Short Foot Length

A Diagnostic Pointer for Harlequin Ichthyosis

Seshadri Suresh, MBBS, RDMS, Raja Vijayalakshmi, RDMS, Suresh Indrani, MD, Murlidharan Lata, MD

Objective. Among the fetal skin disorders, harlequin ichthyosis is the one that has specific sonographic features in the antenatal period. A few cases of antenatal diagnosis of harlequin ichthyosis with typical facial features of ectropion and eclabium have been described. The manifestation of the phenotype is usually in the third trimester. Fetal skin biopsy can be done in the late second trimester for diagnosing fetal skin disorders. We aimed to see whether a short foot length could be a pointer for the diagnosis of harlequin ichthyosis in the second trimester before the full phenotypic manifestation, which is usually seen in the third trimester. ***Methods.*** We report 3 cases of harlequin ichthyosis, 2 of them diagnosed in the third trimester with abnormal facial features and another second-trimester sonographic diagnosis based on short foot length, without eclabium and ectropion. ***Results.*** In all 3 cases, the foot length was considerably smaller than the femur length, especially in the third case, in which the foot length was smaller than the femur length before the manifestation of the typical features of harlequin ichthyosis. ***Conclusions.*** Fetal foot length may be an important and probably the first marker seen in the second trimester for the diagnosis of harlequin ichthyosis. ***Key words:*** foot length; harlequin ichthyosis; prenatal.

Received June 30, 2004, from Mediscan Prenatal Diagnosis and Fetal Therapy Centre, Chennai, India. Revision requested July 29, 2004. Revised manuscript accepted for publication August 12, 2004.

We thank Gurusamy Thangavel, BSMS, MSc, (Mediscan Systems, Chennai, India), for checking the manuscript and compiling the references.

Address correspondence and reprint requests to Raja Vijayalakshmi, RDMS, Mediscan Prenatal Diagnosis and Fetal Therapy Centre, 203 Avvai Shanmugam Rd, Royapettah, Chennai 600 014, India.

E-mail: ssuresh@vsnl.com.

Harlequin ichthyosis is a rare lethal autosomal recessive disorder, characterized by an extremely thickened keratin layer of skin, flattened ears, and diffuse platelike scales.[1] The fetuses have eclabium, ectropion, and scaling of the skin with resultant akinesia. There are few cases of prenatal diagnosis of harlequin ichthyosis reported.[2–4]

Harlequin ichthyosis has classic facial features of edematous eye lids and lips, which are very clearly seen in the third trimester, and the diagnosis is most often not evident during the targeted scan. Several cases of harlequin ichthyosis were diagnosed in our center; all of them were referred in the third trimester. Prenatal diagnosis of harlequin ichthyosis was made on the basis of eclabium and ectropion. Foot length was found to be significantly short compared with femur length. This finding of an abnormal femur–foot length ratio prompted us to look for the presence of short foot length in all the cases of harlequin ichthyosis referred to our perinatal autopsy

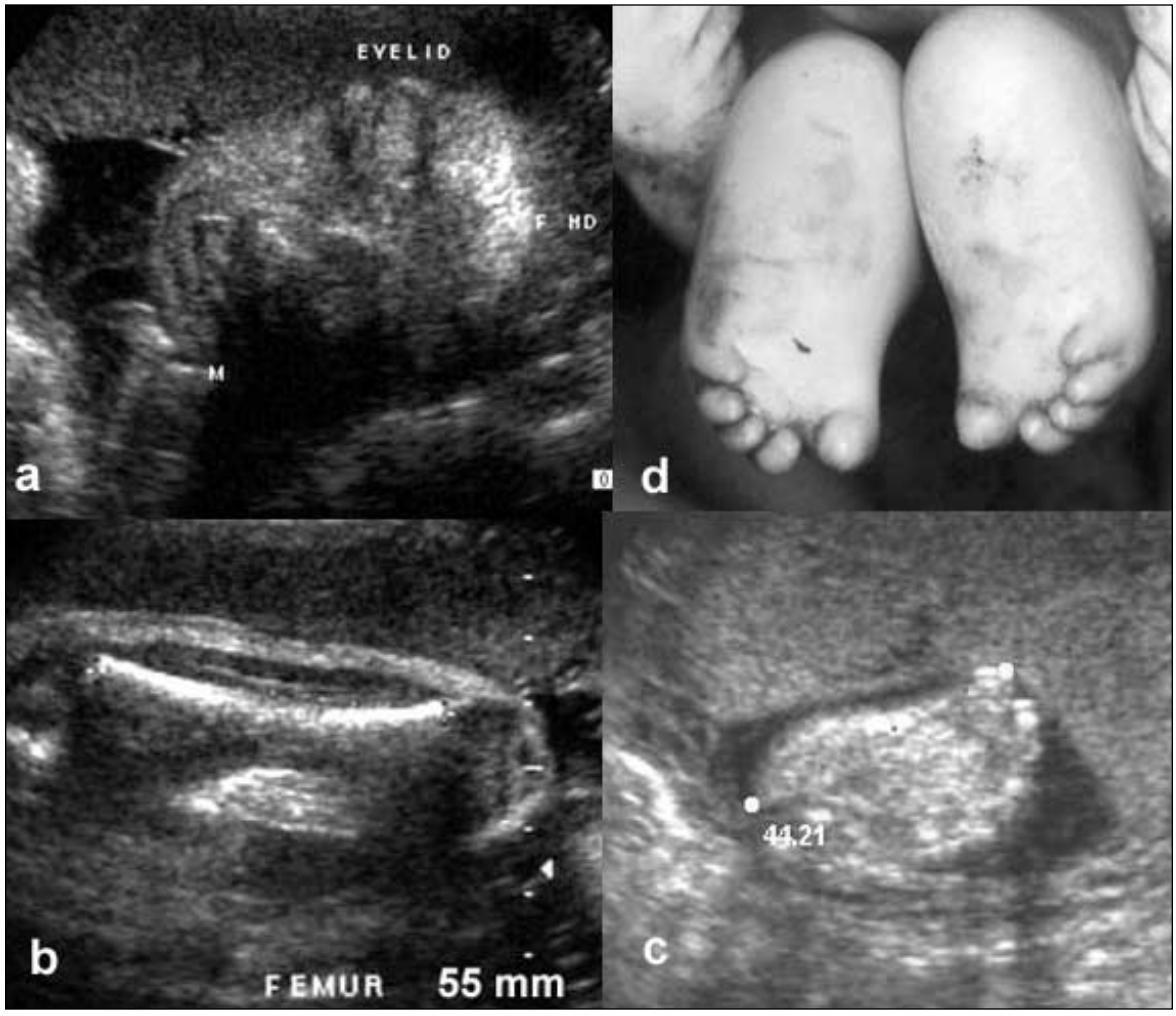
unit. A discussion with our perinatal pathologist confirmed this finding of short foot length unique to harlequin ichthyosis. Here we describe 3 cases of harlequin ichthyosis diagnosed antenatally, of which in 1 case, a targeted scan revealed short foot length with no facial abnormalities.

Case Descriptions

Case 1

A primigravida who conceived after 12 years of married life reported to our center at 34 weeks' gestation to rule out chromosomal abnormalities because a sonographic examination at 24 weeks' gestation at another center revealed polyhydramnios, intrauterine growth restriction, and possible clubfeet and clubhands. At our center, sonography revealed symmetric intrauterine growth restriction, a short forehead, eclabium, ectropion, and abnormal movements of the mouth. The phalanges were abnormally small in both hands and feet. Opening and closing of the hands could not be made out. The foot length measured 47 mm (Figure 1) and was decreased compared with the femur length, which measured 55 mm. A diagnosis of harlequin ichthyosis was considered. At 37 weeks, a live male neonate weighing 1700 g with features of harlequin ichthyosis was delivered. The neonate died 3 days after birth.

Figure 1. a, Coronal view of the face showing an abnormal eye lid (ectropion). F indicates face; HD, head; and M, mouth. **b** and **c**, Comparison between the femur and foot length. Note the abnormal phalanges. **d**, Postnatal photograph of the feet, which is similar to the antenatal picture in **c**.



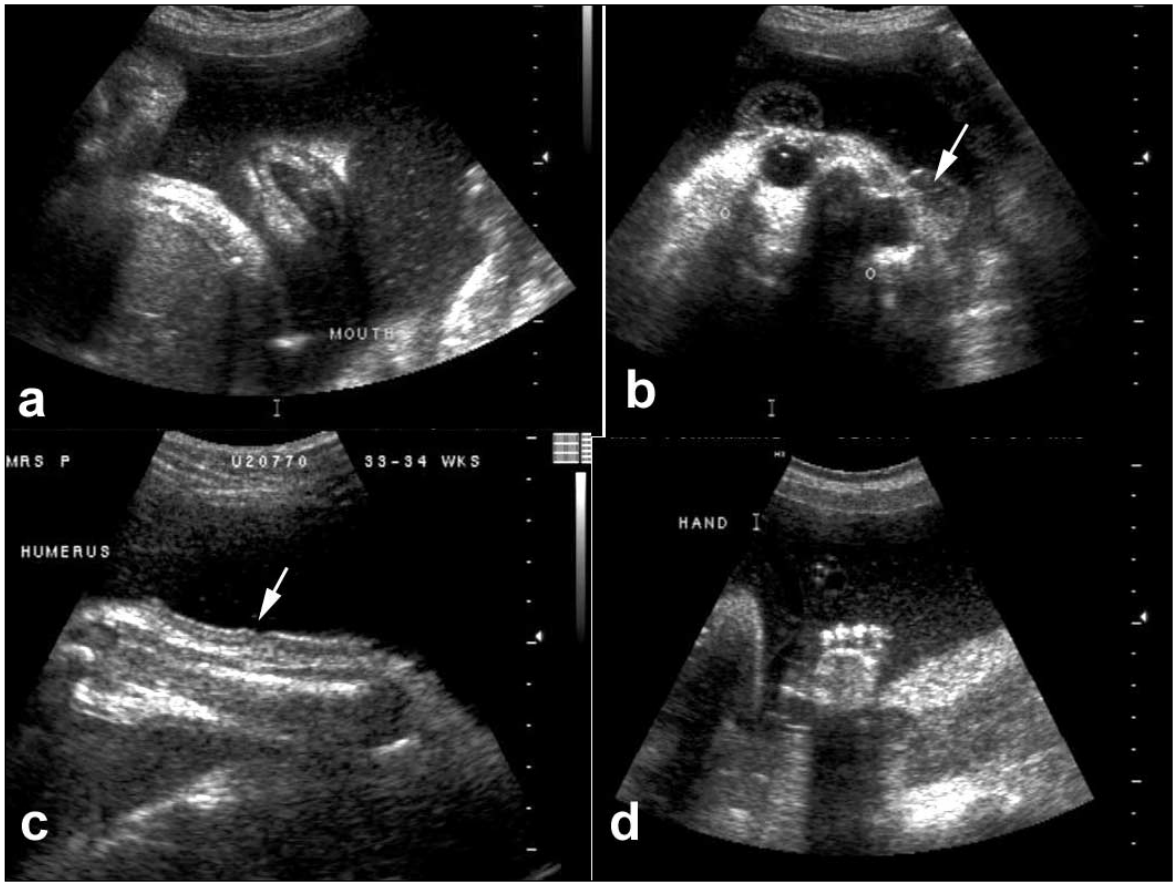
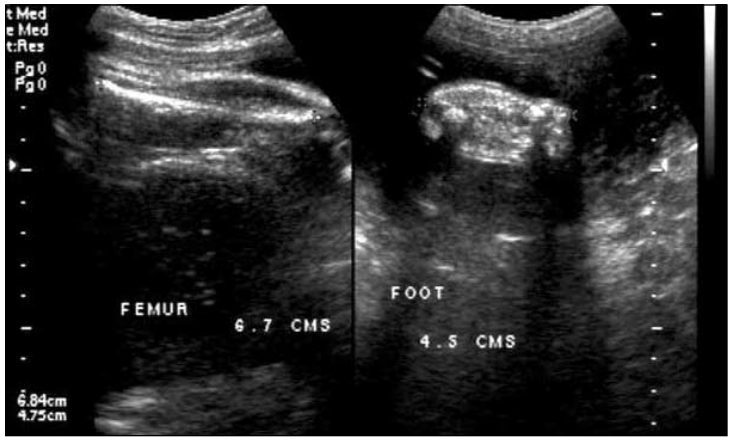


Figure 2. a, Wide open mouth with features of eclabium **b**, Axial view of the face showing orbits and soft tissue swelling (arrow) anterior to the orbits (O). **c**, Irregularity in the skin surface (arrow). **d**, Abnormal phalanges in the hand.

Case 2

A 30-year-old woman, gravida 5, para 3, live 1, aborta 1, with 2 neonatal deaths, cause not known, was referred at 33 to 34 weeks' gestation. She was married to her maternal uncle and, despite the poor obstetric history, sonography was requested in the late third trimester. The biometric parameters corresponded to the period of gestation. There was massive eclabium, ectropion, irregularity in the skin over the forearm, clenched fists, and abnormal phalanges (Figure 2). The femur measured 67 mm, and the foot length measured 46 mm (Figure 3). Harlequin ichthyosis was diagnosed and was confirmed postnatally (Figure 4). The neonate died on the first postnatal day.

Figure 3. Short foot length. Note the considerable difference in the femur and foot length.



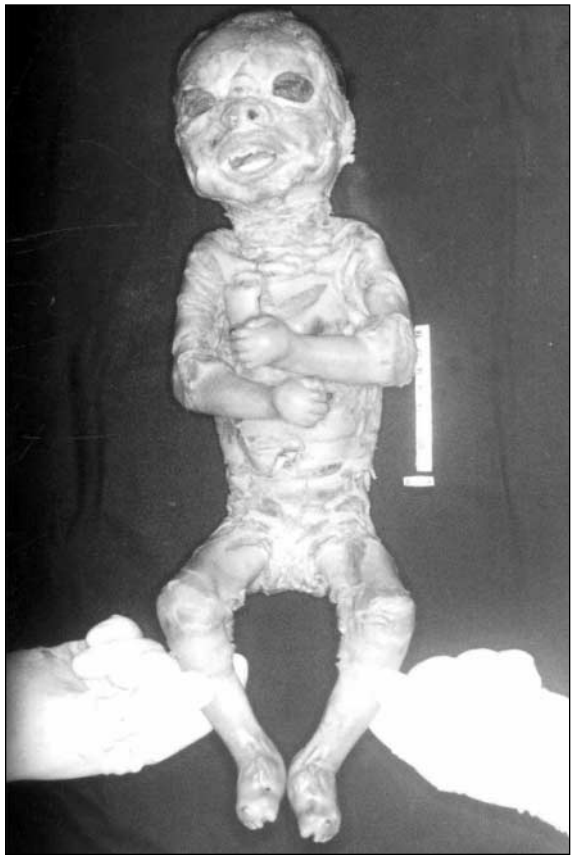


Figure 4. Autopsy photograph of a fetus with harlequin ichthyosis.

Case 3

A 27-year-old woman, gravida 3, para 2, live 1, with a previous fetus with harlequin ichthyosis was referred at 20 weeks to rule out anomalies. Fetal biometric measurements corresponded to the period of gestation. A detailed evaluation of the face revealed mild edema over the forehead and scalp. Orbits, eyelids, the nose, and the mouth appeared normal (Figure 5). The fetal tone was normal at the elbow and knee joints. However, a close look at the hands revealed a clenched fist (Figure 6). Opening and closing of the hands was not observed during a 1-hour scan. Phalanges in the foot and hand were not visualized satisfactorily. The skin line appeared bright and was seen both in the medial and lateral aspects of the foot. The foot length measured 31 mm; the femur length measured 34 mm (Figure 7); and there was mild hydramnios. In view of the above findings, the patient was counseled to have a fetal skin biopsy to confirm ichthyosis. Because the patient could not afford the skin biopsy, she opted for continuation of the pregnancy. At 27 weeks' gestation she spontaneously expelled a stillborn fetus with harlequin ichthyosis. In vitro study of the fetus showed eclabium, ectropion, clenched fists, and decreased foot length.

Figure 5. Coronal view of the face at 20 weeks, showing normal orbits (O) and mouth in a patient with evolving harlequin ichthyosis. N indicates nose.

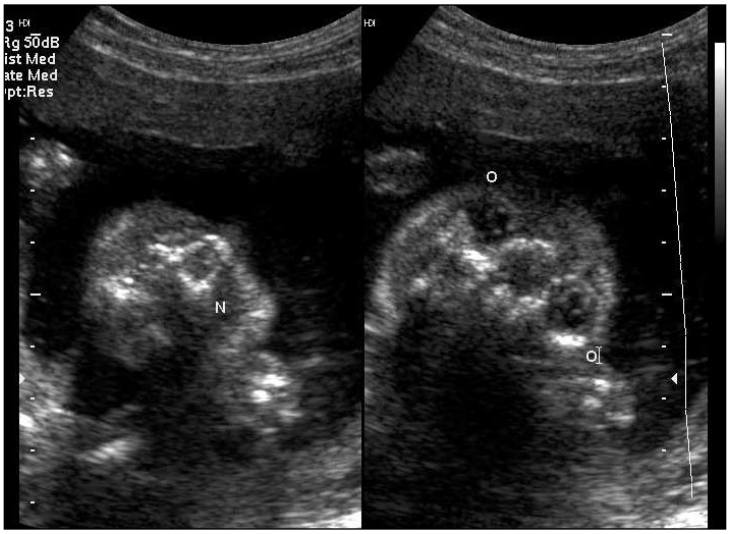
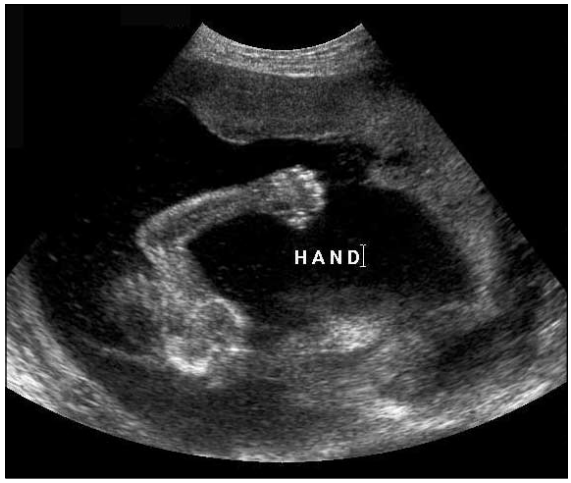


Figure 6. Persistent clenched hands and hydramnios.



Discussion

The femur–foot length ratio is used as a marker for suspecting Down syndrome[5] and skeletal dysplasias.[6] In harlequin ichthyosis, the femur length corresponds to the period of gestation, whereas the foot length is considerably shortened because of severe restrictive dermopathy. Although there is abnormal skin development all over the body, and scaling is present, the long bones are not affected. The phalanges and metacarpal and metatarsal bones are underossified and incurved because of tight wrapping of the skin, leading to decreased foot length.

The development of the skin is completed by 22 weeks' gestation.[1] In harlequin ichthyosis, because of improper development of the skin, the fetus has difficulty in opening and closing of the hands and mouth, which is termed restrictive dermopathy.

Eclabium and ectropion manifest in the third trimester; hence, a diagnosis harlequin ichthyosis on the basis of these findings will be too late. The above conclusion is well documented in the third case, which showed normal orbits and lips, whereas there was considerable incurving of the toes, resulting in a short foot length, which was diagnosed during a targeted scan.

Imaging the feet is much easier than the hand because of the persistent plantar flexion. Short foot length can be observed as early as 22 to 24 weeks' gestation when the development of skin is completed. Hence, measurement of the foot helps when harlequin ichthyosis is suspected, especially with a sibling history because it has an autosomal recessive mode of inheritance.

Recent advances in 3-dimensional sonography have facilitated the phenotypic diagnosis of harlequin ichthyosis. However, the availability of this technology is not widespread, and measurement of fetal foot length is a simpler and more cost-effective option.

In conclusion, on the basis of our observations, fetal foot length may be an early marker that may help in the prediction of harlequin ichthyosis, especially when there is a sibling history of this disorder. More cases are required to determine whether a normal foot length will help exclude this condition, which will obviate the need for fetal skin biopsy.

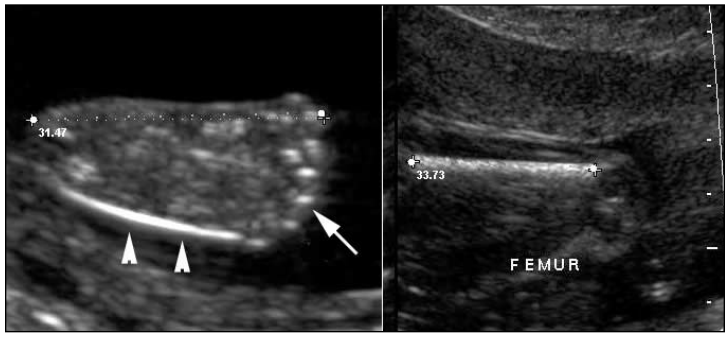


Figure 7. Foot length shorter than femur length. Note the bright skin line in the lateral aspect of the foot (arrowheads) with abnormal phalanges (arrow).

References

1. Machin GA. The skin. In: Wigglesworth JS, Singer DB (eds). Textbook of Fetal and Perinatal Pathology. 2nd ed. Malden, MA: Blackwell Science; 1998: 1111–1142.

2. Vohra N, Rochelson B, Smith-Levitin M. Three-dimensional sonographic findings in congenital (harlequin) ichthyosis. J Ultrasound Med 2003; 22: 737–739.

3. Berg C, Geipel A, Kohl M, et al. Prenatal sonographic features of harlequin ichthyosis. Arch Gynecol Obstet 2003; 268:48–51.

4. Bongain A, Benoit B, Ejnes L, Lambert JC, Gillet JY. Harlequin fetus: three-dimensional sonographic findings and new diagnostic approach. Ultrasound Obstet Gynecol 2002; 20:82–85.

5. Grandjean H, Sarramon MF. Femur/foot length ratio for detection of Down syndrome: results of a multicenter prospective study. Am J Obstet Gynecol 1995; 173:16–19.

6. Campbell J, Henderson A, Campbell S. The fetal femur/foot length ratio: a new parameter to assess dysplastic limb reduction. Obstet Gynecol 1988; 72: 181–184.