Subtle ultrasonographic appearance of Down's syndrome: a case report of prenatal diagnosis of isolated simple fetal syndactyly

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Summary

Syndactyly is an unusual condition in humans where two or more digits are fused together. In our report we present a case of prenatal diagnosis of simple, complete, bilateral syndactyly as the only ultrasonographic anomaly in a fetus with Down's syndrome. The mother, a 30-year-old, gravida 2, was referred to our hospital with an abnormal triple-test at 17 weeks of gestation, with a final biochemical risk for Down's syndrome more than 1: 50. In this pregnancy neither the NT test nor early morphological exam showed typical findings of any chromosomal disorder. The patient underwent amniocentesis. We performed an accurate second level scan at 21 weeks while waiting for genetic results, and we suspected simple, complete, bilateral syndactyly between the third and fourth finger of the hands (rapper sign). The result of the invasive test was 47,XY,+21 and the mother opted for termination of pregnancy; the baby showed simple, complete, bilateral syndactyly of the two digits as suspected during sonography. In presenting our case report, we want to stress the importance of the accuracy of observation of fetal hand morphology, attitude, movements and reactivity. When the observation of fetal hands is not satisfactory (e.g., when the fetus does not open the fist), we recommend external stimulation of fetal reactivity through probe movements on the maternal abdomen (dynamic scan). This approach can make the identification of subtle hand anomalies easier and improve the detection rate of both structural and genetic fetal disorders.

Key words: Down's syndrome; Fetal syndactyly; Dynamic second level scan; Rapper sign.

Introduction

Hand anomalies are difficult to diagnose; they characterize many congenital syndromes including mendelian disorders, skeletal dysplasias, and karyotype abnormalities [1]. Although identification of a hand anomaly alters obstetrical management, evaluation of fetal hands is not included in current ultrasonographic guidelines [2]. Recent advances in ultrasound (US) technology now permit striking visualization of fetal morphology [3]. Evaluation of the hands and feet is an important part of the structural survey of the fetus at all gestational ages, as it provides an adjunct to the diagnosis of many syndromes. Even isolated limb anomalies may be important to diagnose antenatally so that proper care can be instituted postnatally for families and their newborns.

Case Report

A 30-year-old gravida 2 without obstetric, familiar and personal history relevant to risk factors for Down's syndrome was referred to our hospital with an abnormal triple-test at 17 weeks of gestational age, with a final biochemical risk for Down's syndrome more than 1: 50. Lab findings - AFP: 13.5 UI/ml (0.59 MoM, normal value), hCG: 89.9 UI/ml (2.73 MoM, significantly high), and uE3: 0.57 ng/ml (0.33 MoM, significantly low). At 12 weeks of gestation the measurement of nuchal translucency (NT) was 1 mm (10 th percentile) and a subsequent early morphological scan was not able to reveal any anomalies. The patient underwent genetic amniocentesis. At 21 weeks, waiting for genetic results, we performed a morphological second level exam with particular attention to strong and soft markers of trisomy 21.

Fetal biometries were within normal range; amniotic fluid index measured 150 mm, there was normal anterior placenta and the fetal anatomy was normal. In particular we noticed a regular shaped fetal head, normal cerebral anatomy (regular bilateral ventricular width, normal corpus callosum, cerebellar vermis and cisterna magna), regular facial profile (nasal bone: 5.6 mm, regular fronto-maxillary angle and prenasal thickness), nuchal fold less than 6 mm, normal insertion of ears, normal length of long bones (with DBP/LF ratio in normal range), normal cardiac B-mode and echo-color/pulsed Doppler scan (in particular insertion of the septal flap of the tricuspid valve was in normal position, and no signs of ARSA or abnormal position of the aortic arch were found), the renal pelvises were not enlarged, there was a normal echoic bowel, the hands showed five digits bilaterally (with normal length of medial phalanx of the fifth digit), the ankles were in axis and the feet appeared normal (no sandal gap was found). At the beginning of the exam the hands of the baby were closed, in a normal position of fetal tone (and showed five apparently normal digits bilaterally), so we tried to manually stimulate the fetal hand opening through hammering movements of the probe on the maternal abdomen to observe the fine anatomy of the digits; due to this shunting, we noticed a particular finding: fetal hand reactivity was normal in opening the fist, but the third and the fourth finger of both hands appeared constantly adducted. The phalanxes of the hands were all formed and isolated, but the two fingers remained joined, so we suspected simple and complete cutaneous syndactyly between the third and fourth finger of the hands (Figure 1). For this particular condition, we would

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Fig. 1

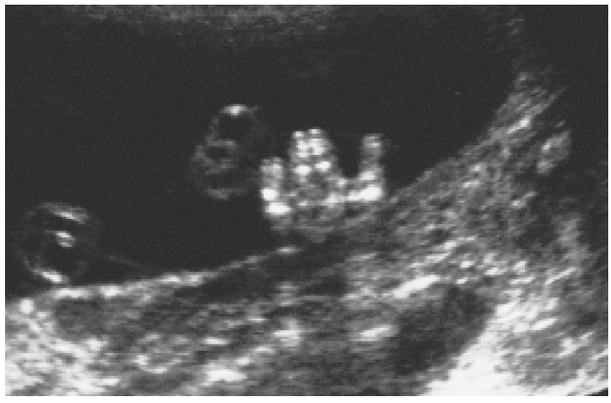

Fig. 2

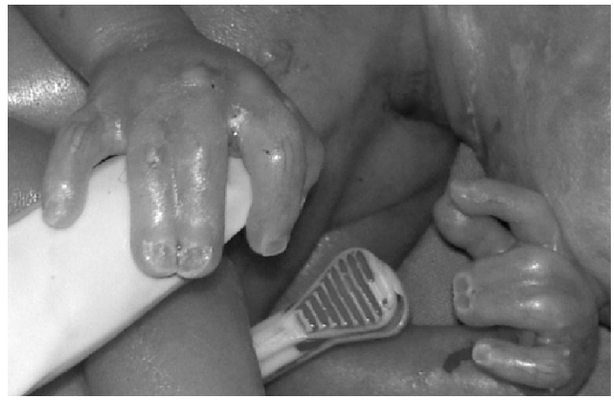

Fig. 3

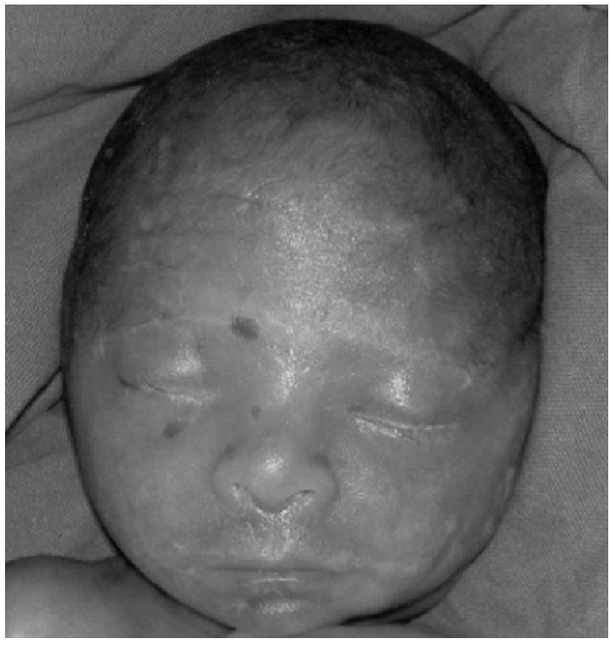

Figure 1. — US: simple and complete cutaneous syndactyly between the third and fourth finger of the hand.

Figure 2. — Simple, complete, bilateral syndactyly of the third and fourth finger (as suspected during US).

Figure 3. — Fetus face did not show typical characteristics of Down's syndrome.

propose the term of "rapper sign" to describe the singular attitude of the hands, similar to that often assumed by rappers while performing their songs.

The result of the invasive test was 47,XY,+21, obtained with the bandage technique G(GTG); AFP in amniotic fluid was normal. The mother opted for termination of pregnancy, and returned for the abortion.

The fetus was delivered stillborn after vaginal stimulation with prostaglandins. The baby had a weight of 600 g and showed simple, complete, bilateral syndactyly of the two digits as suspected during US (Figure 2). The appearance of the baby was completely normal except for the finding of syndactyly; in particular the face did not show typical characteristics of Down's syndrome (Figure 3).

Discussion

What is syndactyly?

Syndactyly (from Greek meaning "together" plus "finger") is a condition where two or more digits are fused together. It occurs normally in some mammals, but is an unusual condition in humans. In early human fetal development, webbing (syndactyly) of the toes and fingers is normal. At about 16 weeks of gestation, apoptosis takes place and an enzyme dissolves the tissue between the fingers and toes, and the webbing disappears. In some fetuses, this process does not occur completely between all fingers or toes and some residual webbing remains [4].

Syndactyly can be *simple or complex, complete* or *incomplete* [1, 2].

In simple syndactyly, which is present at birth (congenital), adjacent fingers or toes are joined by soft tissue and can be full or partial; in complex syndactyly, the bones of adjacent digits are fused.

In complete syndactyly, the skin is joined all the way to the tip of the finger; in incomplete syndactyly, the skin is only joined at part of the distance to the fingertip.

Fenestrated syndactyly means the skin is joined for most of the digit but in a proximal area there is gap in the syndactyly with normal skin.

Five types of syndactyly have been identified in humans and their common phenotypical expressions are as follows [1, 2]:

type I: webbing occurs between the middle and ring fingers and/or second and third toes (as in our case report);

type II: also involves the long and ring fingers, but has a sixth finger merged in between;

type III: small finger is merged into the ring finger;

type IV: involves all fingers and/or toes;

type V: similar to type I, but the metacarpals and metatarsels may also be fused.

Generally isolated simple syndactyly is a benign condition, associated with a good prognosis, but in our case it was secondary to Down's syndrome. Thus we suggest that couples have genetic consultation when this finding is revealed even if it is isolated.

Biochemical Down's syndrome screening

The triple screen

As is well known, combined evaluation of unconjugated serum estriol (fE3), maternal serum hCG, maternal serum AFP, and maternal age has value in predicting risk for fetal chromosomal abnormalities during pregnancy, particularly for trisomy 21. The AFP/hCG/fE3 screening test helps predict 65% of Down's syndrome with a number of false positives of 5%.

It should be emphasized the already known impact of an altered biochemical test in low-risk pregnancies: in our case report neither the NT test nor the early morphological exam showed typical findings of any chromosomal disorder. Biochemical screening is still inserted in a standardized protocol that can differ from each diagnostic center: US screening alone, triple test alone, integrated tests (the most accurate up-to-date), sequential tests, and others. These should never be bypassed because, altered biochemical values can sometimes be the only suspicious finding for the screening of Down's syndrome.

US Down's syndrome markers

Down's syndrome markers are numerous and the scientific literature continuously gives us new soft markers to improve the detection rate of chromosomal abnormalities, but none of these are sensitive enough to reliably discriminate between affected and unaffected fetuses. Clinicians should be very cautious about the use of these markers to counsel women about their risk of having a fetus with Down's syndrome [3, 5].

In our case we noted the importance of an accurate observation of fetal hand morphology and movements with the help of a *dynamic scan* (when necessary).

Sonographers should wait for fetal hand opening and if the fetus does not open the fingers spontaneously, they should stimulate this reactivity through external hammering pressure of the transducer on the maternal abdomen. Only by obtaining fetal digit movements can subtle anatomic anomalies be diagnosed.

Conclusion

From our experience, even if the US investigation cannot be considered indicative of Down's syndrome, we suggest, as many others do, to carefully look for any abnormalities in the fetal hands, their presentation and, especially their movements. Parents should be counseled about the possibility of increased risk for a chromosomal disorder when syndactyly is suspected by US examination, even if the doubt is only for the simple type.

The rapper sign, as we named the singular presentation of simple complete syndactyly of the third and the fourth digits, needs much more study in the future to establish an eventual related OR for Down's syndrome risk adjustment.

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