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The first case of Horn Kolb Syndrome in Turkey, diagnosed prenatally at the 23rd week of a pregnancy: A very rare and unusual case far from the original geography

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Summary

Background:

The aim of this report was to evaluate and announce the first documented appearance of Horn Kolb syndrome in Turkey.

Case Report:

Acheiropodia (Horn Kolb Syndrome) is the bilateral congenital amputation of the distal parts of the 4 extremities. It is an autosomal recessive developmental disorder. The characteristic features are amputation of the upper and lower extremities with aplasia of the hands and feet. The disorder affects only the extremities without other systemic manifestations. In this report, we present the first known case of Horn Kolb syndrome in Turkey, along with the diagnostic features.

Conclusions:

Severe dysmorphic skeletal anomalies should be excluded as soon as the earlier gestational weeks in every pregnancy by visualizing all 4 limbs of the fetus in routine prenatal ultrasound screening.

key words:

acheiropodia • acheiria • transverse limb defect • Horn Kolb syndrome

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BACKGROUND

Acheiropodia (Horn Kolb Syndrome) is the bilateral congenital amputation of the distal parts of the 4 extremities. It is an autosomal recessive developmental disorder. The characteristic features are amputation of the upper and lower extremities accompanied by aplasia of the hands and feet. The disorder affects only the extremities, without other systemic manifestations [1].

Acheiropodia has previously been reported only in Brazilians of Portuguese ancestry. A locus for acheiropodia was mapped on chromosome 7q36 [2]. We report a case of Horn Kolb Syndrome diagnosed prenatally. To our knowledge, this is the first case published from Turkey and the Old World.

CASE REPORT

A 36-year-old woman was referred to our hospital with abnormal findings detected at the 23rd week of her fifth gestation. She had been married to her first cousin for 8 years. After the abortion of her first pregnancy at 2 months gestation, she had subsequently given birth at the 20th week of gestation on 2 separate occasions, both resulting in the death of the baby. Two years prior to the currently described case, she had delivered vaginally at term. The child had had no somatic or developmental abnormalities, but unfortunately, died of pneumonia at age 8 months. Parental karyotype analysis was normal.

The pregnancy had been confirmed at 10 weeks. She had had antenatal visits and ultrasound exams at the 10th and 16th week, both with no remarkable findings. Triple screening and hematological and biochemical test results were also unremarkable.

The woman had used a spironolactone 50 mg and hydrochlorothiazide 50 mg combination daily from 16th of December to 15th of January for mild hirsutism and hypertension, ornidazole 500 mg twice a day orally, and metronidazole 500 mg once a day vaginally from 16 December to 23 December for a genital infection.

Although she was married to her cousin, the family background was unremarkable for congenital anomalies. Despite the couple being blood relatives and there having been several consanguineous marriages discovered during genealogical analysis, no family members were found to have had any congenital anomalies.

She was referred to our tertiary centre based on severe oligohydramnios, inability to visualize the fetal kidneys, urinary bladder and stomach, and minimal right lateral pleural effusion observed during ultrasound.

During the ultrasound examination of the pregnancy, fetal biometry confirmed the 23-week pregnancy using bi-parietal diameter, and abdominal circumference measurements. The amniotic fluid index was measured as 0 cm.

Although the cerebral hemispheres and the cerebellum were evaluated as normal, the cisterna magna was slightly enlarged, with the largest diameter being 15.45 mm. Despite poor visibility, the spinal cord and the vertebral column were



Figure 1. The new born with Horn Kolb syndrome, just after birth.

evaluated as normal in appearance. The fetal heart could be visualized with 4 chambers, but there were periods of arrhythmias dominated with severe bradycardia. We were able to distinguish the fetal kidneys but not the urinary bladder nor the stomach. The fetal sex was female.

During the evaluation of fetal extremities, the fetal femur and humerus were identified and measured, with the measurements showing normal reference levels appropriate for the gestational week. However, we were unable to demonstrate the fetal tibia, fibula, radius, ulna, feet, or hands.

The woman was hospitalized for fetal follow-up and further investigation. However, since fetal death occurred during the first hour of hospitalization, we have obtained consent from the family to terminate the pregnancy and to examine the fetus after birth. Following the administration of misoprostol 200 mcg, vaginally, the fetus, placenta and the associated membranes were delivered 9.5 hours later, and thus, the pregnancy was terminated.

In macroscopic evaluation, the height and weight of the baby were measured as 27 cm and 440 grams, respectively. The face and the skull were normal, but the fetus had bilateral low-set ears. The bilateral forearm and the hand formation were rudimentary. There were no separate identifiable digits in either hand. The bilateral legs and feet were rudimentary. There were no separate identifiable digits in either foot (Figure 1).

The autopsy report showed that there was no development of the distal portions of the lower and upper extremities of the fetus. Although the fetus had normally developed structures of the fetus up to the elbow and the knee joint appropriate for the gestational week, the distal extremities were wing-like, stumpy formations, and had no legs, forearms, wrists or fingers. Other body structures, including the backbone, head, eye, face, heart, intra-abdominal viscera, anus, labium majus and genital area, were normal.

X-ray examination confirmed the clinical diagnosis. There was a single hypoplastic ossification centre in both the forearms and the hands. Moreover, there was a single hypoplastic ossification centre in both legs and feet (Figure 2).



Figure 2. X-ray views the new born.

DISCUSSION

Achairopodia is classified as acheiria under the heading of “dysostoses with predominant involvement of extremities” [3]. However, the nomenclature for skeletal dysplasia is complicated. Classification based on the underlying molecular genetic cause is clinically useful since faulty genes, whose protein products have similar functions, also result in disorders with similar clinical characteristics. Of nearly 300 disorders, the genes responsible for skeletal dysplasia have been identified in more than 150 diseases, most of which are monogenic diseases [4,5].

Achairopodia is an autosomal recessive inherited trait. The heterozygotes are phenotypically normal. Most affected individuals are the offspring of consanguineous matings [1,2,6]. In our case, the parents were cousins and despite this being the 5th gestation for the couple, they had still not managed to have a healthy, living child following 2 previous second-trimester and 1 first-trimester pregnancy losses.

The estimated incidence of achairopodia in Brazil is approximately 1/250,000 births [6]. Moreover, with the exception of 2 cases from Puerto Rico, all known cases are of Brazilian origin. A hospital-based study in Boston, USA by McGuirk et al. found the prevalence rate of all types of limb deficiencies to be 0.69/1000 [7].

Although clinical and experimental studies have not revealed the link between teratogens and achairopodia, it is the authors’ opinion that more trials are needed in order to reach an accurate conclusion concerning their possible role in achairopodia. In one study, smoking was found to be associated with an increase in congenital limb defects [8]. However, although spironolactone and hydrochlorothiazide, which the mother used during the present case,

are classified as risk factor D drugs in pregnancy, no major limb malformations have been reported for these agents. Metronidazole and ornidazole, on the other hand, are classified as risk factor B drugs in pregnancy and, although no significant rise in the number of major limb malformations has been reported for these agents, they have been found to be mutagenic and carcinogenic in animal studies [9]. The possible involvement of teratogenic effects in the specifics of our case (cellular phone base station, spironolactone, hydrochlorothiazide, ornidazole and metronidazole) needs further investigation.

Prenatal diagnosis of achairopodia is extremely difficult due to the rarity and unfamiliarity of the entity. In the evaluation of 226 fetuses and stillbirths with suspected skeletal dysplasia, Sharony et al. was unable to find any sign of skeletal dysplasia or obvious dysmorphic syndrome in 7% of cases. They concluded that skeletal dysplasia could be diagnosed as early as the 14th week of gestation by ultrasound. In addition, they suggested the use of fetal radiographs to reach an accurate diagnosis [10]. In our case, although prenatal diagnosis was inaccurate because of the difficulties created by the severe oligohydramnios, the inability to see the distal parts of the upper and lower extremities was helpful in ascertaining the severity of the condition.

CONCLUSIONS

We recommend that severe dysmorphic skeletal anomalies be ruled out in every single pregnancy and the demonstration of all 4 limbs become routine in prenatal ultrasound screening.

REFERENCE:

- Freire-Maia A, Li WH, Maruyama T: Genetics of achairopodia (the handless and footless families of Brazil). VII. Population dynamics. *Am J Hum Genet*, 1975; 27(5): 665–75
- Escamilla MA, DeMille MC, Benavides E et al: A minimalist approach to gene mapping: locating the gene for achairopodia, by homozygosity analysis. *Am J Hum Genet*, 2000; 66(6): 1995–2000
- International nomenclature of constitutional diseases of bone. *AJR Am J Roentgenol*, 1978; 131(2): 352–54
- Ikegawa S: Genetic analysis of skeletal dysplasia: recent advances and perspectives in the post-genome-sequence era. *J Hum Genet*, 2006; 51(7): 581–86
- Tayel SM, Fawzia MM, Niran A et al: A morpho-etiological description of congenital limb anomalies. *Ann Saudi Med*, 2005; 25(3): 219–27
- Ianakiev P, van Baren MJ, Daly MJ et al: Achairopodia is caused by a genomic deletion in C7orf2, the human orthologue of the Lmbr1 gene. *Am J Hum Genet*, 2001; 68(1): 38–45
- McGuirk CK, Westgate MN, Holmes LB: Limb deficiencies in newborn infants. *Pediatrics*, 2001; 108(4): E64
- Czeizel AE, Kodaj I, Lenz W: Smoking during pregnancy and congenital limb deficiency. *BMJ*, 1994; 308(6942): 1473–76
- Briggs GG, Freeman RK, Yaffe SJ: Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk. 5th ed. Baltimore, Maryland, USA: Williams and Wilkins, 1998; 187–91, 722–26, 976–77
- Sharony R, Browne C, Lachman RS, Rimoin DL: Prenatal diagnosis of the skeletal dysplasias. *Am J Obstet Gynecol*, 1993; 169(3): 668–75