Placental mass in association with neonatal mosaic trisomy 21: genetic makeup consistent with acardiac amorphous twin

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BACKGROUND

Placental Masses

- Placental teratomas thought to arise from germ cells migrating into extraplacental membranes[2]
- Historically, placental teratomas were differentiated from acardiac amorphous twins by presence of multiple tissue types, but lack of axial organization and umbilical cord[1]
- New evidence - previously documented placental teratomas may instead represent acardiac amorphous twin given similar pattern of short tandem repeat (STR) polymorphic loci between placental masses (thought to be teratoma) and adjacent normal placental tissue[1]

Trisomy 21 (T21)

- Most commonly due to spontaneous meiotic non-disjunction[4]
- 1-2% of cases from mitotic errors, causing mosaicism

OBJECTIVES

Describe the genetic profile of a placental mass, initially characterized as a placental teratoma, occurring in association with a newborn with mosaic T21.

CASE

Pregnancy Course:

Mother: 21 yo G1PO, unremarkable medical and surgical history

Prenatal Genetic Testing:

- 2nd Trimester Serum Marker Screen (1/92 risk of T21)
- Noninvasive prenatal screening (68.21% positive predictive value for T21)

Fetal Anatomy Ultrasound: bilateral ventriculomegaly, short humeri, VSD*

Delivery: male infant, 35 wks 1 day gestational age (GA), cesarean section after failed induction of labor

Infant

Weight: 1850 g
APGAR: 6 & 9

Dysmorphology exam: plagiocephaly, fine eyebrows, thin upper lip, smooth philtrum, deep vertical plantar creases, mild 5th finger clinodactyly, overriding 4th toe, grade II/VI murmur, hypospadias with chordee

Postnatal Cytogenetics: 3/22 (14%) cells T21

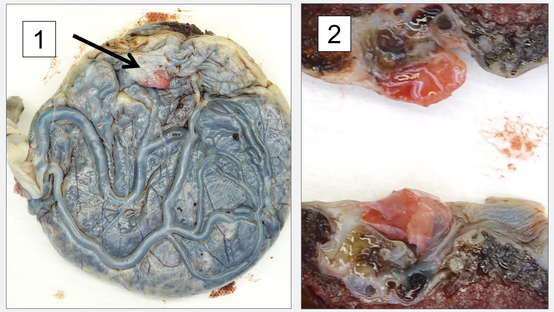
*ventricular septal defect

PLACENTA

Placenta

- 286 g (<10th percentile for GA)
- **Mass:** 0.8 x 0.6 x 0.4 cm, between the amnion and chorion on the fetal surface (Image 1), initial diagnosis benign, non-trophoblastic mature teratoma

Image 1: *Gross Appearance of Placental Mass, intact (1) and transected (2)*



STR (GenePrint 24) Analysis

- Placental mass had extra chromosome 19 allele compared to adjacent placental tissue
- Neither mass nor adjacent tissue had extra chromosome 21 alleles

Table 1: Whole Exome Sequencing of placental mass vs adjacent placental tissue

	Mass vs reference genome	Mass vs Adjacent Placental Tissue
All variants*	45758	159
Exonic variants*	15913	48

*>20x coverage

CONCLUSIONS

- Minimal difference in exome variants between placental mass and adjacent tissue suggests mass likely acardiac amorphous twin (Table 1)
- Explanations for discordant STR findings between placental mass and infant include:
  - Prezygotic meiosis II nondisjunction error caused T21 in the zygote. After twinning, amorphous twin regained normal chromosomal constitution following trisomy rescue.
  - Triplicate chromosome 19 in amorphous twin may represent a parental chromosome 19 duplication not detected on karyotyping or that corrected in infant.
- Our findings support conclusion of McHenry et al[1]

REFERENCES

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