Case summary
A 40-year-old G4P0A3 woman had three first-trimester miscarriages. A NT of 1.6 mm was demonstrated at 12 weeks. NIPT was normal. The ultrasound at 17 weeks showed shortened femur length. Ultrasound 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. An emergency C-section was performed at 34 weeks after reporting reduced fetal movements. A male infant was delivered and resuscitation was required at birth. 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. 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 was identified; this was confirmed by Sanger sequencing.

SLC35A2, located on chromosome Xp11.23, encodes the UDP-galactose translocator. 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. It is likely that the presence of a functional SLC35A2 allele is required for survival. SLC35A2-CDG has never been reported in prenatal cases.

Conclusion
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.