(22,770,421–28,928,730)×1 consistent with the diagnosis of AS or Prader-Willi syndrome. The deletion was not detected in the parents following analysis of DNA extracted from peripheral blood by CMA. The parents were counseled at the time that a third pregnancy was planned, and prenatal diagnosis was not requested.

One year later, the woman came again at her first trimester of gestation. A normal NT (1.2 mm) was measured at 12 weeks with a negative combined first-trimester screening result. However, the mother worried about the pregnancy because of having given birth to an affected child. She required an invasive procedure for prenatal diagnosis. Unexpectedly, CMA of chorionic villi revealed again the familial deletion. The pregnancy was terminated by the parents' request. Mosaicism was then considered in the mother. The maternal germline mosaicism was confirmed by the haplotype analysis of chromosome 15 in this family (Fig. 1).

Mosaicism in AS most often occurs in imprinting defects that do not involve deletions of the imprinting center. Individuals with AS who are imprinting-type mosaics can have relatively higher developmental ability. Maternal germline mosaicism of a UBE3A mutation has also been found [2]. However, germline mosaicism of a deletion in AS has never been reported. Germline mosaicism is a rare but important phenomenon which most of the time occurs in autosomal dominant and X-linked recessive disorders, including osteogenesis imperfecta, neurofibromatosis type I and Duchenne muscular dystrophy [3]. To our knowledge the present case is the first documentation of germline mosaicism for an interstitial 15q11-q13 deletion. This has important implications for genetic counseling. For apparently an isolated case of AS where the mother has been fully investigated, including molecular analysis of genomic DNA directly extracted from peripheral blood leukocytes, and appears unaffected, she is still at risk of another affected child. Indeed, germline mosaicism for other pathogenic microdeletions has also been described in literature [4,5]. The potential for recurrence in future pregnancies should be explained in families with microdeletion syndromes.

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Hai-Shen Tang
De-Gang Wang
Prenatal Diagnosis Unit, Boai Hospital of Zhongshan, Zhongshan, Guangdong, China

Xing-Mei Xie
Dong-Zhi Li*
Guangzhou Women and Children's Medical Center Affiliated to Guangzhou Medical University, Guangzhou, Guangdong, China

* Corresponding author.
E-mail address: drlidongzhi2014@sina.com (D. Li).

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Fetal phenotypes of congenital disorder of glycosylation: A case presentation

Dear Editors,

Congenital disorders of glycosylation (CDG) are a rapidly growing and genetically and clinically heterogeneous family caused by impaired synthesis of glycoconjugates [1]. Affected individuals have multi-systemic manifestations, mainly profound neurological deficiencies, growth failure, facial dysmorphisms, and a wide range of multiorgan symptoms. Currently, all reported CDG cases are child patients. We here first present a prenatal case of CDG due to a *de novo* variant in the X-linked gene *SLC35A2*.

A 40-year-old G4P0A3 woman was referred at 12 weeks of gestation for Down screening. She had three first-trimester miscarriages. Both partner had a normal karyotype. A NT of 1.6 mm with a CRL of 62 mm was demonstrated. Down screening using maternal cell-free DNA screening test was normal. The ultrasound at 17 weeks showed shortened femur length. The anomaly scan at 21 weeks showed retarded growth of both upper and lower limbs with no other abnormality. Genetic amniocentesis showed a 46, XY male and a normal chromosomal microarray. Scoliosis and polyhydramnios were noted at 25 weeks with a normal glucose tolerance test and a normal fetal echocardiogram (Fig. 1). The pregnancy continued to 34 weeks when an emergency caesarean section was performed after reporting reduced fetal movements.

A male infant was delivered with a birth weight of 1.88 kg and length of 43 cm. At birth, resuscitation was required and the boy was transferred to NICU for further management. Physical examination showed coarse facies, broad nasal bridge, thick lips, short stature, mild scoliosis and muscular hypotonia. Unfortunately, the boy developed multiple organ failure and died at the day 3 after birth. The patient's blood sample was sent for investigation of underlying etiology. Whole-exome sequencing (WES) of the patient/parent trio revealed a hemizygous *de novo* c.1A > G (p.M1?) variant in *SLC35A2* associated with CDG in the patient; this was confirmed by Sanger sequencing of the patient and both parents (Fig. 1).

SLC35A2, located on chromosome Xp11.23, encodes the UDP-galactose translocator (UGT), a transmembrane protein important for the supply of nucleotide sugars for various glycosylation pathways. SLC35A2-CDG constituted approximately 7% of all type II CDG [2]. It is inherited with an X-linked dominant pattern. Therefore, the majority of patients reported thus far are females, and only three male patients with mosaic for *SLC35A2* pathogenic variants have been reported [3,4]. It is likely that the presence of a functional SLC35A2 allele is required for survival. Our case is the fourth male patient. Although both WES and Sanger sequencing results showed a non-mosaic pattern, a low-level mosaic wild-type SLC35A2 allele might be present in other tissues.

The c.1A > G, a translation initiation codon (ATG) variant, has been reported in a female patient [4]. Another *de novo SLC35A2* initiation codon variant, c.3 G > A (p.Met1?), was also detected in a female patient [3]. Furthermore, initiation codon (ATG) variants have been clearly associated with other genetic disorders. Therefore, we interpret c.1 A > G to be the disease-causing variant in our patient.

SLC35A2-CDG has never been reported in prenatal cases. As the main characteristics of this disorder are developmental delay, seizures, and ataxia, it is impossible to demonstrate these neurological signs on prenatal sonography. However, there are

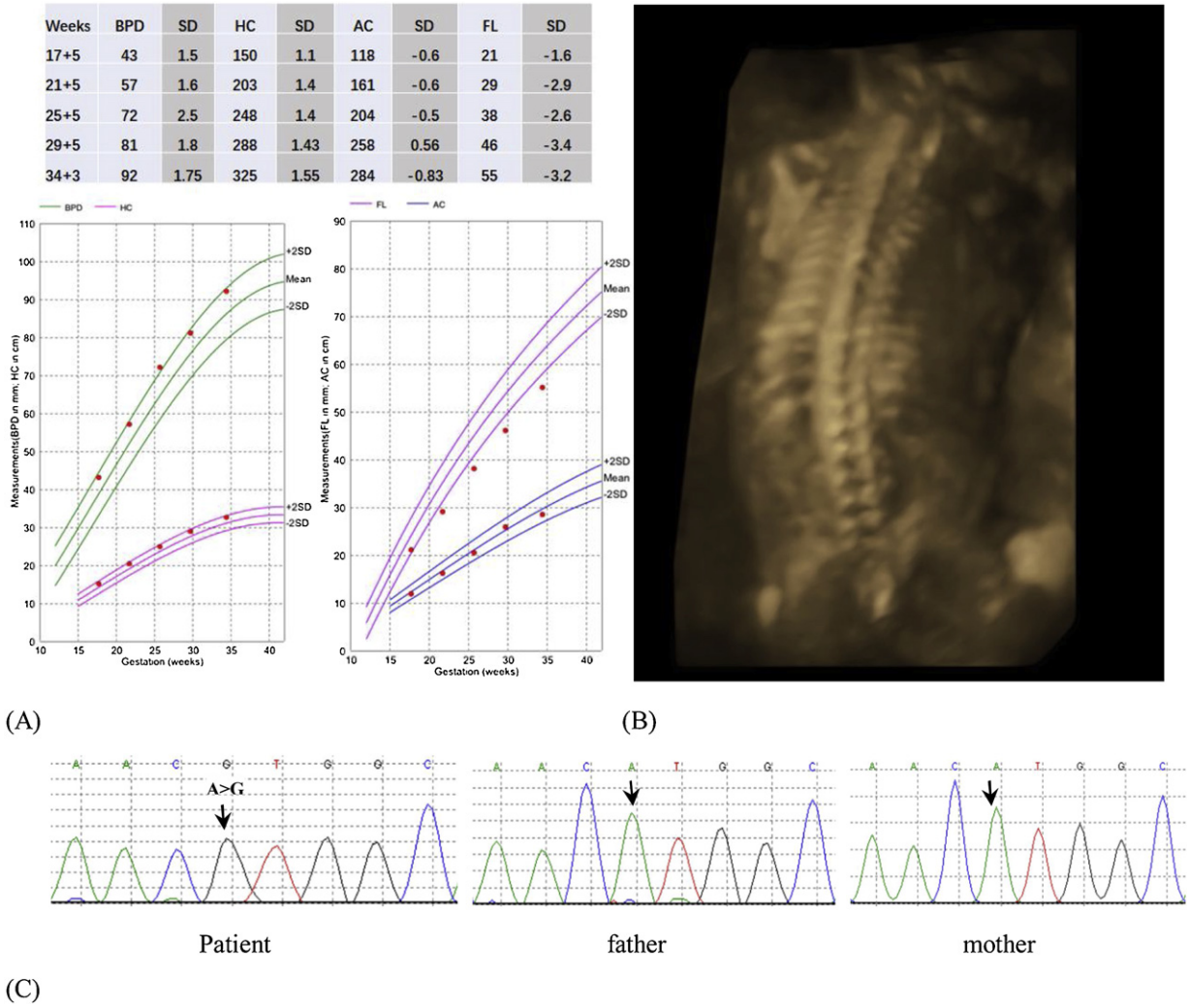

Fig. 1. The prenatal ultrasound and Sanger sequencing data of the patient. (A) Fetal biometric parameters at 17, 21, 25, and 28 weeks' gestation; (B) Fetal scoliosis at 25 weeks' gestation; (C) Sanger sequencing shows *de novo* c.1A > G variant in *SLC35A2*.

some clues in the prenatal diagnosis of SLC35A2-CDG. Our case presented with limb growth retardation, scoliosis and polyhydramnios at mid pregnancy. Indeed, skeletal abnormalities are reported in 9/14 (64%) patients [5]. Features include short stature, limb shortening, scoliosis and bilateral coxa valga. Although these are non-specific pictures, fetal skeletal anomalies should alert clinicians to the possibility of SLC35A2-CDG. WES testing should be considered to accelerating discovery of pathogenic variants related to skeletal dysplasia or other rare genetic disorders such as CDG.

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Yan-Dong Yang
Department of Ultrasound, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

Li-Li Xu
Dong-Zhi Li*
Prenatal Diagnostic Center, Guangzhou Women and Children's Medical Center, Guangzhou, China

* Corresponding author.
E-mail addresses: drlidongzhi2014@sina.com, lidongzhi2013@aliyun.com (D. Li).

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