Parental decision making in fetal callosal abnormalities

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INTRODUCTION

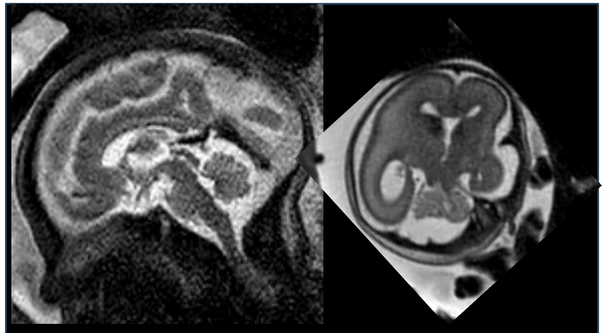
Counseling for fetal callosal abnormalities remains very challenging. Prenatal genetic testing and fetal MRI including an imaging-based scoring system[1] can aid in counseling of parents regarding outcome.

OBJECTIVE

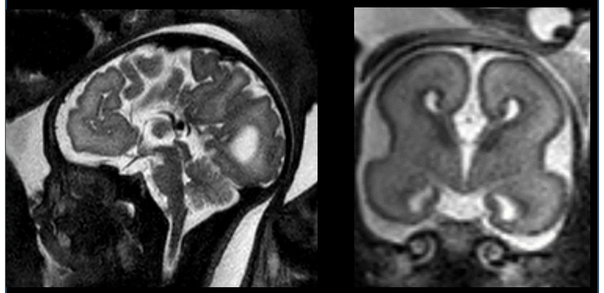
Aim of this study was to investigate the value of prenatal genetic testing and fetal MRI on parental decision making in fetuses with callosal abnormalities.

METHODS

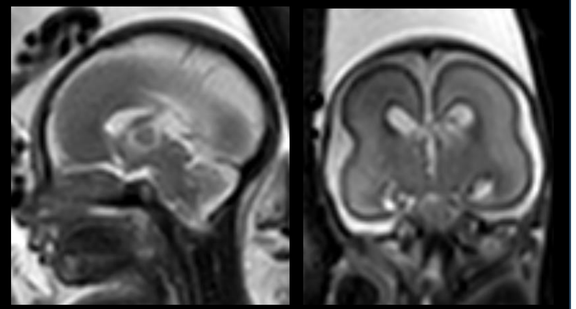
A single center, retrospective case series study. When fetal callosal abnormalities were detected on prenatal ultrasound, parents were referred to the university medical center. After advanced ultrasound, genetic testing (chromosomal microarray, exome sequencing) and/or fetal MRI were offered.



normal CC



complete CC agenesis in fetus with PDHA1 mutation with Diogo score 6: Parents opted for termination of pregnancy



partial CC agenesis in fetus with no variant found and Diogo score 1: Parents decided to continue pregnancy

RESULTS

Forty-nine fetuses were included.

Complete agenesis of the corpus callosum was present in 60% of cases, of which 27% isolated and 33% complex

Partial agenesis of the corpus callosum was detected in 28% of cases, of which 6% isolated and 22% complex

A **too thick corpus callosum, a dilated cavum septum pellucidum vergae and agenesis of the cavum septum pellucidum** was present in each 4% of cases.

Genetic testing was performed in 86% of cases: a genetic diagnosis was established in 60% (24% with chromosomal microarray, 76% with exome sequencing).

Fetal MRI was performed in 30% of cases: 60% had a high (abnormal) imaging score.

A genetic diagnosis and/or high imaging score was very helpful in **parental decision making:**

-67% decided to continue pregnancy in case of normal genetic results and absence of high imaging score;

-96% of parents opted for termination of pregnancy or intra-uterine fetal demise occurred, when abnormal genetic results and/or high imaging score were present.

Results from prenatal genetic analysis

Chromosomal microanalysis

- 1 term del/term duplication
  - agenesis of cavum septum pellucidum
- 1 trisomy 7p/deletion 3p
  - complex partial agenesis
- 1 unbalanced trisomy 18
- 1 triploidia
- 2 terminal del/duplication
  - complex complete agenesis

Incidental finding

- PIK3R1 gene (SHORT)
  - isolated complete agenesis

Prenatal exome sequencing

- 2 DMRTA2 gene → thick corpus callosum
- 1 AMPD2 gene
- 1 GLI3 gene
- 1 NONO gene (IDD X-linked)
- 1 PHF8 gene
- 1 KMT2D gene (Kabuki)
- 1 PTPN11 gene (Noonan)

→ complex partial agenesis

- 1 ACTG1 gene (Baraitser Winter)
- 1 DCC gene

→ isolated complete agenesis

- 1 EHMT1 gene (Kleefstra)
- 2 ZEB2 gene (Mowat Wilson)
- 1 PDHA1 gene
- 1 EPG5 gene (Vici)
- 1 SNAPIN gene
- 1 MYBPC3 gene
- 1 SLC12A6 gene
- 1 OFD1 gene

→ complex complete agenesis

CONCLUSIONS

We show that genetic testing and/or fetal imaging score had a high impact on parental decision making. This warrants implementation in the routine care in fetal callosal abnormalities.

REFERENCES

1. Diogo et al. Improved neurodevelopmental prognostication in isolated corpus callosal agenesis: fetal magnetic resonance imaging-based scoring system. Ultrasound Obstet Gynecol. 2021 Jul;58(1):34-41.

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