

Baby Badger Network ECHO

Case Recommendation Summary

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Case Summary

Prenatal ultrasound of a male fetus identified cystic hygroma, bilateral talipes equinovarus, single umbilical artery, abnormality of the left ventricular outflow tract and aortic valve stenosis.

A Neonatal Crisis Panel was ordered for the Proband sample only. Fifty-two variants passed initial filters of which five were discussed in detail by lab.

- **Heterozygous pathogenic CFTR** (a/w AR Cystic Fibrosis) and **heterozygous pathogenic NPC1** (a/w AR Niemann-Pick) were excluded given poor alignment w/ reported phenotype.
- **Heterozygous VUS in CHD1** (a/w AD Blepharocheilodontic syndrome 1) was excluded given the allele frequency was too high
- **Heterozygous VUS in FGD1** (a/w XLR Aarskog-Scott syndrome) was excluded given the characteristic features are not a strong overlap w/ reported clinical features of proband
- **Heterozygous VUS in RAF1** was subsequently **reclassified to pathogenic after testing parental samples** revealed the variant likely arose de novo in the fetus.

Q: Consideration of alternate genetic testing: In this case, common aneuploidies are on the DDX (if this were a female fetus, Turner syn would be on the DDX).

TAT: karyotype: 7-14d (RUSH: 2-3d), FISH:(RUSH): 2-3d and rapid WES TAT of 7-10d

Recommendation: If a common aneuploidy is suspected (T21, 18, 13, XO), FISH is recommended. However, when ES/GS TATs decrease at some future point, this recommendation may change.

Q: Could karyotype and ES/GS be ordered simultaneously?

Response: rGS can detect structural variants (chromosome rearrangements), homologous regions (which are difficult to sequence), nucleotide repeats, intergenic and regulatory regions, single nucleotide variants (SNV) and Copy Number Variants (CNV) including (X0). Therefore all the information can be obtained in one test. However, currently rGS TAT is typically slower than karyotype.

GS diagnostic yield is approximately 5% higher than ES. However, currently ES is better at detecting mosaicism.