The Association of Carpenter Syndrome and Situs Inversus Totalis: First Case Report

Carpenter Sendromu ve Situs Inversus Totalis Birlikteliği: İlk Olgu Sunumu

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Geliş Tarihi/*Received:* 15.06.2010
Kabul Tarihi/*Accepted:* 17.12.2010

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ABSTRACT Carpenter syndrome (acrocephalopolysyndactyly type II) is a rare autosomal recessive disorder that classically consists of acrocephaly, facial dysmorphism, mental retardation, congenital heart disease and hypogenitalism. To the best of our knowledge, situs inversus totalis has not been demonstrated previously in Carpenter syndrome. We report here a 6- day- old boy with many abnormalities diagnosed clinically and also having situs inversus totalis. As far as we know, this is the first Carpenter syndrome case associated with situs inversus totalis in the literature.

Key Words: Situs inversus; craniosynostoses; mental retardation; craniofacial abnormalities; syndactyly

ÖZET Carpenter sendromu (akrosefalopolisindaktili tip II) klasik olarak akrosefali, fasial dismorfizm, zeka geriliği, doğumsal kalp hastalığı ve hipogenitalizmden oluşan nadir bir otozomal resesif hastalıktır. Bildiğimiz kadarıyla, Carpenter sendromunda daha once situs inversusu totalis tanımlanmamıştır. Burada klinik olarak tanı koyulan pek çok anomalisi olan ve aynı zamanda situs inverus totalisi olan 6 günlük bir erkek bebeği sunuyoruz. Bildiğimiz kadarıyla, bu literatürde situs inversus totalis ile birlikte görülen ilk Carpenter sendromu olgusudur.

Anahtar Kelimeler: Situs inversus; kranyosinostoz; mental retardasyon; kafa yüz anormallikleri; sindaktili

Turkiye Klinikleri J Med Sci 2011;31(2):464-7

Carpenter syndrome or acrocephalopolysyndactyly type II was first described by Carpenter in 1901, but it was not firmly established as an entity until Temtamy's report in 1966.[1] It is a rare autosomal recessive disorder.[1,2] The cardinal features of this syndrome are acrocephaly with variable synostosis of the sagittal, lambdoid, and coronal sutures; peculiar facies; brachydactyly of hands with syndactyly; preaxial polidactyly and syndactyly of the feet; congenital heart defects; growth retardation; mental retardation; hypogenitalism and obesity.[1-5] Besides common clinical manifestations, cerebral malformations, oral and dental abnormalities, coxa valga, genu valgum, hydronephrosis, precocious puberty and hearing loss may be seen.[1-12] Variable rare abnormalities may also accompany the major clinical findings.[1] However, to the best of our knowledge, situs inversus totalis has not been demonstrated previously in Carpenter syndrome. We report a case of Carpenter syndrome associated with situs inversus totalis.

doi:10.5336/medsci.2010-19822

CASE REPORT

A six-day-old boy was referred to our clinic for evaluation of skull and face abnormalities. He was born at term, following an uneventful pregnancy and delivery in a special hospital. The parents were healthy first-degree cousins and had one healthy girl. On his physical examination, the body weight was 4000 g (75-90%), length was 53 cm (75-90%), and head circumference was 36 cm (50-75%). Anterior fontanel was 0.5x0.5 cm, posterior fontanel was closed. He had acrocephaly and a peculiar face characterized by frontal bossing (Figure 1). Acral abnormalities consisted of clinodactyly of the fifth fingers, membranous syndactyly of digits 3 and 4 on the hands, syndactyly of digits 1 and 2 on the feet, and preaxial polidactyly of the big toes bilaterally (Figure 2, 3). Other abnormalities included widely spaced nipples and bilateral cryptorchidism. On cardiac auscultation of the baby, the heart sounds were best heard at the right intersternal border. Examination of the eyes were normal. Standard biochemical and hematological parameters were normal. A lymphocyte culture was a normal male karyotype (46, XY). On abdominal ultrasound, liver was in the left upper quadrant and spleen was in right upper quadrant. Dextrocardia was detected on the chest radiograph and babygram (Figure 4). There were no cardiac abnormalities except mirror-image dextrocardia on the Doppler echocardiography. There were no brain abnormalities detected on the magnetic resonance imaging. Skull roentgenograms and a three-dimensional computerized tomographic (3 DCT) scan of the head revealed metopic anterior and posterior sagittal synostosis (Figure 5).

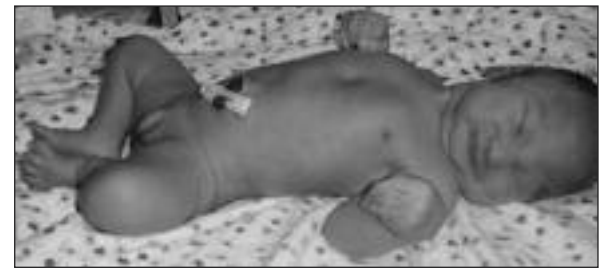

FIGURE 1: Acrocephaly and a peculiar face characterized by frontal bossing.

FIGURE 2: Membranous syndactyly of digits 3 and 4, clinodactyly of the fifth finger on the left hand.

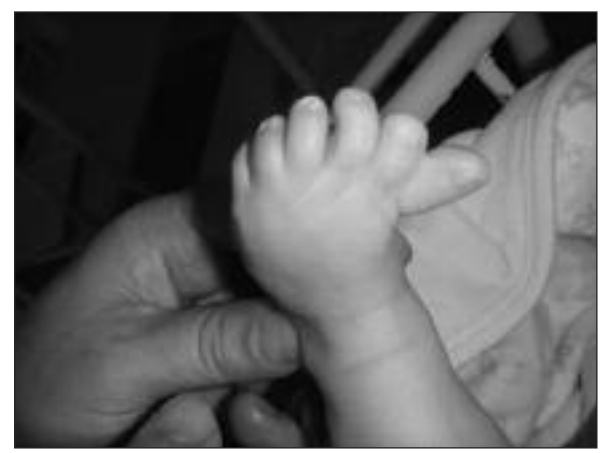

FIGURE 3: Preaxial polidactyly of the big toe.

DISCUSSION

Since Carpenter syndrome was first described in 1901, variable clinical features have been defined (OMIM 201000). The clinical findings of the syndrome show great variations among patients. There is no special test to confirm the diagnosis. In 15 independent families with Carpenter syndrome, Jenkins et al.[2] identified five different mutations (four truncating and one missense) in the RAB23 gene (OMIM 606144). However the RAB23 gene mutations could not been performed in our patient. The diagnosis was based on physical examination. Craniofacial abnormalities are the cardinal features of Carpenter syndrome. It may include acrocephaly; brachycephaly with variable synostosis of coronal, sagittal, and lambdoid sutures; low set and malformed ears; flat nasal bridge; palpebral fis-

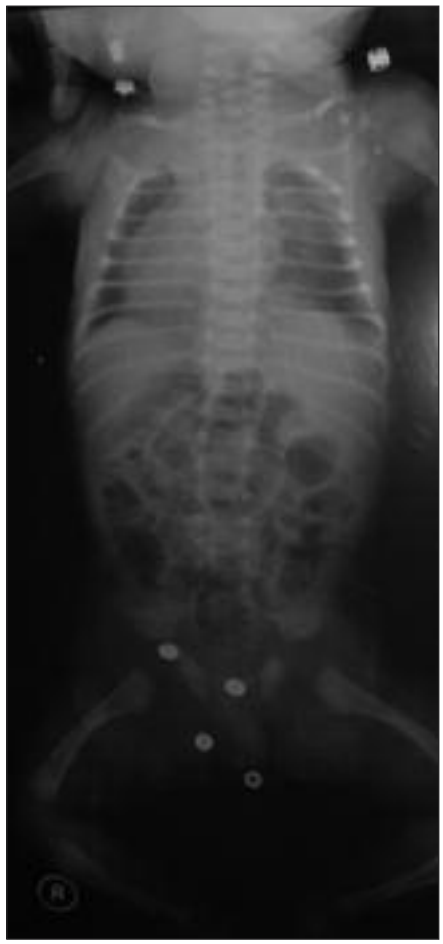

FIGURE 4: Dextrocardia on the chest radiograph and babygram.

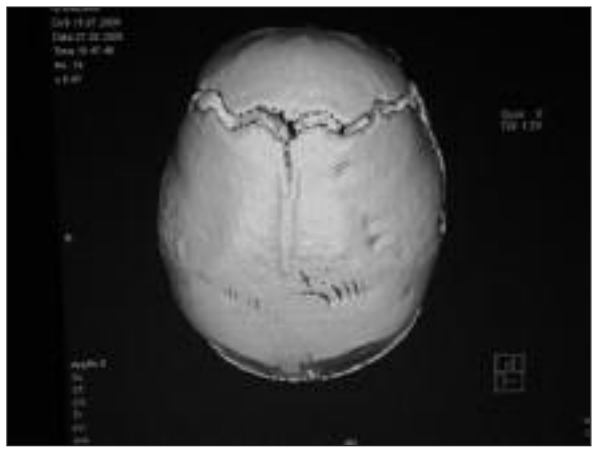

FIGURE 5: Anterior and posterior sagittal and metopic synostosis on the 3-dimensional computerized tomographic (3 DCT) scan of the head.

sures; hypoplastic mandible or maxilla; and highly arched palate.[1-5,7,12] The craniofacial abnormalities may change depending on the timing of early closure of cranial sutures. Our patient had frontal bossing and acrocephaly. There was sagittal synostosis in cranial tomographic scan.

Other cardinal features of Carpenter syndrome are limb abnormalities. They may include brachydactyly of hands with clinodactyly, syndactyly; preaxial polydactyly of the feet with partial syndactyly; short or missing middle phalanges of fingers and toes.[1-5,7,8] Our patient had clinodactyly of the fifth fingers, membranous syndactyly of digits 3 and 4 on the hands, and syndactyly of digits 1 and 2 on the feet, preaxial polydactyly of the big toes bilaterally.

In addition, some individuals with Carpenter syndrome may have congenital heart defects, abdominal hernia, undescended testes, hypogenitalism, hydronephrosis, and obesity.[1-8] In our patient, there were no cardiac abnormalities except for dextrocardia detected with echocardiography. He had bilateral cryptorchidism.

Other rare abnormal features that can be seen in Carpenter syndrome include cerebral malformations (such as cerebral and cerebellar atrophy, absence of corpus callosum); sensorineural hearing loss; eye findings (such as corneal opacity, optic atrophy); mouth and teeth abnormalities (such as prolonged retention of primary teeth, hypodontia,malocclusion); and short stature.[1-4,6,7,9-11] In our patient, auditory brainstem response (ABR) test, examination of eyes and brain magnetic resonance imaging scan were normal. Variable delay can be seen in intellectual performance, IQs can range between 52-104. Mental retardation is not an invariable feature of Carpenter syndrome, and the role of early surgery on the calvarium and its effect on mental development should not be overestimated.[1,4,8,10-12]

To date, a lot of variable abnormalities have been defined in Carpenter syndrome (OMIM 201000). However, to the best of our knowledge, situs inversus totalis has not been demonstrated previously in Carpenter syndrome. Situs invertus totalis was confirmed by radiography, echocardiography and ultrasonography in our patient. This is the first Carpenter syndrome case associated with situs invertus totalis in the literature.

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