ZKTB

CASE REPORT

Cerebro-Oculo-Facio-Skeletal (COFS) Syndrome: Case Report

Serebro-Okülo-Fasio-İskeletal Sendrom: Olgu Sunumu

Ali Karaman [1], Hasan Kahveci [2], Selin Karaman [3], Hatip Aydın [1], Arda Çetinkaya [1]

1. Zeynep Kamil Women and Children Training and Research Hosp, Dept. of Medical Genetics, Istanbul, Turkey
2. Nenehatun Obstetrics and Gynecology Hospital, Neonatal Intensive Care Unit, Erzurum, Turkey
3. Dr. Lütfi Kırdar Kartal Training and Research Hospital, Department of Family Medicine, İstanbul, Turkey

ABSTRACT

Introduction: *Cerebro-oculo-facio-skeletal (COFS) syndrome is a rare autosomal recessive disorder characterized by a wide range of dysmorphic features, including microcephaly, progressive neurologic disorder, optic atrophy, mental retardation, progressive joint contractures and growth failure.*

Case: *The case was two-week-old male infant whose father (29 years old) and mother (25 years old) were non-consanguineous. The present patient had growth deficiency, microcephaly, deep-set small eyes, a prominent beaked nose, micrognathia, micropenis, joint contractures, kyphoscoliosis, short legs, and rocker-bottom feet. A brain magnetic resonance graphy demonstrated cerebral atrophy and hypoplasia of the corpus callosum. The patient was hospitalized at neonatal intensive care unit. However, he died at age 2 weeks*

Conclusion: *Here in, we report a rare patient with the features of COFS*

Keywords: *Cerebro-oculo-facio-skeletal syndorme, microcephaly, progressive joint contractures*

ÖZET

Giriş: *Serebro-okülo-fasio-iskeletal sendrom, mikrosefali, ilerleyici nörolojik bozukluk, optik atrofi, mental gerilik, ilerleyici eklem kontraktürleri, ve büyüme geriliğini içeren çok çeşitli dismorfik özellikler ile karakterize nadir bir otozomal resesif bozukluktur.*

Olgu: *Olgu iki haftalık erkek bebek idi, 29 yaşındaki babası ve 25 yaşındaki annesi akraba değildi. Hastamız büyüme geriliğine, mikrosefaliye, derinde olan küçük gözlere, çıkıntılı bir gaga buruna, küçük ağıza, mikropenise, eklem kontraktürlerine, kifoskolyoza, kısa bacaklara ve fırlak topuğa sahipti. Beyin magnetik rezonans grafisi serebral atrofi ve korpus kallosum hipoplazisi gösterdi. Hasta yenidoğan yoğun bakım ünitesine yatırıldı. Ancak hasta iki haftalık iken öldü.*

Sonuç: *Burada, biz COFS sendromu özellikleri ile nadir bir hastayı rapor ettik.*

Anahtar Kelimeler: *serebro-okülo-fasio-iskeletal sendrom, mikrosefali, ilerleyici eklem kontraktürleri*

Contact:
Corresponding Author: Ali Karaman
Address: Zeynep Kamil Women and Children Training and Research Hosp., Dept. of Medical Genetics, Istanbul, Turkey
E-mail: alikaramandr@gmail.com
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INTRODUCTION

Described initially by Pena and Shokeir in 1974 the the cerebro-oculo-facio-skeletal (COFS) syndrome has been recognized as an autosomal recessive, apparently degerative problem of the brain and spinal cord that is usually manifest before birth (1). An associated genetic mutation were first found, in a patient with COFS syndrome, by Hamel et al (2).

In another study, Sigmundsson et al. reported patient with COFS syndrome, with both microphthalmia and cataracts and with an XPG-gene defect (3). As part of the Nucleotide Excision Repair (NER) process, the endonuclease XPG is involved in repair of helix-distorting DNA lesions, but the protein has also been implicated in several other DNA repair systems, complicating genotype-phenotype relationship in XPG patients (4).

CASE REPORT

The boy was born at term and was the first child of non-consanguineous parents, aged 29 (father) and 25 (mother). Delivery was by cesarean section due to breech positon. His birth weight was 2.600g, length was 43cm, and head circumference was 31cm.

On examination at birth, he was noted to have growth deficiency, microcephaly, deep-set small eyes, a prominent beaked nose, micrognathia, micropenis, joint contractures, kyphoscoliosis, short legs and rocker-bottom feet (Figure 1).

He had no cataract or optic atrophy. The patient had no abnormal organs on ultrasound examination. A brain magnetic resonance graphy demonstrated cerebral atrophy, hypoplasia of the corpus callosum. Karyotype analysis were normal. The patient was hospitalized at neonatal intensive care unit. However, he died at age 2 weeks. The hospital Ethical Committee approved the human study. We obtained written informed consent from the parents of the patient.

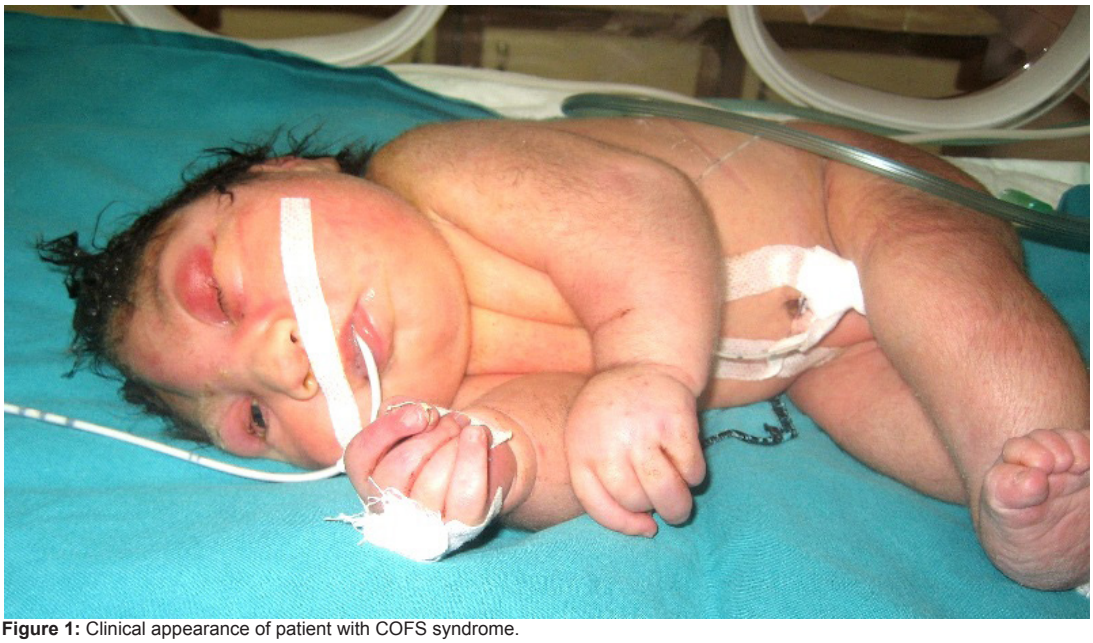

Figure 1: Clinical appearance of patient with COFS syndrome.

DISCUSSION

Cerebro-oculo-facio-skeletal (COFS) syndrome is a recessively inherited rapidly progressive neurologic disorder leading to brain atrophy, cataracts, microcornea, optic atrophy, progressive joint contractures, and growth failure (5).

Our patient had growth deficiency, microcephaly, deep-set small eyes, a prominent beaked nose, micrognathia, micropenis, joint contractures, kyphoscoliosis, short legs and rocker-bottom feet. Key features of COFS syndrome include congenital microcephaly, with subsequent brain atrophy, reduced white matter, patchy gray matter, hypotonia, deep-set eyes with microphthalmia and cataracts, and camptodactyly with rocker-bottom feet. Movement is markedly decreased, leading to joint contractures, and life span is usually severely limited (5-7). Our patient died at age 2 weeks. In children with COFS syndrome, failure to thrive is prevalent, because of feeding problems, aspiration, and repeated lower respiratory-tract infections.

Neuropathology studies reported in the initial publications discussing COFS syndrome revealed generalized subcortical gliosis and decreased white matter with reduced myelin content, and Del Bigio et al. reported neuropathology in eight children with COFS syndrome, seven of whom were from the same Manitoba Aboriginal families (8). They noted progressive cortical neuronal loss with patchy absence of myelin and gliosis in white matter, as well as pericapillary and parenchymal mineralization in the globus pallidus, putamen, and cerebral cortex. In older children, there was severe cerebellar degeneration involving the internal granular layer and the Purkinje cell layer, and, in the younger cases, swollen ubiquinated granular cells were found in the white matter shortly after birth. Such progressive demyelination with brain calcification is quite similar to what is seen in the severe infantile form of Cockayne syndrome(CS). In both conditions, intrauterine growth can be close to normal, but, after birth, growth deficiency is striking and unrelenting, and it has become increasingly more difficult to distinguish between early-onset CS and COFS syndrome in siblings who have congenital cataracts, microphthalmia, intracranial calcifications, and progressive demyelinating diseases similar to early-onset CS (7, 9, 10).

This disorder has an outosomal recessive inheritance pattern. Mutations in three DNA-repair genes, CSB, XPG and XPD have been documented in some babies with COFS syndrome (1,11). It has been clear for some time that a specific biochemical or genetic marker would be of great benefit. Specific XPG deletion in neurons and glia of the forebrain creates a progressive neurodegenerative phenotype that shows many characteristics of human XPG deficiency (4). The relationship between COFS syndrome and differential diagnoses, Cockayne syndrome (CS), Pena-Shokier phenotype (PSP) and Neu-Lexova syndrome (NLS) must discuss (12).

The present report is the rare patient with COFS. The prognosis is dependent on the severity of the associated defects. Besides it stresses the importance of the genetic counseling and prenatal diagnosis in such syndromes with 25% the recurrence risk. Prenatal diagnosis by means of ultrasonography is possible. Pre-natal diagnosis followed by appropriate management in time may be helpful to reduce its incidence in the community.

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