings of del(1q) Syndrome.

	Previously Reported Patients					
Clinical Features	Puretype of 1q deletion (n=23) M/F= 20:23	1q42 deletion (n=22) M/F= 9:13	1q43 deletion (n=17) M/F= 3:14	1q44 deletion (n=6) M/F= 3:3	Interstitinal deletion (n=8) M/F= 5:3	Our case q42.1-qter Female
Growth retardation	37/42	14/16	14/14	5/5	4/7	+
Psychomotor retardation	48/50	20/20	17/17	5/5	6/6	+
Hypotonia	25/28	13/15	8/8	3/4	1/1	+
Central nervous system anomalies	35/39	10/13	14/15	5/5	6/6	+
Craniofacial anomalies	41/47	18/20	15/17	5/7	3/4	+
Extremity anomalies (hands ,feet)	19/33, 20/29	12/15, 7/12	4/11, 9/10	2/4 4/5	1/3 0/2	+
Genital anomalies (male/female)	18/18, 5/11	9/9, 2/4	3/3, 3/6	2/2, 0/0	4/4, 0/1	+
Kidney/urine pathway anomalies	6/15	0/6	4/6	1/1	1/2	+
Cardiac anomalies	18/37	9/18	4/12	3/3	2/4	+

Table 2: Cardiac anomalies of del(1q) Syndrome.

Patient	Deletion chromosome	Cardiac anomalies
1	1q43-44	Atrial septal defect
2	1q43-44	Ventricular septal defect
3	1q43-44	Tetrology of Fallot
4	1q43-q43	Left ventricular noncompaction myocardium
5	Terminal deletion of chromosome 1(q43)	Pulmonary atresia with intact ventricular septum
6	Pure 1q terminal deletion	Ventricular septal defect
7	q42-q44	Congenital cardiomyopathy / noncompaction

not been noted [6]. Congenital cardiomyopathy/noncompaction of left ventricular myocardium[5], pulmonary atresia with intact ventricular septum [1] and ventricular septal defect [2] had been reported in patients with del(1)(q43). In 3 of six patients with 1(q 43-q44) deletion tetralogy of Fallot, atrial septal defect, ventricular septal defect had been reported [4]. Also in a patient with 1(q42-q44) deletion noncompaction of left ventricular myocardium had been reported [3]. Cardiac anomalies of del(1q) Syndrome are also given in Table 2. Our patient has a specific association with (1q) (q42.1-qter).

Some genetic syndromes or extracardiac abnormalities had been reported to be associated with CHDs in 30% of the patients [8]. In about 11% of 9727 children with CHD, genetic abnormalities had been diagnosed [9]. As the associated genetic abnormalities are major risk factors for cardiac surgery in children [8], their preoperative diagnosis has major importance. Tetralogy of Fallot had been first defined in 1888, and it is the most frequent cyanotic CHD with a relatively better prognosis [10]. It has been frequently associated with genetic syndromes, and this association increases the morbidity and mortality of tetralogy of Fallot [8]. The most frequent genetic abnormalities reported to be associated with tetralogy of Fallot is 22q11.2 deletion (10-16%) and Down syndrome (3-8%) [10]. Besides many syndromes like Wolfram syndrome and Myhre syndrome and chromosomal anomalies like dup (9q34-13qter) and del(q13.1-q13.2) had been reported to be associated tetralogy of Fallot.

Our case has a rare togetherness (tetralogy of Fallot with del (1q) (q42.1-qter). All patients with dysmorphic phenotypic features should be evaluated in terms of associated heart diseases and chromosomal abnormalities.

Financial Support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors

Ethical Standards

Informed consent was provided from the family for this report.

References

1. Wagner, N., Guengoer, E., Mau-Holzmann, UA., Maden, Z., Hoopmann, M., Abele, H., et al. (2011) Prenatal diagnosis of a fetus with terminal deletion of chromosome 1 (q43) in first-trimester screening: is there a characteristic antenatal 1q deletion phenotype? A case report and review of the literature. Fetal Diagn Ther, 29(3): 253-256.

2. Hiraki, Y., Okamoto, N., Ida, T., Nakata, Y., Kamada, M., Kanemura, Y., et al. (2008) Two new cases of pure 1q terminal deletion presenting with brain malformations. Am J Med Genet A, 146A(10): 1241-1247.

3. Van Linthout C, Emonard, V., Gatot, JS., Capelle, X., Kridelka, F., Emonts, P., et al. (2016) Prenatal diagnosis of a terminal chromosome 1 (q42-q44) deletion: original case report and review of the literature. Facts Views Vis Obgyn, 8(2): 101-103.

4. Nagamani, SC., Erez, A., Bay, C., Pettigrew, A., Lalani, SR., Herman, K., et al. (2012) Delineation of a deletion region critical for corpus callosal abnormalities in chromosome 1q43-q44. Eur J Hum Genet, 20(2): 176-179.

5. Kanemoto, N., Horigome, H., Nakayama, J., Ichida, F., Xing, Y., Buonadonna, AL., et al. (2006) Interstitial 1q43-q43 deletion with left ventricular noncompaction myocardium. Eur J Med Genet, 49(3): 247-253.

6. Gentile, M., Di Carlo, A., Volpe, P., Pansini, A., Nanna, P., Valenzano, MC., et al. (2003) FISH and cytogenetic characterization of a terminal chromosome 1q deletion: clinical case report and phenotypic implications. Am J Med Genet A, 117A(3): 251-254.

7. van Bever, Y., Rooms, L., Laridon, A., Reyniers, E., van Luijk, R., Scheers, S. (2005) Clinical report of a pure subtelomeric 1qter deletion in a boy with mental retardation and multiple anomalies adds further evidence for a specific phenotype. Am J Med Genet A, 135(1): 91-95.

8. Formigari, R., Michielon, G., Digilio, MC., Piacentini, G., Carotti, A., Giardini, A., et al. (2009) Genetic syndromes and congenital heart defects: how is surgical management affected? Eur J Cardiothorac Surg, 35(4): 606-614.

9. Hoang, TT., Goldmuntz, E., Roberts, AE., Chung, WK., Kline, JK., Deanfield, JE., et al. (2018) The Congenital Heart Disease Genetic Network Study: Cohort description. PLoS One, 13(1): e0191319.

10. Piran, S., Bassett, AS., Grewal, J., Swaby, JA., Morel, C., Oechslin, EN., et al. (2011) Patterns of cardiac and extracardiac anomalies in adults with tetralogy of Fallot. Am Heart J, 161(1): 131-137.