Original Article

Study of the Association between Congenital Heart Defects and Neuroblastoma in Abdominal Sonography

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Abstract

Background

A higher prevalence of congenital heart defects (CHD) in neuroblastoma patients in general population is reported in some publications, however, some authors did not find such an association. The evidence for this relation comes from the observation that, the neural crest cells accompany to the development of the heart and neuroblastoma as well.

Materials and Methods

We prospectively investigated this relation for the first time, in a cohort of 114 patients with CHD. Echocardiographic evaluations were made as two-dimensional morphological examination and the patients with CHD were evaluated with through physical examination, especially for the stigmata of neuroblastoma, telecardiogram and abdominal ultrasonography.

Results

In a period of 6 months, 114 children were diagnosed as CHD. Ventricular septal defect (VSD), atrial septal defect (ASD), pulmonary stenosis (PS) and tetrology of Fallot (TOF) were the most common diagnoses. We did not find any evidence for the association between CHD and neuroblastoma.

Conclusion

The possible association between the two entities was generally investigated by retrospective evaluation of echocardiographic studies in neuroblastoma patients. However, according to our preliminary results the presence of CHD is not a predilection for neuroblastoma. Detailed laboratory and radiological studies for neuroblastoma are not necessary in patients with CHD.

Keywords

Heart Defects, Congenital; Neuroblastoma;Child

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Introduction

The association between congenital heart defects (CHD) and neuroblastoma was generally investigated by reviewing echocardiographic studies retrospectively in neuroblastoma patients (1,2). The rationale for this relation is based on the observation that in the embryonic period, the neural crest cells accompanie to the development of some organs, including the heart as well as neuroblastic tumors (3). However, some researchers did not find such an association between CHD and neuroblastoma (4,5). The aim of this study was to find the incidence of neuroblastoma in patients with CHD. To the best of our knowledge, in the present study, the association between neuroblastoma and CHD was prospectively investigated for the first time, in a cohort of patients with CHD.

Materials and Methods

Patients suspected with CHD were evaluated by the same pediatric cardiologist (BA) in Diyarbakir Children's Diseases Hospital, Diyarbakir, Turkey and the patients with CHD, diagnosed with echocardiographic findings, were included in the study for a period of September 2010 to February 2011. The institutional review board approved the study before patient enrollement. Echocardiographic evaluations were made as two-dimensional morphological examination (G.E., vivid 4) in continued doppler mode, with linear S3 or S7 probes depended on the age of the patient. After taking informed consent from the legal guardians of the patients, children were evaluated with through physical examination especially for the stigmata of neuroblastoma and the findings of the patients were recorded in Pediatric Oncology Unit. Evaluation of the telecardiograms routinely taken for the cardiologic disease and abdominal ultrasonography (USG) of each patient were undertaken by the same radiologist (AB).

The patients were followed-up with three-month intervals and laboratory studies were made upon indication by the clinician. Detailed laboratory and radiological studies were planned for the patients with suspected thoracal or intraabdominal mass.

Statistical Analysis

We could not make a statistical analysis because we could not find a neuroblastoma patient among the cohort of patients with CHD during the study.

Results

In a period of 6 months, 114 children were diagnosed as CHD based on echocardiographic evaluation in Pediatric Cardiology Unit in Diyarbakir Children's Diseases Hospital, Diyarbakir, Turkey. Seventy patients were male and 44 female (M/F= 1.59). The ages of the patients were between 7 days and 14 years (median= 12 months). Ventricular septal defect (VSD), atrial septal defect (ASD), pulmonary stenosis (PS) and tetrology of Fallot (TOF) were the most commonly diagnoses (Table 1). In physical examination, there was no finding compatible with neuroblastoma such as subcutaneous nodules, Horner's syndrome, massive hepatomegaly, racon eyes, cervical or abdominal mass. Evaluation of the telecardiograms revealed thymic enlargement in 13 patients and cardiomegaly in 4 patients.

Abdominal USG showed unilateral renal agenesis in 2 patients, simple right renal cyst in another patient and pelvicaliceal ectasis in 23 patients. For these abnormalities, Pediatric Nephrology consultation was made. Down syndrome in 7 patients and situs inversus totalis in one accompanied to the CHD. None of the patients were diagnosed as neuroblastoma neither in first visit nor in follow-up examinations.

Table1: Cardiac malformations in patients with CHD

Cardiac malformation	Frequency	**Percent**
Ventricular septal defect	51	44.7
Atrial septal defect	50	43.8
Pulmonary stenosis	13	11.4
Tetrology of Fallot	9	7.8
Aortic insufficiency	5	4.3
Aortic stenosis	4	3.5
Bicuspid aortic valve	3	2.6
Transposition of great arteries	2	1.7
Mitral insufficiency	2	1.7
Tricuspid insufficiency	2	1.7
Pulmonary insufficiency	2	1.7
Atrioventricular septal defect	1	0.8
Mitral valve prolapsus	1	0.8
Sole ventricle	1	0.8
Truncus arteriosus	1	0.8
Double outlet right ventricle	1	0.8

Discussion

Some researchers suggest a higher prevalence of CHD in neuroblastoma patients than in general population. However, others did not find such an association (1-5). Although data on the frequency of CHD in neuroblastoma patients are equivocal, a possible association between CHD and neuroblastoma may require cardiac screening in neuroblastoma patients to Institute prophylaxis against infective endocarditis, to choose appropriate chemotherapeutic agents and for the early treatment of CHD (2). Similarly, a possible association between the two entities may indicate detailed laboratory and radilogical studies for neuroblastoma in patients with CHD. In the present study, for the first time, we planned to define a possible association between CHD and neuroblastoma in a prospective manner. An association between CHD and neuroblastoma was proposed to be a result of neural crest abnormalities during development (6). Changes within the cardiac neural crest cells have been implicated in many congenital cardiac abnormalities incuding tricuspid atresia, tetrology of Fallot, transposition of great arteries, common arterial trunk, aortic arc lesions, double inlet left ventricle and double outlet right ventricle (3). Bicuspid aortic valve and coarctation of the aorta were proposed to be derived by neural crest cells (3,7). Another possible explanation of the association between the two entities was proposed by using the two-hit theory of carcinogenesis with a first mutational event in preconceptional period might lead to an expression of a cardiovascular anomaly and predisposing the child for later development of neuroblastoma after a second mutation (8). We did not find any evidence for the association between CHD and neuroblastoma in a series of 114 patients with CHD. We hypothesised that, if a real association exists between CHD and neuroblastoma, patients with CHD will be realized generally earlier than neuroblastoma due to signs and symptoms related with cardiac pathology and such an

association warrant screening for neuroblastic tumors. The knowledge of median age of diagnosis for various CHD varies between 45 days and 5.3 years (9), and that for neuroblastoma is 19 months (10) supports our hypothesis.

Conclusion

Our preliminary results suggest that the presence of CHD is not a predilection for neuroblastoma and detailed laboratory and radilogical studies for neuroblastoma is not necessary in patients with CHD.

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Conflict of Interest

The authors have no conflict of interest.

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