Kraniofrontonazal Sendrom'lu bir Türk olgu

A Turkish Case with Craniofrontonasal Syndrome

Kadri Karaer
MD
Department of Medical Genetics
Faculty of Medicine, Gazi University
kadrikaraer@yahoo.com

Kemali Baykaner
Prof., M.D.
Department of Neurosurgery
Faculty of Medicine, Gazi University

Emriye Ferda Perçin
Prof., M.D., Ph.D.
Department of Medical Genetics
Faculty Of Medicine, Gazi University
ferdaep@yahoo.com

Abstract
Craniofrontonasal syndrome is a very rare X-linked disorder characterized by abnormalities of the craniofacial area, mental deficiency, longitudinally grooved nails and various skeletal and soft tissue abnormalities. Following first description of the syndrome, approximately 180 additional cases have been published in medical literature. We describe here a new female Turkish patient with craniofrontonasal syndrome and discuss the common features of previously reported cases.

Key Words: **Craniosynostosis, Facial asymmetry, Abnormal nail.**

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Özet
Kraniofrontonazal sendromu, kraniofasyal anomaliler, mental gerilik, uzunlamasına çizgili tırnaklar, iskelet ve yumuşak doku anomalileri ile karakterize, X'e bağlı kalıtılan oldukça nadir görülen bir hastalıktır. Tıbbi literatürde, sendromun ilk tanımlanmasının ardından yaklaşık 180 ilave hasta yayınlanmıştır. Biz, burada kraniofrontonazal sendrom'lu yeni bir Türk kız hasta tanımladık ve daha önce yayınlanan olgularla ortak bulgularını tartıştık.

Anahtar Kelimeler: **Kraniosinostosis, Fasyal asimetri, Tırnak Anomalisi.**

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Corresponding Author:
Dr. Kadri Karaer
Department of Medical Genetics
Faculty Of Medicine, Gazi University
Ankara - Turkey

Telephone : +90 - 3122026944
E-mail : kadrikaraer@yahoo.com

Introduction

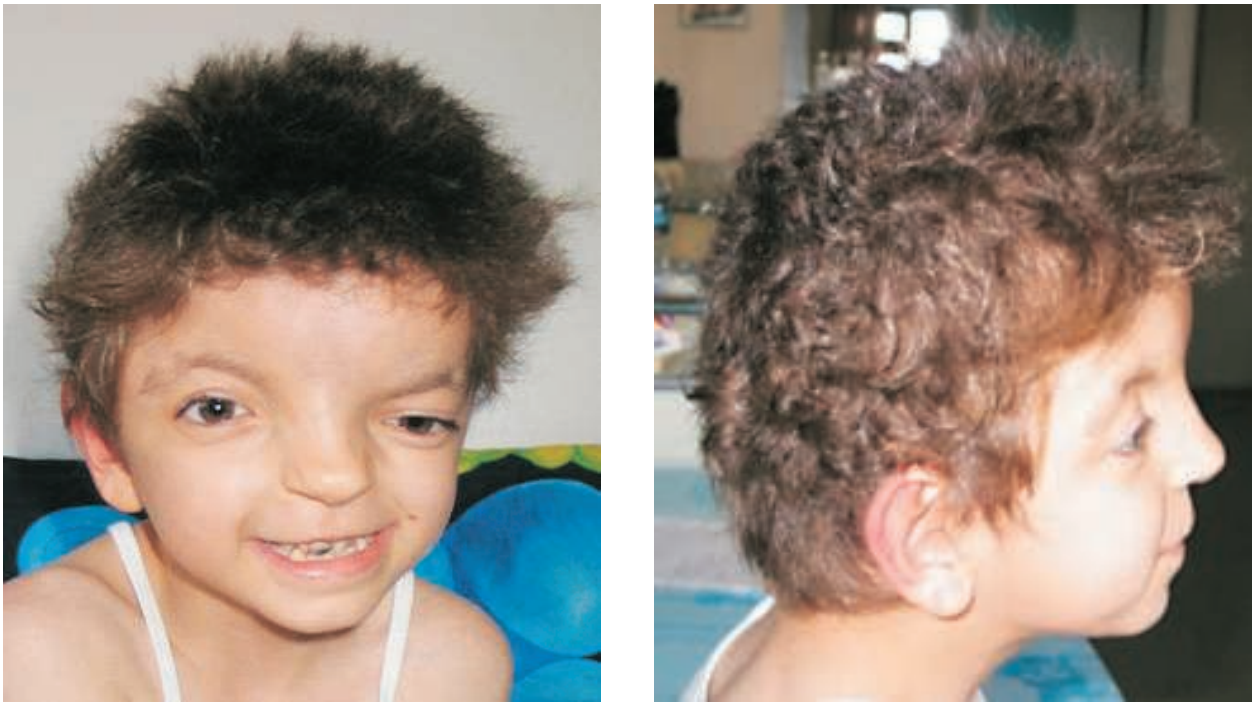
Craniofrontonasal syndrome (MIM #304110) (1), is a rare malformation syndrome. It was firstly identified as a subgroup of frontonasal dysplasia by Cohen in 1979. He described a 14 year old girl with coronal synostosis, brachycephaly, limitation of shoulder movement and various digital anomalies (2). Pedigree analysis is consistent with an X-linked dominant mode of inheritance in most families. In females this condition is characterized by craniofacial asymmetry, coronal craniosynostosis, frontal bossing, hypertelorism, downslanting palpebral fissures, broad bifid nose, low posterior hairline, curly hair, occasionally cleft lip and palate, longitudinally grooved fingernails and other digital anomalies. However, males have mostly been more mildly affected with only hypertelorism and occasionally cleft lip or palate (3). This inconsistent manifestation of craniofrontonasal syndrome in females and males led to the proposal of several inheritance possibilities including the interacting craniofrontonasal syndrome gene products from different cells in heterozygous females. Accordingly, the severity of disease manifestation in heterozygous females has been mainly attributed to expression of the EFN1 gene in a mosaic pattern due to random X-inactivation. There are several possible explanations for this inconsistent phenotypic pattern of X-linked inheritance with more severely affected females than males. Craniofrontonasal syndrome also might be a sex-limited disorder, in which the greater severity in females is explained by different interaction of the mutant gene with sex-specific developmental pathways (4, 5).

Following first description of the syndrome, approximately 180 additional cases have been published in medical literature. We report here on an additional case of Turkish girl with craniofrontonasal syndrome.

Case report

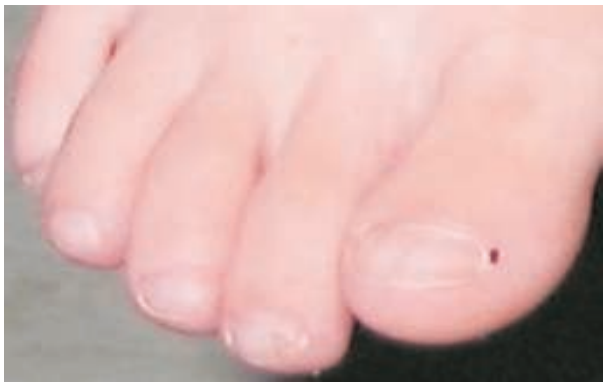
The patient, a 5,5 year old girl, admitted to our clinic with plagiocephaly from neurochirurgia department. She was born to a healthy, 34-year-old mother and 41-year-old father. This couple was non-consanguineous. She had healthy brother and sister. Pregnancy, delivery, and the neonatal period were uneventful. Her birth weight was 4200 g (>97th centile), birth length was 52 cm (90-97th centile), but her occipitofrontal (OFC) circumference was not recorded. She began to sit without support at 6 months; started walking at 2 years and began to speak at 1.5 years old.

At the time of 5.5 years old, her height was 104 cm (10th centile), weight was 16 kg (10-25th centile), occipito-frontal circumference 47.5 cm (-2SD-50SD). On craniofacial examination; plagiocephaly, brachycephaly, kinky and thick hair pattern, posteriorly low-set ears, sparse eyebrows, hypertelorism with asymmetrical placed eyes, downslanting palpebral fissures, high and broad nasal bridge, bifid nose, prominent columella, crowded teeth and low posterior hairline was observed (Picture 1). She have had hyperextansible elbow and finger joints. On her hand examination; bilaterally thenar and hypothenar muscle atrophy and fifth fingers clinodactyly found (Picture 2). Feet examination showed; third and fourth toes had mediodorsal curve. All fingers and toes had longitudinally grooved nails (Picture 3).



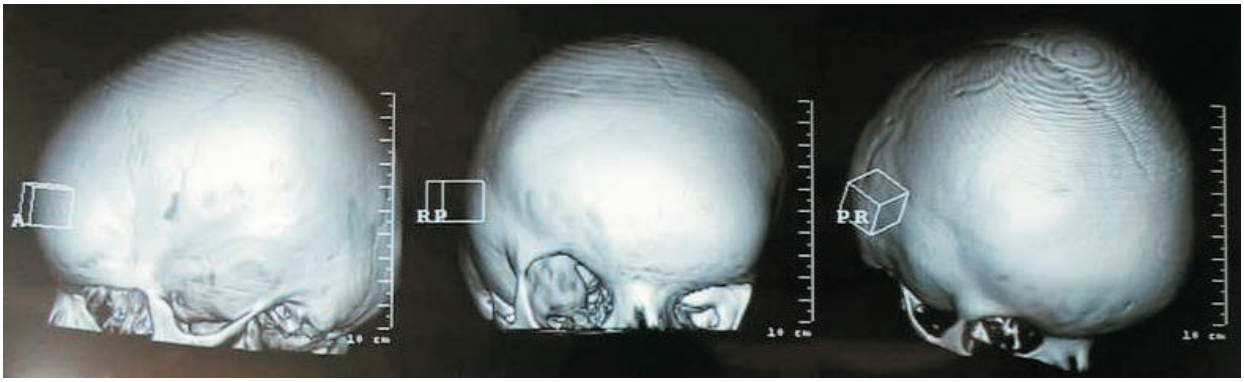
Picture 1. Frontal (left) and lateral (wright) view of the patient at 5.5 years old showing brachycephaly, kinky and thick hair pattern, posteriorly low-set ears, sparse eyebrows, hypertelorism with asymmetrical placed eyes, downslanting palpebral fissures, high and broad nasal bridge, bifid nose, prominent columella, crowded teeth and low posterior hairline.

Picture 2. On her hand examination shows fifth fingers clinodactyly and grooved finger nails.



Picture 3. Feet examination shows all toes have longitudinally grooved nails.

Ophthalmologic examination revealed that inferior dystrophia and nystagmus had existed in left bulbus oculi. Laboratory studies demonstrated that, routine biochemistry tests for renal, liver and thyroid function were found as normal but complete blood count (CBC) indicated that she had had a hypochromic microcytic anemia**.** Cranial Magnetic Resonance Imaging showed an agenesis of corpus callosum. Three-dimensional computerized tomography (3D-CT) scan demonstrated unilateral (right) coronal synostosis (Picture 4). Chromosome analysis of peripheral leukocytes by using high resolution binding technique showed a normal 46, XX female karyotype.



Picture 4. Three-dimensional computerized tomography (3D-CT) scan demonstrates unilateral (right) coronal

Discussion

Craniosynostosis is a common birth defect (1 in 2100-2500 infants) which affects the premature fusion of one or more of the cranial sutures and leads to an abnormal head shape (6). The most likely diagnosis in our patient is Craniofrontonasal syndrome, which is characterized in females by abnormalities of the craniofacial area, grooved nails, normal intelligence and various skeletal and soft tissue abnormalities. We compared the clinical features of the previously published cases of craniofrontonasal syndrome with our case (Table 1). Common findings in all reports, including our case, are thick curly hair with low posterior hairline, coronal craniosynostosis, craniofacial asymmetry, hypertelorism, downslanting palpebral fissures, broad bifid nose, malocclusion, longitudinally grooved fingernails. Occasionally, strabismus, bulbous oculi dystrophia and agenesis of corpus callosum in syndrome were also demonstrated (7) Also, occasional cleft lip and palate, abnormal clavicles and thorax, asymmetric lower limb shortness, unilateral breast hypoplasia, unilateral absence of pectoralis major muscle (8) were noted but not in all of the cases as well as not seen in our case.

Table I. Comparison of previously reported clinical findings 184 patients (9, 10) with craniofrontonasal syndrome patients and features of present case.

Clinical findings	Our	Females	Males
Brain and Development			
Normal intelligence	+	117/119	19/20
Corpus callosum hypoplasia or agenesis	+	7/62	
Delayed motor development	-	1/62	
Craniosynostosis			
Coronal	+	74/89	1/22
Craniofacial			
Thick, wiry and curly hair	+	27/59	1/19
Widow's peak	-	16/62	3/14
Low posterior hairline	+	11/35	0/8
Brachycephaly	+	32/34	0/9
Frontal bossing	-	20/30	2/4
Hypertelorism	+	147/148	27/27
Bifid nose	+	73/114	6/27
Cleft lip-palate	-	13/153	4/27
Other			
Abnormal clavicles	-	28/36	7/16
Abnormal thorax	-	27/115	1/19
Grooved nails	+	30/78	6/20
Unilateral breast hypoplasia	-	14/63	
Strabismus	+	48/54	6/14
Deafness	-	1	
Cutaneous syndactyly	-	21/96	0/10
Polydactyly	-	18/54	0/10

The defects in craniofrontonasal syndrome bear some likeness to Teebi hypertelorism syndrome (MIM 145420), such as brachycephaly, telecanthus/hypertelorism, shallow orbits and broad nasal tip. However absence of craniosynostosis and brittle grooved nails are the main points which distinguish disorder from craniofrontonasal syndrome (1).

Differential diagnosis between craniofrontonasal syndrome and craniofacial dyssynostosis syndrome (MIM 218350) should be considered because of common clinical features, such as agenesis of corpus callosum, hypertelorism, craniosynostosis, ophthalmologic findings. Normal intelligency, specific hair pattern, asymmetric face, grooved nails which are found in the craniofrontonasal syndrome, as well as in our patient but are not seen in the craniofacial dyssynostosis syndrome (1).

There is no specific treatment for craniofrontonasal syndrome. The phenotypic expression of craniofrontonasal syndrome is described to recognize patients early. In the first year of life synostotic sutures of the skull are released. The aim of this surgery is decompression of the brain and remodeling of the skull. A treatment algorithm for craniofrontonasal syndrome based on timing and technique is offered to decrease the need for revision and secondary complications (11). Genetic counseling may be of benefit for affected individuals and their families. We hope this information may be compared with findings in other patients in the future to assist in clarifying the phenotype of the craniofrontonasal syndrome.

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