

Research Letter

## Prenatal diagnosis of microvillus inclusion disease

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Accepted 13 June 2011

A 23-year-old, gravida 3, para 1, woman underwent amniocentesis at 20 weeks of gestation because of a previous child affected with microvillus inclusion disease (MVID). The child died of intractable diarrhea, sepsis, malnutrition, and multiple organ failure at the age of 6 months. Mutation analysis of the family revealed a c.445C>T nonsense mutation in Exon 4 of the *MYO5B* gene in the affected child and the father and a c.1021C>T nonsense mutation in Exon 9 of the *MYO5B* gene in the child and the mother [1]. During this pregnancy, routine sonographic findings were normal. There was neither intestinal dilation nor polyhydramnios. The pregnancy was uneventful and did not have antepartum hemorrhage. Amniocentesis revealed a karyotype of 46,XX. The level of amniotic fluid  $\alpha$ -fetoprotein (AFAFP) at 20 weeks of gestation was 67,420 ng/mL (7.69 multiples of the median). Molecular analysis of the *MYO5B* gene using both uncultured and cultured amniocytes revealed compound heterozygous nonsense mutations in the *MYO5B* gene. The mutation of c.445C>T or CAG>TAG predicts a p.Q149X, and the mutation of c.1021C>T or CAG>TAG predicts a p.Q341X in the affected fetus (Fig. 1). The maternal serum AFP level at 23 weeks of gestation was not elevated. The parent elected to terminate the pregnancy, and a 634-g affected fetus was delivered at 23 weeks of gestation. The fetus did not have structural abnormalities. The placenta was grossly normal. Postnatal analysis of the fetal tissues confirmed the prenatal diagnosis.

MVID (OMIM 251850) is an autosomal recessive disorder of intestinal epithelial cells and is characterized by intractable life-threatening watery diarrhea during infancy. MVID is caused by mutations in the *MYO5B* gene (OMIM 606540) [2]. *MYO5B* encodes myosin Vb or the unconventional class V dimeric nonfilamentous myosin that regulates membrane trafficking along the recycling pathway in polarized epithelial cells [2,3]. Loss-of-function mutations of the *MYO5B* gene that cause disruption of epithelial cell polarity are a major cause of MVID [2,4,5]. *MYO5B* mutations have been shown to correlate with an aberrant subcellular distribution of the myosin Vb protein and apical recycling endosomes [6]. The present case had compound heterozygous nonsense mutations in the *MYO5B* gene causing early truncation of MYO5B and the loss of its function.

The present case is the first report of prenatal molecular diagnosis of MVID. The present case did not present polyhydramnios and bowel dilation in the second trimester. Ruemele et al [7] suggested that in cases of MVID, the pregnancy is uneventful, and there is no polyhydramnios. However, Kennea et al [8] and Chen et al [1] reported polyhydramnios and bowel dilation associated with MVID in the third trimester. The peculiar aspect of this presentation is elevated AFAFP in the second trimester, which has not been previously described in pregnancy with MVID. Elevated AFAFP can be associated with fetal anomalies such as ventral wall defects, esophageal atresia, fetal teratoma, cloacal extrophy, and epidermolysis bullosa as well as placental abruption and hemorrhage. Because there were no other uteroplacental and fetal factors of elevated AFAFP in this case, we speculate that the AFAFP elevation may possibly be caused by *in utero* body fluid leakage into the amniotic fluid through fetal enteropathy.

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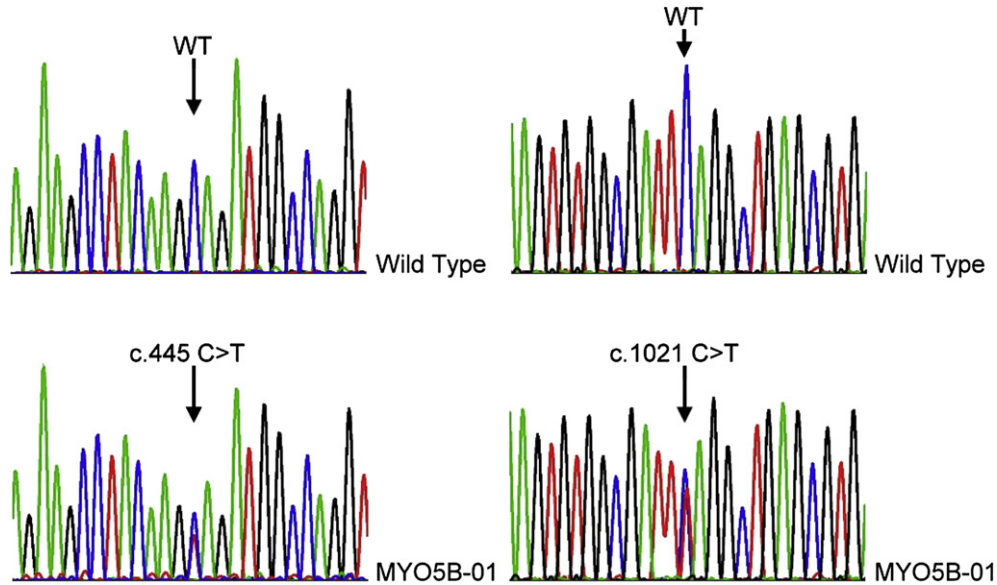


Fig. 1. Compound heterozygous nonsense mutation of c.445C>T, p.Q149X in Exon 4 and c.1021C>T, p.Q341X in Exon 9 of the *MYO5B* gene in the fetus. MYO5B-01 = fetus; WT = wild type as control.

## Acknowledgments

This work was supported by research grants NSC-97-2314-B-195-006-MY3 and NSC-99-2628-B-195-001-MY3 from the National Science Council and MMH-E-100-04 from Mackay Memorial Hospital, Taipei, Taiwan.

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