Prenatal diagnosis of KAT6B-related disorders based on ultrasound scan findings.

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Introduction
Mutations of KAT6B cause KAT6B-related disorders including genitopatellar syndrome (GPS, MIM#606170) and Say-Barber-Bieseker-Young-Simpson syndrome (SBBYSS, MIM#603736, Ohdo syndrome MIM#249620). Here, we report two fetuses with highly consistent ultrasonography and autopsy features carried two novel mutations of KAT6B.

Pictures
Case 1: An ultrasound (US) examination was performed at 24.3 gestational weeks (GW) on a woman aged 26 who had her first pregnancy. Ultrasound imaging showed abnormal development of corpus callosum, pyelic separation and congenital talipes equinovarus (Figure A-C).

Case 2: A 35-year-old woman who had her second pregnancy with an ultrasound at 23.3 GW demonstrated a male fetus with abnormal development of corpus callosum, pyelic separation and congenital talipes equinovarus (Figure E-G). Septum pellucidum was absent. The fetus had small low-set ears and congenital talipes equinovarus (Figure H).

Results
Whole-genome sequencing (WGS) was performed on the two subjects. We detected two new frameshift mutations in the same gene KAT6B: Case 1 carried a heterozygous c.3747delA mutation in exon 18, resulting in Gly1251Glufs*21 (RefSeq NM_012330.2); Case 2 carried a heterozygous c.3660_3661insT in exon 17, resulting in Arg1221* (RefSeq NM_012330.2). Both mutations were confirmed by Sanger Sequencing. Neither of them has been reported previously.

Conclusion
In conclusion, we described, herein, two fetuses with two novel heterozygous KAT6B variants. To the best of our knowledge, this is the first report of antenatal ultrasound findings in KAT6B-related disorders.

Figure. (A-D) Obstetric ultrasonography at 23+6 GW in Case 1 showing a typical 'teardrop' configuration of the lateral ventricles (A), pyelic separation (B) and congenital talipes equinovarus (C, D). (E-H) Obstetric ultrasonography at 22+1 GW and autopsy in Case 2 showing a typical 'teardrop' configuration of the lateral ventricles (E), pyelic separation (F, H), congenital talipes equinovarus (G, H), and agenesis of the corpus callosum (H).