Congenital cardiac defects with 22q11 deletion

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SUMMARY: Giray Ö, Ülgenalp A, Bora E, Sağın-Saylam G, Ünal N, Meşe T, Hüdaoğlu S, Erçal D. Congenital cardiac defects with 22q11 deletion. Turk J Pediatr 2003; 45: 217-220.

New cytogenetic techniques have promoted progress in determining the role of chromosomal abnormalities in the cause of congenital cardiac defects. Some patients with congenital cardiac defect have a microdeletion within chromosomal region 22q11, and a majority of them are conotruncal cardiac defects. To determine frequency in our population, we evaluated 36 patients with congenital cardiac defects, 23 of them with conotruncal cardiac defects. Microdeletion of 22q11 was detected in seven of 36 patients (19.4%), and in all deleted cases cardiac pathology was conotruncal.

Key words: 22q11 deletion, conotruncal anomalies, congenital cardiac defects, fluorescent in situ hybridization.

Congenital cardiac defects (CCD) are the most common major congenital anomalies, occurring in approximately 0.6-1.3% of livebirths[1,2]. The importance of genetic factors in the cause of congenital cardiac defects has been shown by previous studies[3,4]. Although associated extracardiac anomalies can be seen, the majority of congenital cardiac defects may also occur as isolated malformations. There have been several hypotheses and studies to determine the etiology[3]. Epidemiological studies have indicated a variable, but increased risk of recurrence in families with one affected proband[5,6-8]. This suggests a genetic predisposition to cardiac malformation which may be influenced by in utero environmental or genetic background. Microdeletion of chromosomal region 22q11 is an important cause of selected conotruncal cardiac defects (CTCD) of the heart and account for about 6.9% to 68% of cases[9-12].

Material and Methods

To determine the frequency of congenital cardiac defects with or without conotruncal anomalies with 22q11 deletion in our population we evaluated 36 newly diagnosed cases who were admitted to the Genetic and Pediatric Cardiology Departments of Dokuz Eylül University, Faculty of Medicine.

Twenty-one of the 36 patients had isolated CCD and 15 patients also had distinct significant malformations, including narrow upslanting palpebral fissures, prominent nose with hypoplastic nares, microcephaly, mental motor retardation, slender fingers and laryngomalacia. The characteristics of our cases are listed in Table I.

There were conotruncal cardiac defects in 23 cases. Sixteen of the cases had isolated cardiac defect and seven had additional extracardiac clinical features. None of the 36 patients had previous family history with congenital heart disease (CHD).

Fluorescence in situ hybridization analysis was performed to detect 22q11 deletion. Lymphocytes were cultured by standard methods. Samples were analyzed by using dual-color FISH probes specific to the commonly deleted area (22q11). Signals were visualized using a Nikon fluorescent microscope. Fifty metaphases and 200 interphase nuclei from each patient

Table I. Characteristics of 36 Cases with Congenital Cardiac Defect

Case	Cardiac defect	Extracardiac abnormalities	Deletion
1	TOF		
2	TOF		
3	TOF	Abnormal immune function, nephrolithiasis	
4	TOF		
5	TOF		
6	TOF		
7	TOF	MR, umbilical hernias, pectus carinatum	+
8	TOF+ASD	Imperforate anus, short philtrum, low nasal bridge, laryngomalacia	
9	TOF	Inguinal hernias, hypertelorism	+
10	TOF		
11	TOF		
12	TGA		+
13	TGA+VSD		
14	TGA	Umbilical hernia, hypertelorism	+
15	DORV+VSD		
16	DORV+VSD		
17	DORV+VSD		
18	VSD+PA		
19	VSD	BGG, microcephaly, fish mouth, nail hypoplasia	
20	VSD+PA		+
21	VSD+PS	Hypertelorism, high arched palate, prominent nasal brigde, Simian crease	
22	VSD+PA	Prominent nasal bridge, narrow upslanting palpebral fissures	+
23	VSD+ASD	Microphthalmia, epicanthus, low-set ears, long eyelashes	
24	VSD+PA		
25	VSD+PS		
26	VSD+PA		+
27	AVSD	MMR, long philtrum, long slender fingers, aquiline nose	
28	AVSD		
29	AVSD		
30	AVSD		
31	ASD		
32	ASD+VSD	Trigonocephaly, hypertelorism, coloboma of iris, high arched palate	
33	ASD+PS	Umbilical hernia	
34	AS+MVP	MMR, low nasal bridge, prominent forehead	
35	ASD+PDA	High arched palate, low nasal bridge, inguinal hernia, horse shoe kidney	
36	ASD	Epicanthal fold, retrognathia, renal dysplasia	

ASD: atrial septal deceft, AVSD. atrioventricular septal defect, DORV: double outlet right ventricle, MVP: mitral valve prolapse, PA: pulmonary atresia, PDA: patent ductus arteriosus, PS: pulmonary stenosis, TOF: tetralogy of Fallot, TGA: transposition of great arteries, VSD: ventricular septal defect, MMR: mental motor retardation, MR: motor

Fig. 1. Interphase nucleus with normal signals.

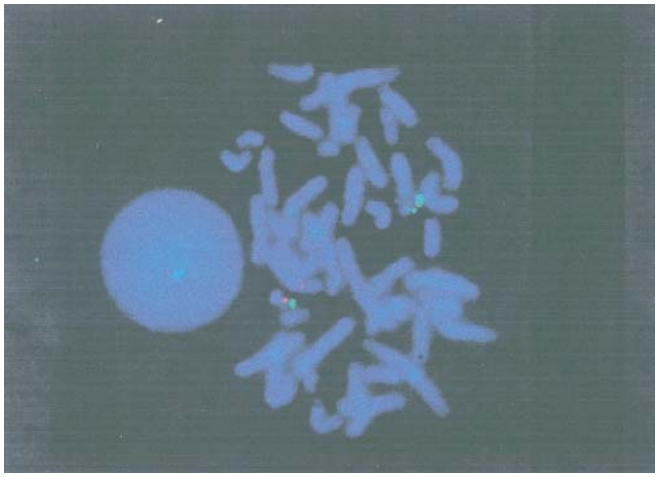

Fig. 2. Metaphase of case 20 with deleted signal.

were evaluated (Figs 1, 2).

Results

Microdeletion of 22q11 were detected in seven cases (19.4%). In all seven patients with deletion, the cardiac pathology was in the conotruncal region (30.4%). Three cases had an isolated conotruncal defect four had additional extracardiac abnormalities (Table I).

Discussion

Chromosomal abnormalities (5%), environmental factors (1%) such as intrauterine exposure to alcohol and drugs, viral infections, maternal diabetes and gene mutations can be the cause of CCD[13].

In our study, we detected seven cases with 22q11 microdeletion among 36 patients with CCD by FISH. Del 22q11 was identified in 19.4% of all the patients (7/36), in 14.2% (3/21) of the cases with isolated conotruncal defect and in 30.4% (7/23) of CTCD.

Some studies suggest that conotruncal anomalies in nonsyndromic cases are very rarely related to 22q11 deletion and some authors point out the importance of accurate phenotypic evaluation in selecting patients with CTCD at risk for 22q11 deletion. However, three our 7 deletion-positive patients had isolated defects (45%)[12,14,15].

Our results show that a patient with CTCD with or without extracardiac anomaly should alert the cardiologist to suspect 22q11 microdeletion.

Subjects with a 22q11 deletion should be evaluated for accurate genetic counseling. We want to point out the importance of accurate clinical evaluation in selecting patients with CCDs at substantial risk for 22q11 deletion. Our study suggests that in conotruncal cardiac defects with or without extracardiac abnormalities, investiga-tion for 22q11 deletion should be performed.

The results of our investigation were higher than the report of Alikaşifoğlu et al.[9] and this may be explained with the probe technology used in that study. Lüleci et al.[16] reported no 22q11 deletion in patients with CCD, a finding that might stem from different criterial selection and evaluation of the patients.

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