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Congenital contractural arachnodactyly suspected by abnormally long extremities by fetal ultrasound

Ryuta Miyake, Mayuko Ichikawa, Katsuhiko Naruse

OB/GYN, Nara Medical University Hospital, Kashihara, Japan

Correspondence to
Dr Ryuta Miyake;
ryuta-miyake@naramed-u.ac.jp

Accepted 8 February 2021

SUMMARY

Congenital contractural arachnodactyly (CCA) is a rare disease with the clinical features of limited extension of multiple joints, arachnodactyly, camptodactyly, thin and long extremities, and so on. In the point of long extremities, CCA resembles Marfan syndrome (MFS). CCA is easily differentiated from MFS after birth due to the flexion of multiple joints, including elbows, knees, hips and fingers. During the fetal period, observation of arachnodactyly and folded fingers by fetal ultrasound is the means of differential diagnosis between these two diseases. We report on a case of CCA diagnosed with prenatal symptoms of long extremities, and introduced physiotherapy in early childhood for a better physical prognosis.

BACKGROUND

Congenital contractural arachnodactyly (CCA) was first reported in 1971 by Beals and Hecht[1] and, thus, called 'Beals and Hecht syndrome' or 'Beals syndrome'. The clinical features are limited extension of multiple joints, arachnodactyly, camptodactyly, thin and long extremities, bowed long bones, crumpled ears, scoliosis, adducted thumb and so on.[2] CCA occurs because of fibrillin 2 (FBN2) gene mutation. The prognosis is typically not poor, unless there are severe cardiovascular complications. In terms of physical prognosis, physiotherapy from early childhood increases joint mobility and lessens muscle hypoplasia.[2]

CASE PRESENTATION

A woman in her 30s, gravida 2, para 1, live birth 1, was seen in our hospital at 36 weeks of pregnancy due to fetal ultrasound abnormality. Her 20-month-old child has no congenital anomalies or developmental disorders. The patient had no medical history and no family history of cardiovascular disease, such as aortic dissection and aortic aneurysm. The patient has never smoked a cigarette and not consumed alcohol. She had taken multivitamin supplements from the first trimester of pregnancy, including folic acid and vitamin B_6. She got spontaneous pregnancy and the expected delivery date was determined from the last menstrual period matched with ultrasound finding. The pregnancy was initially uncomplicated; at 31 weeks of pregnancy the fetal ultrasound showed the femur length (FL) to be 58 mm, which was still considered acceptable. After 33 weeks of pregnancy the FL became longer than the average; the FL was 68 mm (+2.7 SD on Japan Society for Ultrasound in Medicine formula) at 33 weeks, 72 mm (+2.9 SD) at 35 weeks and 75 mm (+3.0 SD) at 36 weeks (figure 1). The patient referred to our hospital at 36 weeks and 5 days; the fetal ultrasound (figure 2) showed abnormally long extremity bones. The FL was 77.9 mm (+3.7 SD), the tibia was 70.0 mm (+4.1 SD), the fibula was 71.9 mm (+5.4 SD), the humerus was 70.0 mm (+4.6 SD), the radius was 65.4 mm (+5.4 SD) and the ulna was 73.2 mm (+6.6 SD), and they were curved in a bow shape. The length of the finger bones could not be measured because the fingers were folded. The amount of amniotic fluid was within the normal range and no other major anomalies, including that of the cardiovascular system, were detected.

DIFFERENTIAL DIAGNOSIS

We suspected CCA and Marfan syndrome (MFS) due to the long extremity bones. The long extremity is a common feature of CCA and MFS, but the joint contracture and arachnodactyly are only seen in CCA. CCA is easily distinguished from MFS by observing the condition of the joints and hands after birth. The distinguishing features in the fetal period are camptodactyly and folded fingers.[3] In the reported case by Kölble *et al*,[4] whose father has CCA and was genetically diagnosed after birth, pes adductus, contractures of the elbows, camptodactyly and moderately deformed ears were found in fetal ultrasound. In contrast to MFS, patients with CCA rarely have the complications of aortic aneurysm or ectopia lentis.

By the fetal ultrasound findings, respectively, syphilis could be suspected by bowed bones, trisomy 18 by overlapped fingers, Achard syndrome

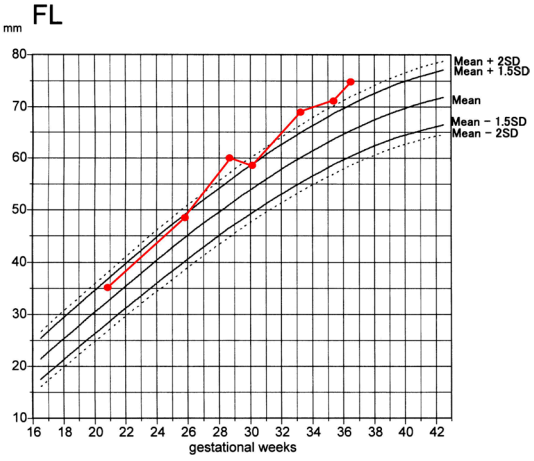

Figure 1 Regression curve of femur length and gestational weeks in Japanese fetus. FL, femur length.

To cite: Miyake R, Ichikawa M, Naruse K. *BMJ Case Rep* 2021;**14**:e237904. doi:10.1136/bcr-2020-237904

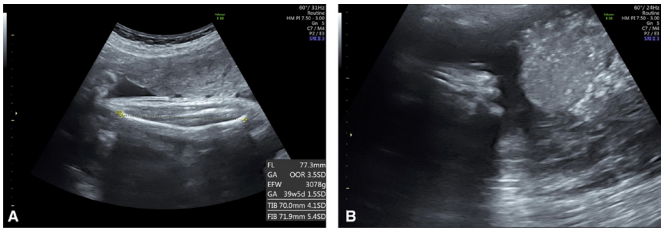

Figure 2 Fetal ultrasound at 36 weeks of gestation. (A) The length of right tibia is 70.0 mm (+4.1 SD). (B) The left fingers are folded.

by arachnodactyly, VACTERL by scoliosis and distal arthrogryptosis by multiple joint contractures.

OUTCOME AND FOLLOW-UP

On 39 weeks and 1 day of pregnancy, the patient gave birth to a female neonate by spontaneous vaginal delivery. Infant's birth weight was 3100 g, and the Apgar scores were 9 at 1 min and 10 at 5 min. The baby had crumpled ears, long extremities, limited extension of the hips, knees and elbow joints, arachnodactyly, camptodactyly, adducted thumb, and scoliosis (figure 3). The clinical features were matched to the characteristic of CCA. The neonate received physiotherapy from day 3. In the admission period, the neonate received an automated auditory brainstem response test, eye fundus examination, and brain and cardiac ultrasounds, which revealed no other complications. At day 4, X-rays showed bowed long bones and scoliosis (figure 4). The neonate was discharged from our hospital at day 12.

Genome sequencing by next generation sequencer did not detect abnormal variant in genetic connective tissue disease gene panel (HCTDv4) including FBN2 gene.

The prognosis of CCA is typically not poor, unless there are severe cardiovascular complications. In terms of physical prognosis, physiotherapy from early childhood increases joint mobility and lessens muscle hypoplasia.[2] In some patients, scoliosis is progressive and requires surgical treatment, which severely restricts the physical prognosis. Routine physical examination for spinal deformities and early intervention for scoliosis can prevent morbidity later in life. In Japan, CCA cases are reported in the orthopaedics societies and the age of diagnosis ranges between 18 months and 15 years.[5] The diagnosis during the fetal period through ultrasound, or soon after birth, is essential for early intervention to improve the physical prognosis.

DISCUSSION

In this case, we suspected CCA and MFS by long extremities and bowed long bones prenatally.

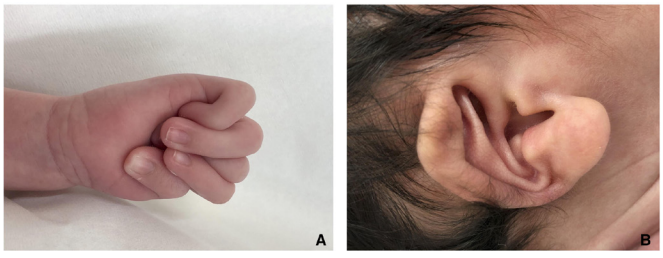

Figure 3 Pictures of the baby after birth. (A) The baby holds her hands tightly. The index finger and ring finger are folded over the middle finger. The thumb is adducted. (B) The baby's ear is crumpled. All photographs are provided after written informed consent by the patient's mother.

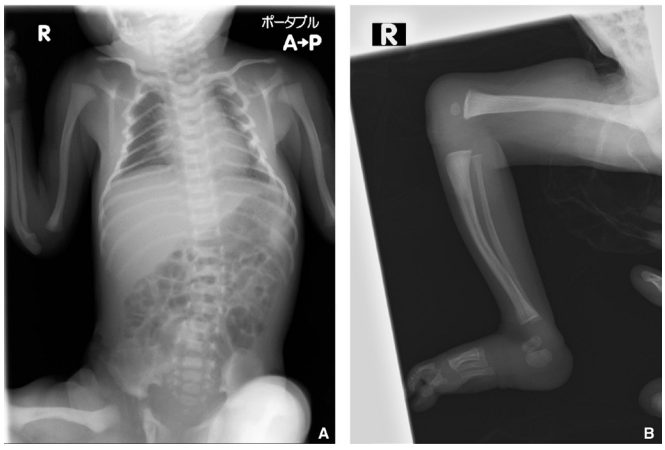

Figure 4 The X-ray of the baby on day 4. (A) The baby has scoliosis and her humerus is bowed. (B) The tibia is bowed which resembles the one shown in fetal ultrasound.

It is believed that the first case of CCA was reported by Marfan in 1896. The case Beals and Hecht reported was a 5-year-old girl with limited knee and elbow joints extension, followed by the complication of scoliosis, but the patient never developed cardiovascular and ocular complications. In this case, arachnodactyly, camptodactyly, limited extension of the elbow, knee and hip joints, crumpled ear, adducted thumb, scoliosis, and bowed long bones are matched to the clinical features of CCA.

CCA and MFS have the same clinical features as long extremities and bowed long bones. CCA and MFS are caused by fibrillin protein abnormalities. CCA is caused by a deficit in the FBN2 gene, which is mapped on 5q23-31. Previously, constitutional interstitial deletion of chromosome 5(q15q31) or 5(q23q31) patients were reported and they have the same clinical features as CCA.[6] On the other hand, MFS is caused by FBN1 gene mutation mapped on chromosome 15q15-21. Both mutations result in errors in fibrillin production; fibrillin is composed of extracellular filaments and is distributed throughout the whole body, found in fascia, tendons and blood vessels. The FBN2 gene mutation is detected in 27%–43% of patients with CCA,[7 8] and the maximum lod score is 6.2 (θ=0.005; 95% CI).[9] In this case, genome sequencing revealed no abnormality in FBN2 gene region. Because of the low detection rate of FBN2 gene mutation in patients with CCA, this result does not deny the clinical diagnosis of CCA.

The long extremity is a common feature of CCA and MFS, but the joint contracture and arachnodactyly are only seen in CCA. CCA is easily distinguished from MFS by observing the condition of the joints and hands after birth. The distinguishing features in the fetal period are camptodactyly and folded fingers.[3] Cardiovascular complications and ectopia lentis are characteristic

Learning points

- If long extremities and bowed long bones are seen in fetal ultrasound, congenital contractural arachnodactyly, in addition to Marfan syndrome, should come to mind.
- The distinguishing features in the fetal period are camptodactyly and folded fingers.
- Physiotherapy should be started from early childhood to increase joint mobility and lessen muscle hypoplasia, and have better physical prognosis.

symptoms of MFS. Cardiovascular complications in CCA include mitral valve prolapse, atrial septal defects, ventricular septal defects[10–12] and transient cardiomyopathy,[13] with dilated cardiomyopathy,[14] rarely reported in Japan. In CCA, 20% of patients have heterotropia as an ophthalmological complication,[10] and blue sclerae, glaucoma optic disc cupping, partial coloboma of the lens and abnormal ciliary body morphology have also been reported. In this case, cardiovascular and ophthalmological diseases were not present.

Contributors Concept and design—RM, MI and KN. Data analysis—RM and MI. Writing (original draft)—RM. Writing (review and editing)—RM and KN.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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