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Case report

Cerebro-oculo-facio-skeletal syndrome : A case report

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= Abstract =

The Cerebro-oculo-facio-skeletal (COFS) syndrome is a rare autosomal recessive disorder characterized by multiple abnormalities that involve the brain, face, eyes, and extremities. COFS syndrome is regarded as a degenerative disorder of the brain and spinal cord caused by a mutation of the DNA repair genes. We report on an 8-month-old girl with COFS syndrome who exhibited growth and developmental delay, hypotonia, microcephaly, nystagmus, cleft palate, widely separated nipples, inguinal hernia, camptodactyly, and rocker-bottom feet with vertical talus. **(Korean J Pediatr 2007;50:435-438)**

Key Words : Cerebro-oculo-facio-skeletal (COFS) syndrome

Introduction

The Cerebro-oculo-facio-skeletal (COFS) syndrome, first described by Pena and Shokeir[1] in 1974, is a rare autosomal recessive disorder. The COFS syndrome is regarded as a degenerative disorder of the brain and spinal cord caused by the mutation of the DNA repair genes. It shows multiple abnormalities of the brain, face, eyes, and extremities.

In Korea, only one case has been reported of a newborn with COFS syndrome who died at 1 month of age[2]. We experienced an 8-month-old female infant with multiple abnormalities in the brain, face, eyes, and extremities, which led to a diagnosis of COFS syndrome.

Case report

An 8-month-old female infant was hospitalized due to fever, vomiting, and cough that had persisted for three days. She was born in the 39th week of gestation through repeated Cesarean section delivery at the local obstetric clinic. Her birth weight was 2,120 g (less than 3 percentile). Her parents and five-year-old twin sisters were normal, without noticeable genetic disorders. She had feeding difficulty and had a persistent cough since birth, and was hospitalized because of severe dehydration, and aspiration pneumonia at 1 month of age. At that time, she was found cleft palate, and she started orogastric-tube feeding at 2 months of age. She was also underwent herniorraphy on both sides. A short leg splint was applied to both lower extremities to correct vertical talus from 2 to 7 months of age. She achieved incomplete head control in her fifth month and partially turns over her body in her seventh month. At that time, TORCH Ig M antibody tests were negative and the chromosome study revealed normal female karyotype (46, XX). On the physical examination, she was measured to be 5,100 g in weight, 58 cm in length, and 35 cm in head circumference (all parameters are less than 3 percentile). Her skin and buccal mucosa were severely dry, and there was no sign of photosensitivity on her skin. In gross appearance, she exhibited microcephaly, coarse and sparse hair, low-set ears, cleft palate, and micrognathia on the head and face; deep-set eyes and pendular-type nystagmus on the eyes (Fig. 1, 2). There were widely separated nipples on the chest (Fig. 3) and subcostal retraction on her chest wall, and moist rales on both lung fields. The heart sound was normal. She exhibited camptodactyly, mild flexion contracture, and rocker-bottom feet with vertical talus on the extremities (Fig. 4). Laboratory findings at admission were within normal limit except thyroid function test. Thyroid function test showed thyroid stimulating hormone (TSH) 1.88 μU/mL, free thyroxine (T_4) 1.05 ng/dL and triiodothyronine (T_3) 127 ng/dL. In consequence she diagnosed as hypothyroidism. Chest radio-

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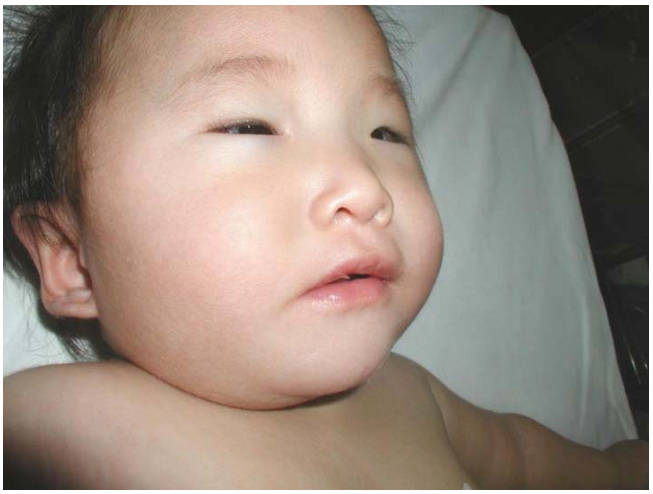

Fig. 1. A picture of her face at 12 month of age. She exhibited microcephaly, low-set ears, micrognathia on the head and face, deep-set eyes and pendular-type nystagmus on the eyes.

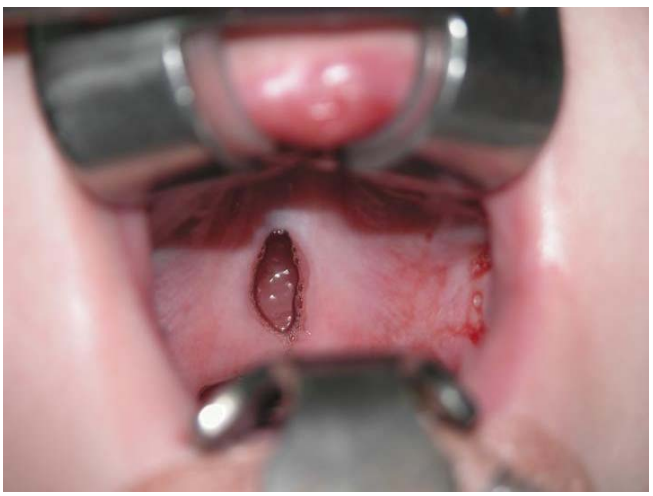

Fig. 2. A picture showing the cleft palate during Von Rarrgenback operation.

graphy showed streaky infiltration in both perihilar areas. Radiography of the pelvis did not show shallow acetabular angle and coxa valga. The weight-bearing lateral radiographs of foot showed a typical vertically oriented talus (Fig. 4). The auditory evoked potential test and echocardiograph were normal. A brain magnetic resonance imaging (MRI) at 8 month of age showed a microcephaly and myelination that seemed to be about 6 months old, with no structural abnormality. In the initial management, she was administered with intravenous fluid to correct dehydration and antibiotics for pneumonia. Orogastric-tube feeding was attempted after there was clinical improvement of dehydration and pneumonia, but it led to recurrent vomiting and aspiration

Fig. 3. A full-length figure was taken. Note that microcephaly, widely separated nipples, camptodactyly, and rocker-bottom feet with vertical talus was presented.

pneumonia. Thus, total parenteral nutrition was instilled for nutritional support. At 10 months of age, a Von Rarrgenback operation was performed to correct her cleft palate and to allow her to attempt oral feeding. A V-tube insertion was also conducted on ear drums for concomitant otitis media with effusion. Oral feeding was attempted after correcting the cleft palate, but her swallowing difficulty led to lack of ingestion and aspiration pneumonia. Ultimately she underwent gastrostomy at 11 months of age, which made subsequent enteral feeding successfully. Levo thyroxine was administered to treat hypothyroidism. She was 6,800 g and 79.5 cm in length, and the head circumference was 37 cm (all parameters are less than 3 percentile) at 28 month of age. At that time, the patient could completely control her head, but had been unable to turn over her body and sit alone.

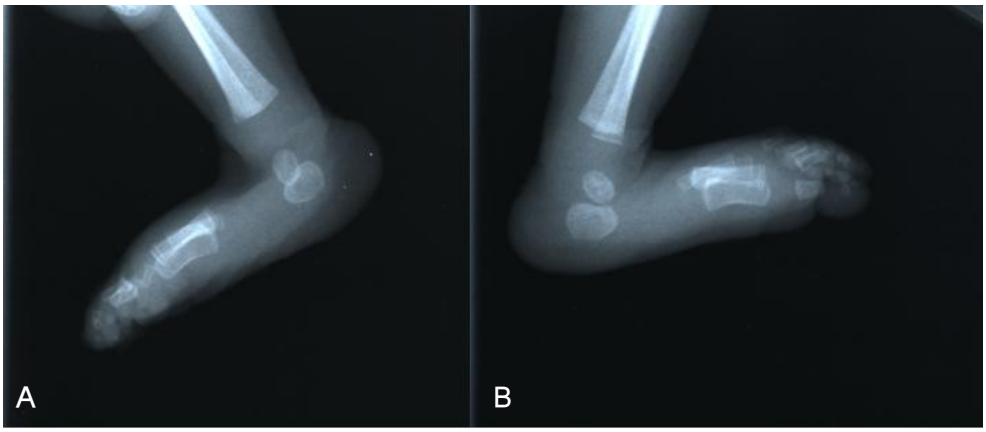

Fig. 4. The weight-bearing lateral radiographs of both feet showed a typical vertically oriented talus.

Discussion

The COFS syndrome is a rare autosomal recessive disorder characterized by various abnormalities that involve the brain, face, eyes, and extremities[3].

The etiology and pathogenesis of the COFS syndrome are unknown, but it is thought to be related to the mutation of the cockayne syndrome group B (CSB), xeroderma pigmentosum group D (XPD), or xeroderma pigmentosum group G (XPG) gene, known as the DNA repair genes[4, 5]. Meira et al[4] reported that the mutation of the CSB gene causes COFS syndrome and COFS syndrome is a variant of Cockayne syndrome in a study conducted on typical COFS syndrome patients. In addition, the other study reported a type of COFS syndrome that gave patients skin photosensitivity because of the mutation of the XPD gene[5].

The diagnosis of COFS syndrome is led clinically from characteristic craniofacial and skeletal deformities[3]. And the neuro-imaging study is necessary in almost cases because of neurologic malformation. According to a neuro-imaging study of the COFS syndrome, the brain CT scan shows intracranial calcification and brain MRI shows partial agenesis of the corpus callosum, the dilatation of the polymicrogyria and the lateral ventricle, an irregular gyral pattern of the cerebral cortex, and atrophy of the optic nerve or chiasm, mostly with a normal brainstem[8-10]. In our case microcephaly, deep-set eye, nystagmus, cleft palate, widely separated nipples on the chest, comptodactyly, and rocker-bottom feet with vertical talus was found. Because our patient did not perform brain CT, we could not confirm intracranial calcification. And brain MRI showed microcephaly and delayed myelination without structural anomaly. In this respect, our patient is different from most reported COFS syndrome patients. Other cases of patients with COFS syndrome who had oligohydramnios-accompanied renal agenesis[6] or congenital muscular dystrophy[7] were reported.

Because the course of COFS syndrome is unfavorable, prenatal diagnosis has an important role in COFS syndrome. A study reported that COFS syndrome could be diagnosed antenatally from a fetus who exhibits unusual combination of micrognathia, multiple joint contractures, and rocker-bottom feet, which are detected in an antenatal ultrasonic examination[11].

COFS syndrome should be differentiated from Cockayne syndrome (Pena-Schokeir phenotype), MICRO syndrome, lethal multiple Pterygium syndrome, and intrauterine infection[9, 10].

The management of COFS syndrome is mainly conservative and the majority, COFS syndrome patient had a feeding dysfunction and poor weight gaining, therefore gastrostomy was performed. Some patients with COFS syndrome have a seizure, for that reason patients were maintained on anticonvulsants[10]. And the other patient was bed- ridden with inability to sit, minimal vocalizations, and progressive neuromuscular scoliosis with recurrent pneumonia[10].

Most patients with COFS syndrome reveal severe failure to thrive as well as recurrent aspiration pneumonia, and die before their fifth year[1, 2]. One case of neonate with COFS syndrome in Korea died at the age of 1 month, because of persistent respiratory failure. In addition various cases have

been reported in other countries, a male infant was born at 39 weeks gestation weighing 2,180 g, and he was shown clinical features in COFS syndrome. This patient died at the age of 5 months, because of feeding difficulties with gastroesphageal reflux and recurrent pneumonia[12]. Our patient improved with feeding and weight gaining after gastrostomy. After this, she was hospitalized for recurrent pneumonia. But, hospitalization days and frequencies of hospital care have been decreased.

In this study we report on an 8-month-old infant with COFS syndrome who is living at present in Korea.

한 글 요 약

COFS 증후군 1례

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Cerebro-Oculo-Facio-Skeletal (COFS) syndrome은 뇌, 안면, 안구 및 사지의 기형을 특징으로 하는 상염색체 열성 유전질환이다. COFS 증후군은 DNA-repair gene의 돌연변이로 인한 뇌와 척수의 퇴행성 질환으로 여겨지며, 대뇌, 안구, 안면 및 사지의 복합 기형을 보인다. 국내에서는 신생아기에 진단되어 생후 1개월에 사망한 1례만이 보고 되어 있다. 저자들은 뇌, 안면, 안구, 그리고 사지의 복합 기형을 보여 COFS 증후군으로 진단된 환아를 경험하였으며, 이를 문헌 고찰과 함께 보고한다.

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