OLGU SUNUMU / CASE REPORT

Carpenter sendromu ve çift çıkışlı sağ ventrikül birlikteliği

Co-occurrence of Carpenter syndrome and double outlet right ventricle

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Özet- Carpenter sendromu (Akrosefalopolisindaktili tip 2, OMIM 201000), nadir görülen ve otozomal resesif olarak geçen bir hastalıktır. Akrosefali, kraniyosinostoz, fasiyal asimetri polidaktili ve sindaktili, obezite, hipogonadizm, mental gerilik ve kornea opasitesi gibi anomalilerin yanında en sık olarak ventriküler septal defekt, patent duktus arteriyozus ve pulmoner stenoz olmak üzere doğuştan kalp hastalıklarıyla da birlikte olabilir. Çift çıkışlı sağ ventrikül, her iki büyük damarın tamamen veya büyük oranda morfolojik sağ vent- rikülden çıktığı bir hastalıktır. Bildiğimiz kadarıyla bu send- romla birlikte çift çıkışlı sağ ventrikül hastalığı literatürde tanımlanmamıştır. Bu yazıda, Carpenter sendromu ve çift çıkışlı sağ ventrikül birlikteliği olan bir hasta sunuldu.

Summary- Carpenter syndrome (acrocephalopolysyndactyly type 2, OMIM 201000) is a rarely seen autosomal recessive disorder. In addition to abnormalities such as acrocephaly, craniosynostosis, facial asymmetry, polydactyly and syndactyly, obesity, hypogonadism, mental retardation, and corneal opacity, it may frequently be accompanied by congenital heart diseases such as ventricular septal defect, patent ductus arteriosus and pulmonary stenosis. Double outlet right ventricle is a defect in which both major arter- ies originate in the morphological right ventricle. To the best of our knowledge, this is the first report in the literature of double outlet right ventricle disease in combination with Carpenter syndrome.

Carpenter Syndrome (acrocephalopolysyndactily type 2, OMIM 201000), is a rarely seen autosomal recessive hereditary disorder which is seen one in million cases.[1] Firstly it was described by Carpenter in the year 1901, and its first case was reported in 1966 by Temtamy.[U] The patient's head resemble a typical cloverleaf due to the development of cranicraniosynostosis. Other frequently seen anomalies include facial asymmetry secondary to developmental retardation of maxillary, and mandibular bones, low-set ears, syndactyly in hands and feet, preaxial polydactyly, obesity, hypogonadism, mental retardation, corneal opacity, and mental retardation.[3-5] Prenatal diagnosis of the disease can be made based on fetal ultrasonographic evaluation.[6] In nearly half of the patients congenital heart disease (CHD) was detected.

Abbreviations:
CHD. Congenital heart disease
PD Pulmonary stenosis
VSD Ventricular septal defect

In this paper a patient with double onset right ventricular anomaly followed up with the diagnosis of Carpenter syndrome was presented.

CASE PRESENTATION

A 6.5-year- old baby girl who was diagnosed as Carpenter syndrome with double outlet right ventricle during her neonatal period when she was 8-month-old whose chromosomal analysis revealed 46XX karyotype was presented . The patient was under our surveillance for two years and, she had complaints of cyanosis, shortness of breath, and easy fatigability for the last two months. her parents were third degree relatives, and any family member had not any similar disease. She hadn't undergone any medical of surgical treatment or experienced a hypoxic episode. On physical examination her general health status was good, and her vital signs, and symptoms were unremarkable. Her height was within 25-50 percentile, and her body weight was above 90 percetile when compared with her age-matched peers.

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Oxygen saturation of the patient was measured as 70 percent. Macrocephalus, facial asymmetry, low-set ears, preaxial polydactyly (her right and left hands had six fingers, and right, and left feet had six, and seven toes, respectively), syndactyly, short fingers, club fingers, and toes were detected (Figure 1). A grade 3/6 systolic murmur was heard more prominently along the left edge of the sternum, and other systemic examinations of the patient was not remarkable. On electrocardiographic examination normal sinus rhythm with a heart rate of 90 bpm, 1. degree atrioventricular block, and p pulmonale were detected (Figure 2). Hematological, and biochemical values of the patient with a 61% hematocrit were within normal limits. On echocardiographic examination two major vessels arising from the right ventricle, and aorta localized at the right side and behind the pulmonary artery were seen. A large subaortic ventricular septal defect, and infundibular, and valvular pulmonary stenosis (PS) with a maximum pressure gradient of 65 mm Hg was detected on CW Doppler US. A fibrous band between mitral, and aortic valve was not detected (Figure 3).

On 3-D computed tomogram craniosynostosis was observed (Figure 4). Oxygen saturation of the patient within the last two years decreased gradually. Cardiac catheterization was planned for hemodynamic examination of the heart, and pulmonary balloon valvuloplasty for the treatment of the valvular component of the stenosis.. However, her family declined this procedure, so the patient was monitored closely. Her family gave their informed consent for the use of her clinical findings, laboratory results, and photos for this case report.

DISCUSSION

As a rarely seen disease, the typical manifestation of Carpenter syndrome which may have various clinical findings is craniofacial abnormality which includes acrocephaly associated with craniosynostosis of sagittal, lambdoid, and coronal sutures.[4] Many different mutations have been detected on RAB23 gene associated with this syndrome, and more rarely it may be related to sporadic mutations.[7]

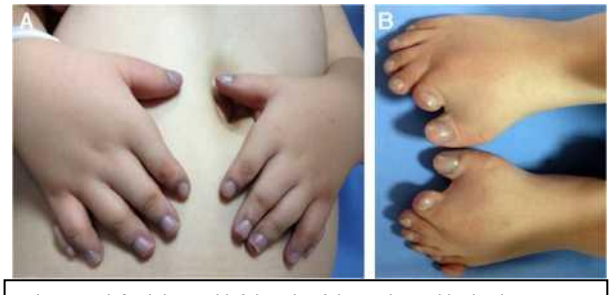


Figure 1. (**A)** Right, and left hands of the patient with six short fingers, and a club finger (**B)** Her right foot with six, and left foot seven toes, in addition syndactyly is seen

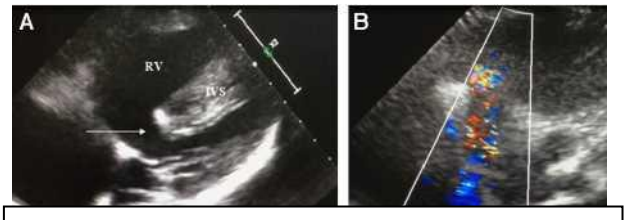


Figure 3. On echocardiogram ventricular septal defect (arrow) **(A),** and mosaicism associated with pulmonary artery stenosis **(B)** are seen

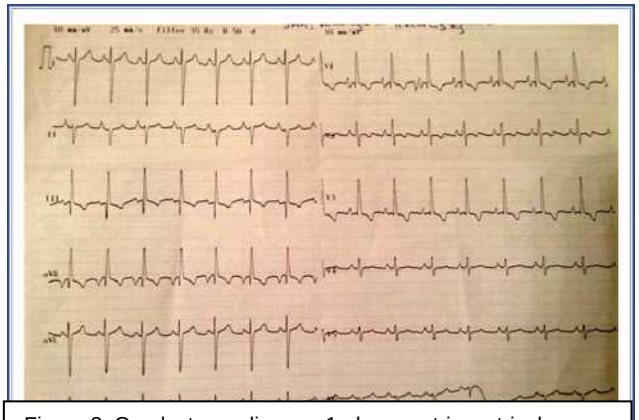
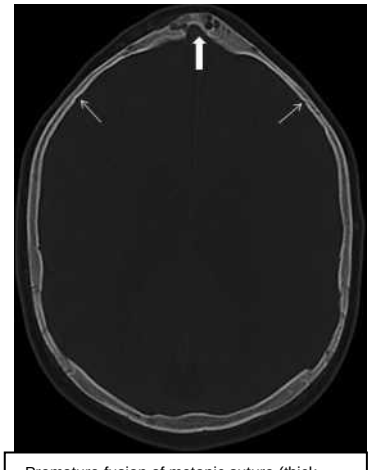


Figure 2. On electrocardiogram 1. degree atrioventricular block, and p pulmonale are seen



Premature fusion of metopic suture (thick arrow) gives the calvaria a triangular appearance which is termed as trigonocephaly. Besides coronal (thin arrow) and other sutures also close prematurely (craniosynostosis)

In our patient any mutation could not be demonstrated, and diagnosis was based on clinical findings. As one of the congenital forms of craniosynosthosis Carpenter syndrome is generally diagnosed based on the degree of morphological disorders during neonatal period or infancy. Acrocephaly which is one of the other genetic disorders associated with craniosynosthosis can be discriminated from other genetic disorders with its special facial appearance, and facial asymmetry.[7] Our case was also diagnosed as Carpenter syndrome during neonatal period. In addition, obesity, short stature, and central nervous system malformations as mental retardation, cerebral or cerebellar atrophy, sensorineural hearing loss, corneal opacity, optic atrophy, umbilical hernia, hypogonadism, undescended testis, hydronephrosis, dental anomalies, and CHD can be seen in patients.[48] Obesity was detected in our case. Her height, mental motor functions were normal when compared with her age-matched peers, and any urogenital abnormality was not detected.

In the literature, in nearly half of the patients, mainly ventricular septal defect (VSD), patent ductus arteriosus, PS, atrial septal defect, Fallot tetralogy, and transposition of major arteries, and CHD have been reported. Patients exited from congestive heart failure, and sudden cardiac death have been also cited in the literature.[89]

Double outlet right ventricle is a form of ventriculoarterial connection anomaly which constitutes less than 1% of all cases with CHD. Its incidence is six cases out of every 100.000 live births.[10] Although its etiology is not known exactly, it is known to be related to Di George syndrome, trisomy 13, 18, and 21, Noonan syndrome, Ellis-van Creveld syndrome, maternal diabetes, and use of valproic acid, and retinoic acid during prenatal period. Both of greater vessels arise from wholly or at a great extent from morphologic right ventricle, and left ventricular outlet is mostly enlarged VSD. From anatomic, and physiopathologic perspective, it may manifest many clinical different conditions, ranging from cyanosis up to congestive heart failure. Its classification is based on the associations between major vessels, and between ventricular septal defect, and major vessels, and also presence of PS, and decision for type of surgical treatment is determined based on these associations. Based on the relationship of ventricular septal defect wit major vessels, it is categorized into four groups as: subaortic, subpulmonic,*double committed* , and *noncommitted.* The most important lesion of the disease is VSD which is the only outlet of the left ventricle.[1011] In our patient the most frequently seen types were subaortic dilated VSD, and enlarged VSD, and PS, and increased pulmonary stenosis with time was detected. As seen in Fallot tetralogy, the disease progresses with symptoms related to decrease in pulmonary blood flow, and cyanosis. We aimed to determine hemodynamic parametres with cardiac catheterization, and to decrease valvular PS component, and cyanosis using balloon valvuloplasty, however her family did not give their consent.

In conclusion, since CHD is frequently detected in patients with Carpenter syndrome, at the time of diagnosis the patient should be evaluated in detail , and then followed up by the department of pediatric cardiology. Because Carpenter syndrome associated with double onset right ventricle has not been encountered in the literature, we deemed it appropriate to present this rarely seen case.

Patient's consent

Informed patient consent was obtained from parents of the patient .

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Conflict of interest: *None declared*

REFERENCES

1. Jones KL. Smith's Recognizable patterns of Human Malfor- mation. 6th ed. Philadelphia: WB Saunders; 2006. p. 484-5.
2. Temtamy SA. Carpenter's syndrome: acrocephalopolys-yndactyly. An autosomal recessive syndrome. J Pediatr 1966;69:111-20.
3. Robinson LK, James HE, Mubarak SJ, Allen EJ, Jones KL. Carpenter syndrome: natural history and clinical spectrum. Am J Med Genet 1985;20:461-9.
4. Altunhan H, Annagür A, Örs R. The association of Carpenter syndrome and situs inversus totalis: First case report. Turkiye Klinikleri J Med Sci 2011;31:464-7.
5. İşlek I, Küçüködük S, İncesu L, Selçuk MB, Aygün D. Carpenter syndrome: report of two siblings. Clin Dysmorphol 1998;7:185-9.
6. Begum S, Khatun N, Rayhan SM, Rahman SA. Carpenter syndrome: a case report. Mymensingh Med J 2012;21:547-9.

7. Jenkins D, Seelow D, Jehee FS, Perlyn CA, Alonso LG, Bueno DF, et al. RAB23 mutations in Carpenter syndrome imply an unexpected role for hedgehog signaling in cranial-suture development and obesity. Am J Hum Genet 2007;80:1162-70.
8. Ramos JM, Davis GJ, Hunsaker JC, Balko MG. Sudden death in a child with Carpenter Syndrome. Case report and literatüre review. Forensic Sci Med Pathol 2009;5:313-7.
9. Balci S, Haytoglu T, Ozer S. A case of a four-day-old male with Carpenter's syndrome with transposition of great arteries. Turk J Pediatr 1998;40:461-6.
10. Wright GE, Maeda K, Silverman NH, Hanley FL, Roth SJ. Double outlet right ventricle. Ed: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. Heart Disease In Infants, Children and Adolescents. Eight Edition Lippincott Williams & Wilkins Philadelphia 2013:1161-74.
11. Atay Y, İyem H, Yağdı T, Levent E, Özyürek R, Alayunt EA. Double outlet right ventricle. Turkish J Thorac Cardiovasc Surg 2004;12:64-9.

Anahtar sözcükler: **Carpenter sendromu; çift çıkışlı sağ ventrikül; çocuk; doğumsal kalp hastalığı.**

Keywords: **Carpenter syndrome; double outlet right ventricle; child; congenital heart disease.**