# Early Prenatal Detection of Recessive Split-hand/Foot Malformation Caused by a Homozygous Variant of *WNT10B*

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Dear Editor,

Split-hand/foot malformation (SHFM) is a malformation of the limb involving the central rays of the autopod. It can occur as a single entity or as a part of the syndrome. SHFM is mainly inherited as an autosomal dominant trait with incomplete penetrance, involving different genetic variants.[1] The recessive SHFM has also been described.[2] We report a nonsyndromic fetal case of SHFM due to a homozygous *WNT10B* variant, which was diagnosed by ultrasound in the first trimester.

A 31-year-old Chinese woman, gravida 2 para 1, came for a routine first-trimester scan at 13 weeks of gestation. Both partners were healthy, in particular, did not show any hand or foot malformation, and their teeth examinations were normal. Both had a nonsignificant family history. They had a healthy 6-year-old daughter. The first-trimester scan identified a nuchal translucency (NT) of 2.0 mm with a crown-rump length of 70 mm. Notably, split defects were seen in both feet, with more severe in the left foot than in the right foot [Figure 1]. Further detailed examination showed a normal appearance of the head, face, heart, stomach, bladder, and hands. Pregnancy termination was required by the parents. Postnatal examination confirmed the prenatal findings. Trio-exome sequencing detected a causative *WNT10B* (NM_003394.4) variant, homozygous nonsense c.786G>A, p.(Trp262*) in the fetus. Both parents were carriers for this variant which was classified as likely pathogenic according to the American College of Medical Genetics and Genomics guidelines.

Autosomal recessive SHFM (Type 6) is caused by *WNT10B* pathogenic variants.[2] The Trp262* variant in a heterozygous state was first reported in a sporadic Chinese patient with oligodontia as the cause of tooth agenesis.[3] However, no information was available for the dental conditions of that patient's family members. In the present study, oligodontia was not identified in any family members who carried this variant. Therefore, the Trp262* might be an incidental finding in that study.[4]

Interestingly, only the foot was affected in our case. Indeed, one characteristic of SHFM caused by *WNT10B* variants is that the feet were more severely affected than the hands.[5] This characteristic is usually reflected in a *WNT10B*-related SHFM family, in which some siblings have mildly affected hands while all members have relatively severe foot defects. Traditionally, ectrodactyly was detected by sonography in mid-pregnancy. The fingers and feet can be visualized on ultrasound as soon as the long bones begin to ossify at 12 weeks gestation. Therefore, the hands and feet can potentially be visualized late in the first trimester, which is also an ideal time as the fetus has enough room to move for the limbs, and the hands are often open. Accordingly, the diagnosis of a split hand/foot is possibly achieved during the first trimester of pregnancy.[6]

In summary, we first reported the prenatal identification of recessive SHFM at the time of NT measurement. An early diagnosis has allowed the couple to make an informed decision in a timely manner before a viable fetus. Molecular investigation of such defects will be helpful in assessing the recurrent risk for future pregnancies and guide prevention.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her names

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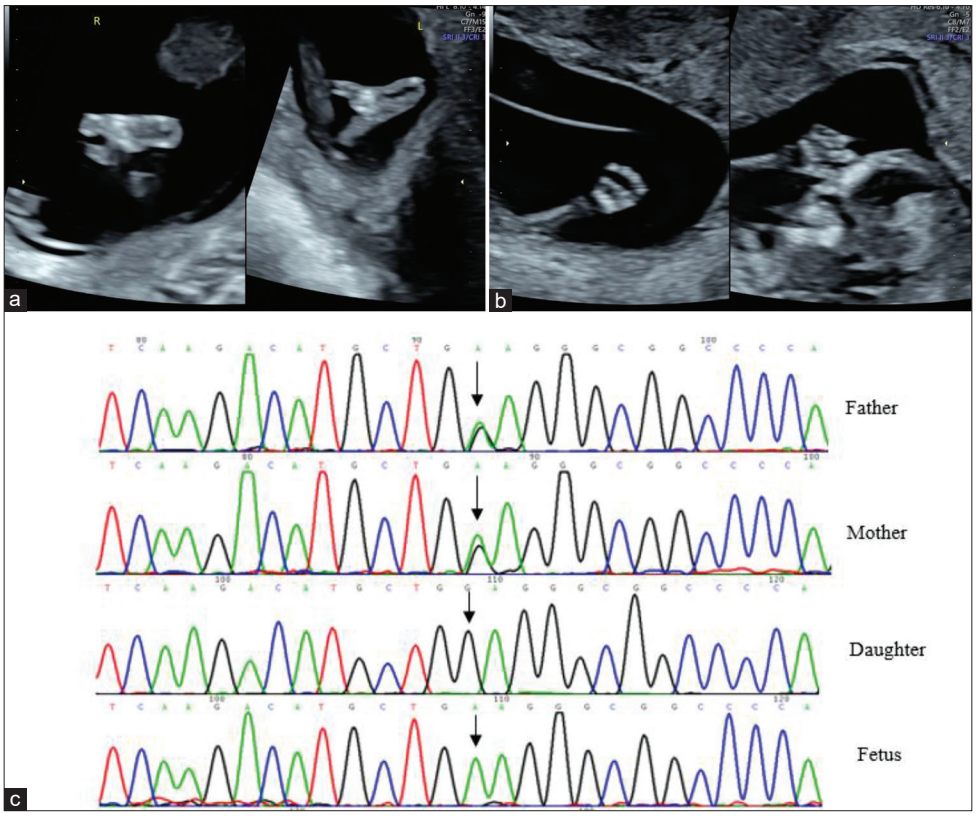


**Figure 1:** Prenatal sonographic findings in the first trimester and sequence variations of *WNT10B* in family members. (a) Split defect in both feet, with more severe in the left foot, (b) normal morphology of both hands, (c) chromatograms of the *WNT10B* variant (c.786G > A), showing the homozygous state in the fetus, heterozygous state in the parents, and free from this variant in the daughter

and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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