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Correspondence

Fetal phenotype of Galloway-Mowat syndrome 3 caused by a specific *OSGEP* variant

Dear Editors

Galloway-Mowat syndrome (GAMOS) is an autosomal recessively inherited condition characterized by the association of nephrotic syndrome and central nervous system involvement [1]. The consistent hallmarks are early-onset steroid-resistant nephrotic syndrome and microcephaly which is often present at birth. Most patients die in the first years of life. Prenatal diagnosis of GAMOS is rare. We here describe the prenatal sonographic features of a case with GAMOS3, in which the diagnosis was achieved by exome sequencing.

A 31-year-old G2P1 woman was referred at 16 weeks for further assessment because of an abnormal reproductive history. During that pregnancy two years previously, a 12-week ultrasound revealed a normal NT and biometrics consistent with the gestation calculated from her last menstrual period. A 20-week anatomic ultrasound showed mildly reduced head dimension. No major structural anomalies were noted. Subsequent fetal ultrasounds showed gradual aggravation of arrested head growth (Fig. 1). A caesarean section was performed at 36 weeks due to oligohydramnios (amniotic fluid index 28 mm). A female infant was delivered weighing 1850 g (<3rd percentile) with Apgar scores of 8 each at one and five minutes. The girl manifested microcephaly and an "aged face" comprising peculiar facial dysmorphisms: large and floppy ears, micrognathia, hypertelorism, microphthalmia, sunken eyeballs, a receding forehead, and prominent glabella with a broad nasal bridge. The patient also had hypotonia, clenched hands, and arachnodactyly. The girl was transferred to neonatal intensive care unit (NICU) for further evaluation. She developed nephrotic syndrome at day 6, and died of multi-organ failure at 3 months. Genetic testing of the patient reported a normal karyotype and microarray.

In a subsequent pregnancy at 16 weeks, a detailed ultrasound showed normal fetal biometric parameters with no notable structural anomalies except bilateral clenched hands (Fig. 1). Amniocentesis was offered, and after obtaining a normal cytogenetic result, the fetal sample with parental blood samples was sent for further testing using exome sequencing. This identified a homozygous c.740 G > A (p.R247Q) variant in the *OSGEP* gene on chromosome 14q11 in the fetus, and heterozygous state for this variant in both parents (Fig. 1). The DNA sample of the index patient was retrieved, and Sanger sequencing detected the homozygous c.740 G > A variant. Therefore, GAMOS3 was confirmed in this family. The current pregnancy was terminated.

OSGEP is one of the members of KEOPS complex genes responsible for GAMOS. The KEOPS complex is required for a universal tRNA modification, which is necessary for translational accuracy and efficiency [2]. GAMOS3 is used for this syndrome with mutations in *OSGEP*. Interestingly, the c.740 G > A is the only variant reported in Chinese patients. All of the 9 reported patients with GAMOS3 were of Taiwanese ethnic origin and had homozygous state for this variant [3]. Our case is the first one found in a mainland Chinese patient. Considering sharing the same *OSGEP* variant and geographical location of the patients, it might suggest that there is a founder effect among GAMOS3 cases in Chinese population.

Microcephaly, oligohydramnios, and IUGR in late gestation have been reported in patients of GAMOS [4,5]. We first delineated that the growth retardation was only restricted to fetal head and abdomen, and the growth of long bones was not affected. We also first found that an abnormal limb might be present in affected fetuses which could be detected in early second trimester. These fetal phenotypes should alert clinicians to the possibility of GAMOS3. Prenatal diagnosis of GAMOS in early pregnancy, currently, requires molecular confirmation. The c.740 G > A variant might be served as the first-line targeted allele for rapid testing in suspected prenatal cases of GAMOS3. A search of other candidate variants is possible by exome sequencing.

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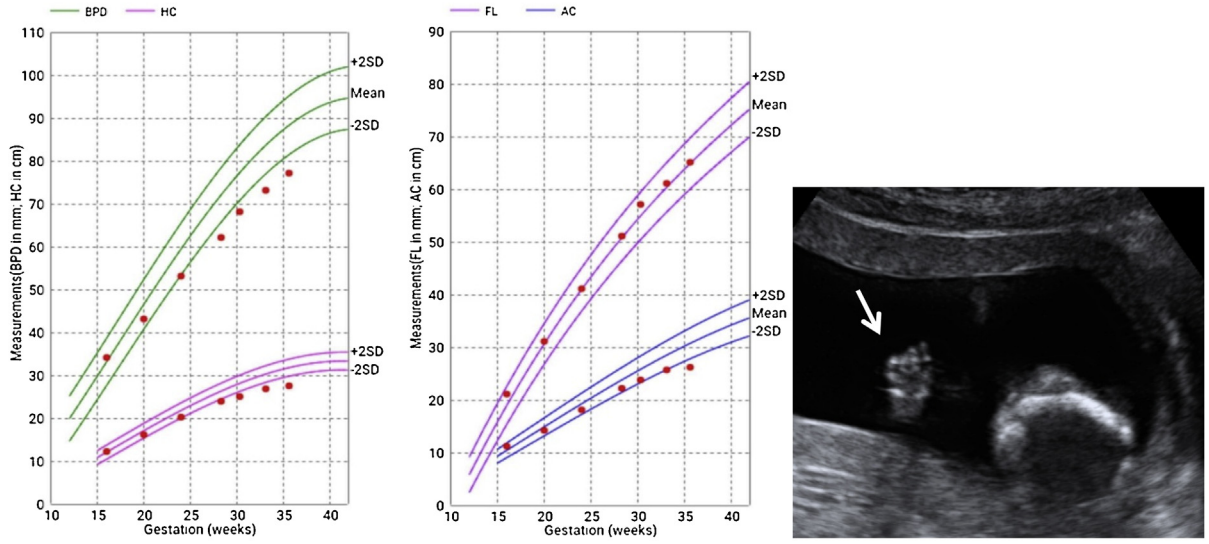
Weeks	HC	SD	BPD	SD	FL	SD	AC	SD
16+0	121	0.18	34	0.36	21	1.19	111	1.12
20+0	160	-1.09	43	-1.18	31	0.25	141	-0.79
24+0	201	-1.75	53	-2.08	41	0.07	180	-1.15
28+2	238	-2.55	62	-3.12	51	0.15	221	-1.36
30+2	249	-3.26	68	-2.81	57	0.97	237	-1.60
33+1	267	-3.55	73	-3.15	61	0.32	256	-2.04
35+4	274	-4.27	77	-3.26	65	0.10	261	-3.09



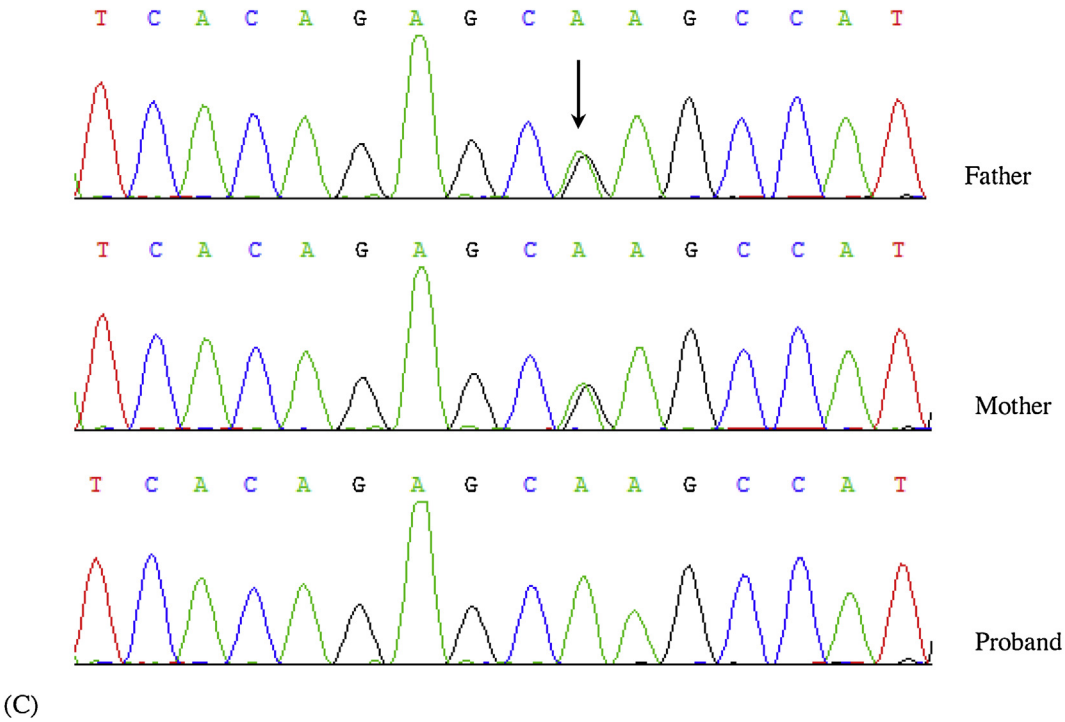


Fig. 1. The prenatal ultrasound and Sanger sequencing data of the patients. (A) Fetal biometric parameters identified by ultrasound during gestation; (B) Clenched hand identified by ultrasound at 16 weeks. (C) Sanger sequencing shows a homozygous *OSGEP* c.740 G > A variant in the fetus and a heterozygous state in the parents.

Declaration of Competing Interest

The authors report no conflicts of interest.

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References

[1] Steiss JO, Gross S, Neubauer BA, Hahn A. Late-onset nephrotic syndrome and severe cerebellar atrophy in Galloway-Mowat syndrome. Neuropediatrics 2005;36(5):332–5.
[2] Braun DA, Rao J, Mollet G, Schapiro D, Daugeron MC, Tan W, et al. Mutations in KEOPS-complex genes cause nephrotic syndrome with primary microcephaly. Nat Genet 2017;49(10):1529–38.
[3] Lin PY, Tseng MH, Zenker M, Rao J, Hildebrandt F, Lin SH, et al. Galloway-Mowat syndrome in Taiwan: OSGEP mutation and unique clinical phenotype. Orphanet J Rare Dis 2018;13(1):226.
[4] Chen CP, Lin SP, Liu YP, Tsai JD, Chen CY, Shih SL, et al. Galloway-Mowat syndrome: prenatal ultrasound and perinatal magnetic resonance imaging findings. Taiwan J Obstet Gynecol 2011;50(2):212–6.
[5] Horton AL, Smith JK, Strauss RA. Recurrence of Galloway Mowat syndrome and associated prenatal imaging findings. Prenat Diagn 2009;29(3):280–2.

Yu Yang[1]
Guangzhou Women and Children's Medical Center affiliated to Guangzhou Medical University, Guangzhou, Guangdong, China

Yi He[1]
Dongguan Maternal Women and Children Healthcare Hospital, Dongguan, Guangdong, China

Li Zhen
Dong-Zhi Li*
Guangzhou Women and Children's Medical Center affiliated to Guangzhou Medical University, Guangzhou, Guangdong, China
[1]*The two authors contributed to this work equally.*

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

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Flexible endoscopic decompression for treatment of sigmoid volvulus in pregnancy

Dear editor,

A 26-year-old healthy gravida 5 para 2 woman at 36 weeks' gestation presented to the emergency department with a 5-days history of abdominal pain followed by constipation, obstipation and urine retention. Despite the use of antispasmodics and laxatives, her pain worsened, and she had become unable to pass stool, flatus or urine. The vital signs were normal. The physical examination revealed a gravid woman with a distended and tender abdomen. Abdominal plain X-ray demonstrated a distended sigmoid loop with an inverted U shape, also known as 'coffee bean sign' with no free intraperitoneal gas. Computed tomography (CT) showed a dilated colon with a transitional zone and swirling of the mesentery, the "whirl sign". The presence of gas was not observed in the distal obstructed region, corresponding to a diagnosis of sigmoid volvulus (Fig. 1).

The mother underwent an urgent flexible sigmoid decompression. The sigmoid was grossly dilated with liquid stool and a twist was evident 20–35 cm from the rectum. The colon was decompressed with immediate relief of symptoms. The rectal tube was left in place for 24 h. She remained well and was discharged two days later, in good general condition and still pregnant.

Intestinal obstruction in pregnancy is rare with incidence reported from 1 in 1500 to 1 in 66,431 deliveries [1,2] Differential diagnosis of gestational intestinal obstruction include volvulus, adhesions, intussusceptions, hernia or appendicitis [2]. Volvulus of the sigmoid colon is the most common cause of intestinal obstruction complicating pregnancy, accounting for up to 44 per cent of cases [3]

Sigmoid volvulus in pregnancy is a serious complication associated with significant maternal and fetal mortality; the diagnosis usually delayed by the pregnancy-related similar symptoms and reluctance to use radiologic investigations. Most cases of volvulus occur during the third trimester because of the displaced sigmoid colon out of the pelvis, leading the colon to twist around its fixation points [4].

In the absence of peritonitis or bowel perforation, endoscopic decompression is safe for mother and fetus, despite the uterine enlargement related technical challenge of the third trimester [5].

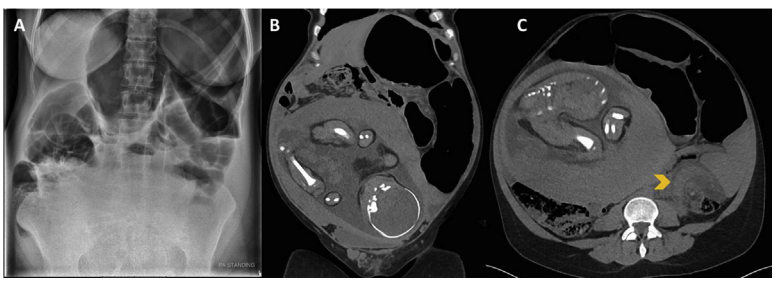

Fig. 1. Abdominal plain X-ray demonstrated a distended sigmoid loop with an inverted U shape, 'coffee bean sign' (**A**). Computed tomography (CT) showed a dilated colon with a transitional zone and swirling of the mesentery,"whirl sign"(**B&C**).