

Unusual cases of Non immune hydrops fetalis (NIHF) With Variants of Uncertain Significance (VOUS)

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INTRODUCTION

- Non-immune hydrops fetalis (NIHF) is a life-threatening fetal condition characterized by an abnormal accumulation of fluid in at least two different fetal compartments
- Underlying causes include- structural abnormalities, intrauterine infections, lymphatic dysplasia and genetic causes.
- Several known monogenic conditions are responsible for recurrent NIH too and advancement in next generation sequencing technology has expanded the spectrum of genetic causes of NIHF

Aims & Objectives

- This study is a case series of NIHF cases where whole exome sequencing revealed rare monogenic variants which matched the fetal phenotype and history

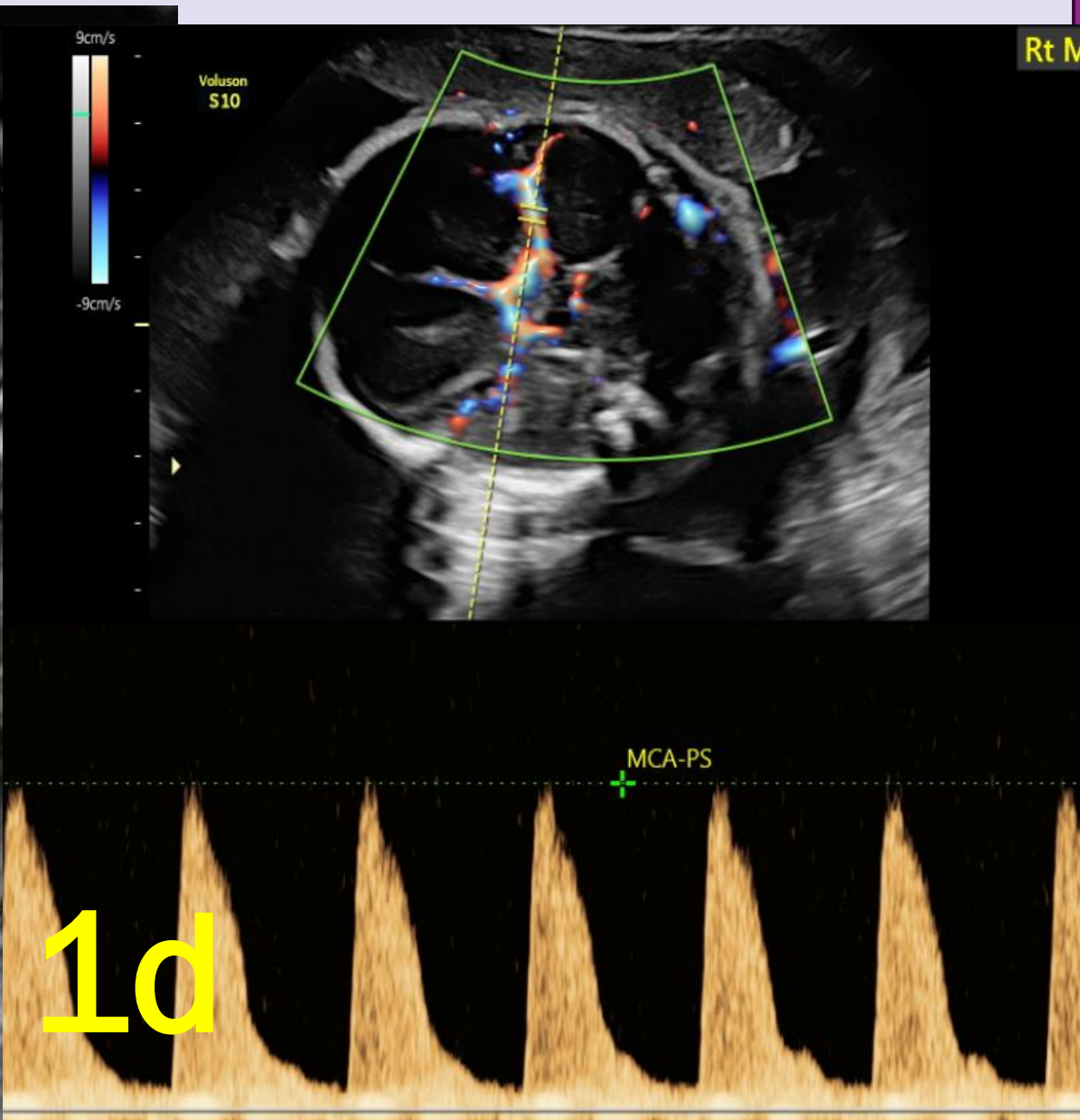
Case 1 - G3P1LOA1, previous 2 IUFD with features of hydrops fetalis. In current pregnancy amniocentesis was done for mild pericardial effusion and increased MCA PSV at 21wk GA. WES revealed **homozygous missense variant c.6151C>G p.(His2051Asp) in the SPTB gene VOUS**. At 25 weeks Fetal MCA PSV MoM was at 1.7 and cordocentesis revealed an Hb of 4 gm/dl. IUT was refused and fetal demise was noted at 28 weeks. Couple was heterozygous for the same on sanger's sequencing.



Image 1a – Mild pericardial effusion at 21 weeks

Image 1b & 1c – Pericardial effusion and Ascites at 27 weeks

Image 1d – Increased MCA PSV MoM at 27 weeks



RESULTS

Case 2 – G1 at 31wks GA, fetus showed NIHF, DVSS shunt, dilated IVC and umbilical artery aneurysm. The MCA PSV was at 1.55 MoM. Fetal Cordocentesis showed a Hb of 4gm/dl, negative DCT. WES identified the same **homozygous missense variant c.6151C>G p.(His2051Asp) in the SPTB gene VOUS**.

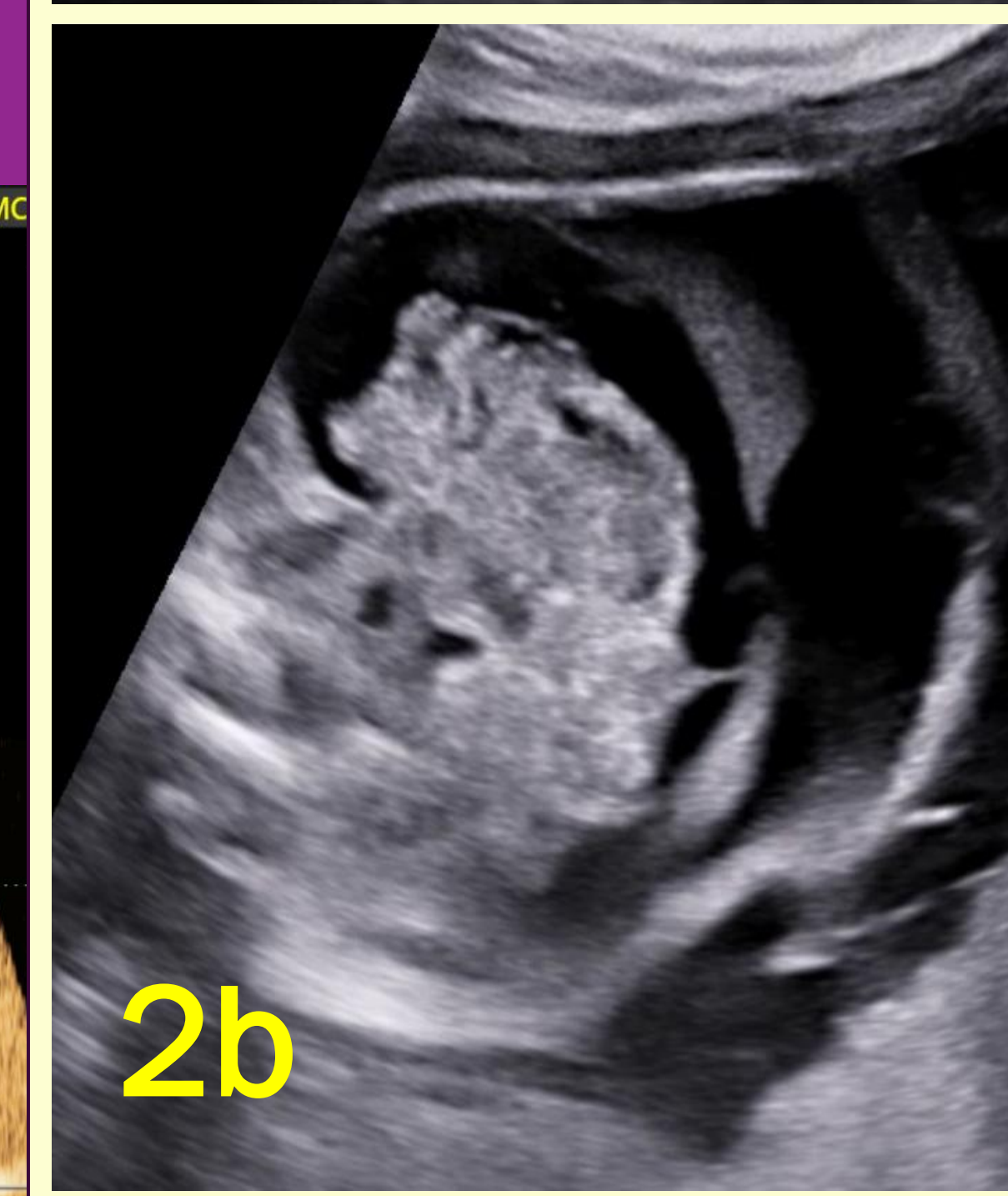


2a

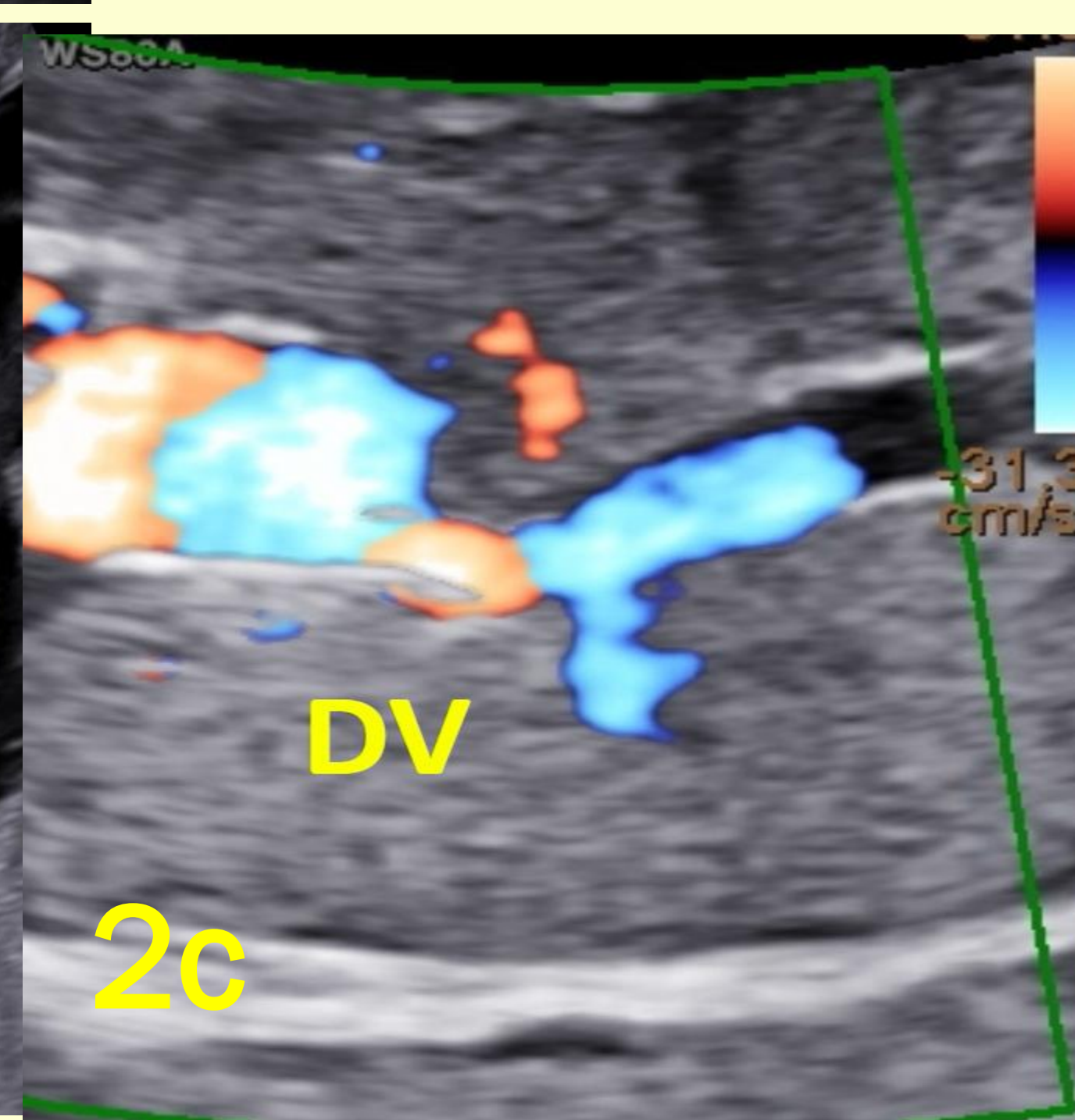
Image 2a & b – Pericardial effusion and Ascites s/o Hydrops Fetalis

Image 2c – DVSS shunt with dilated IVC

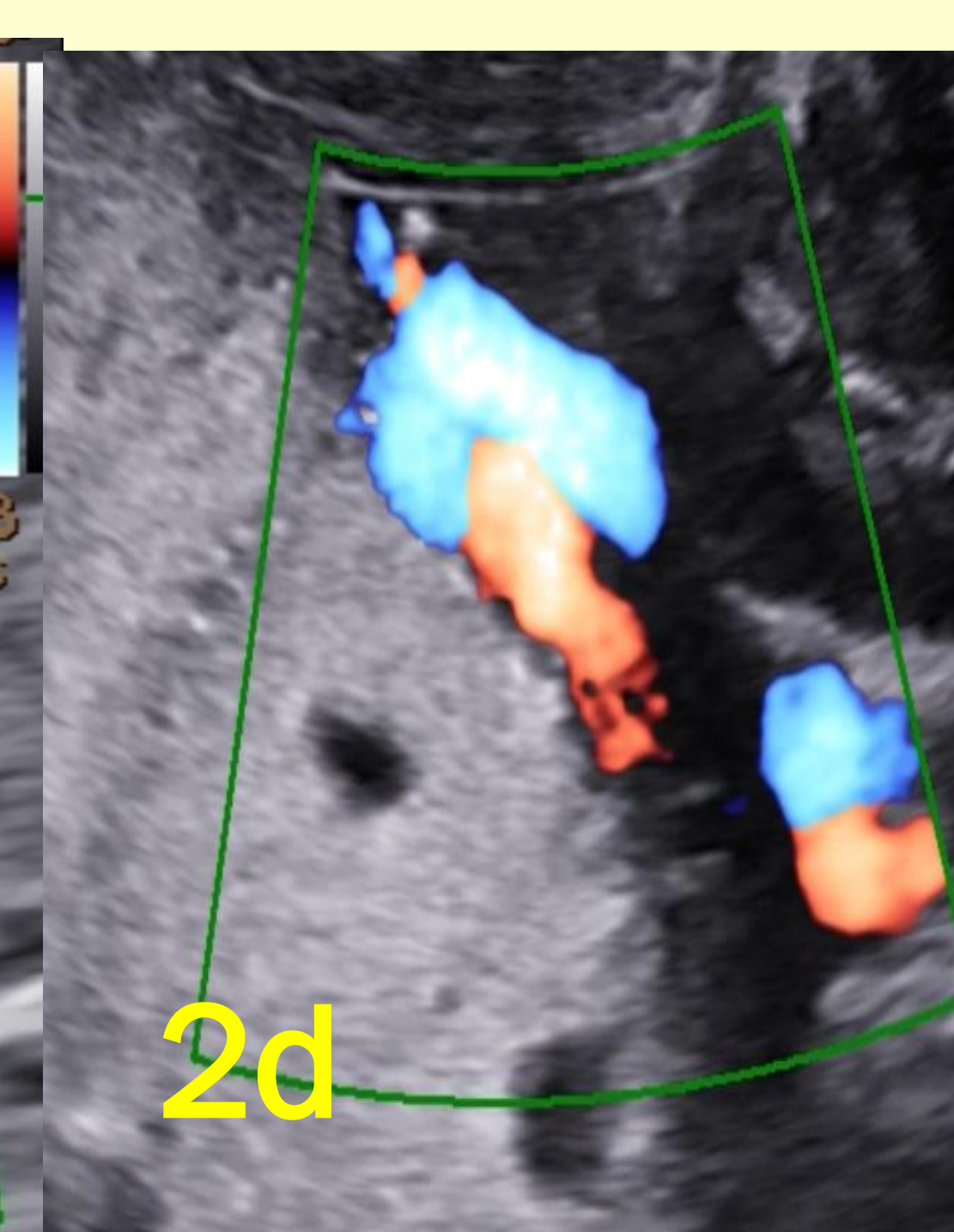
Image 2d – Umbilical artery Aneurysm with SUA



2b

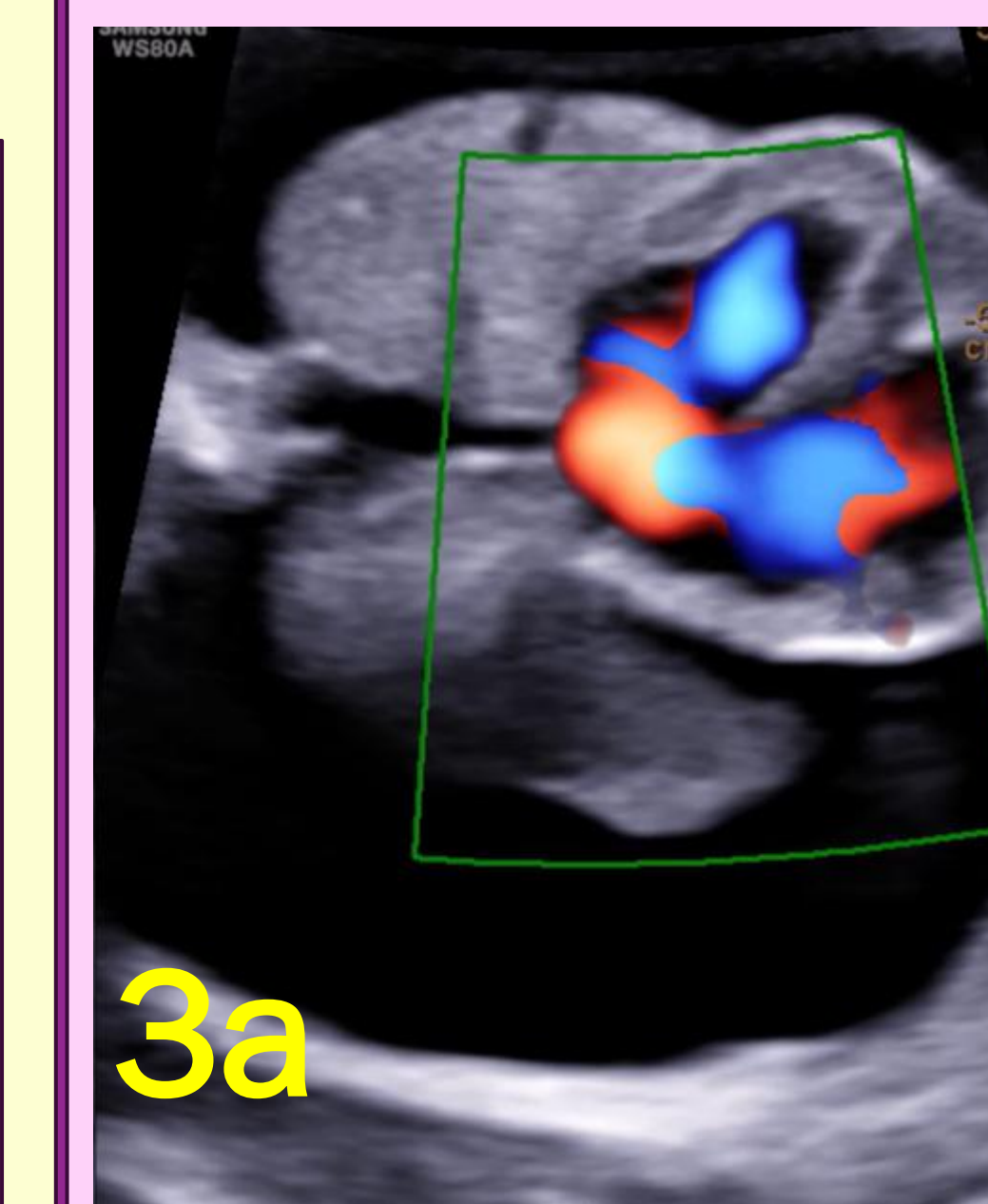


2c

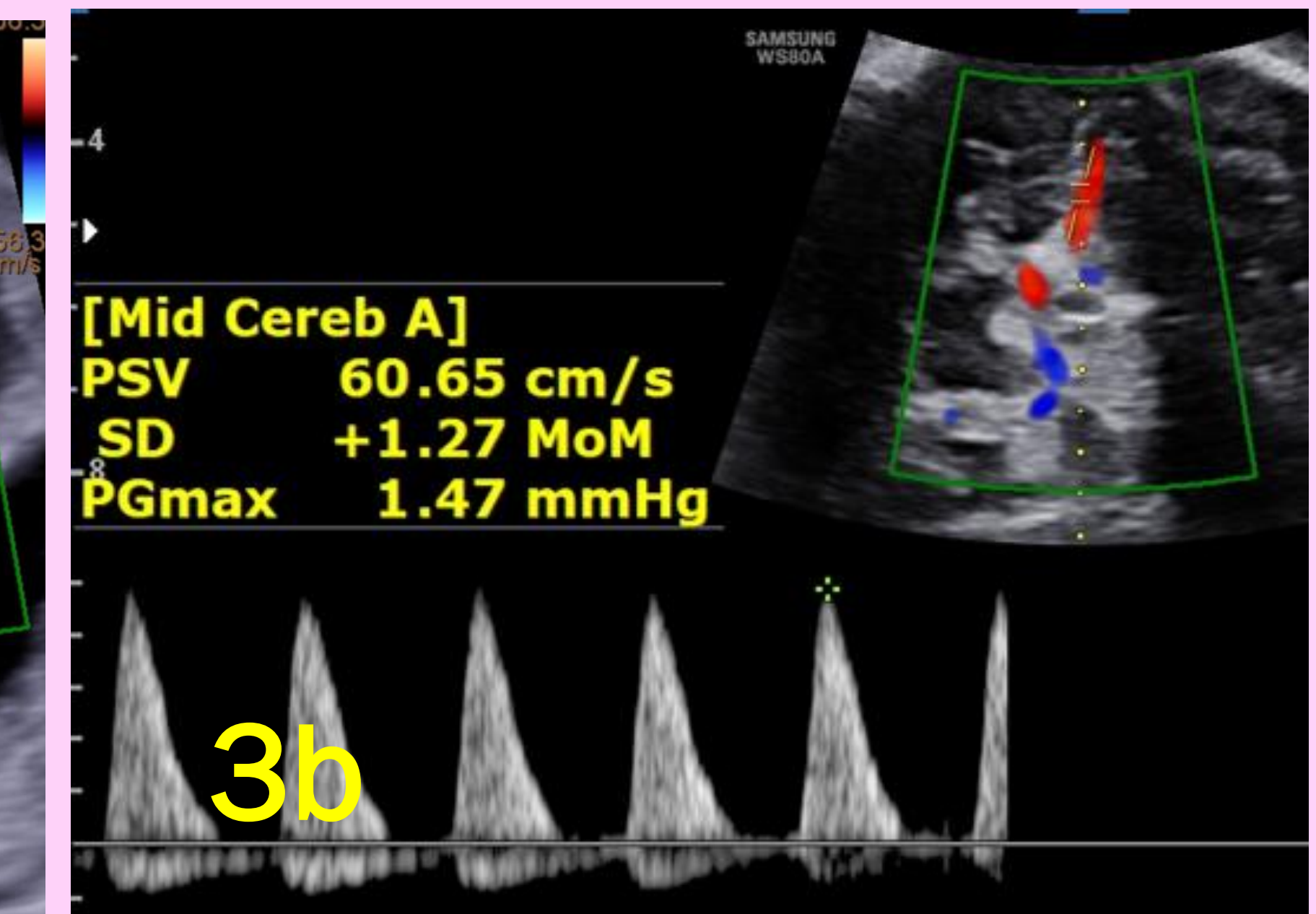


2d

Case 3 – G1 at 34wks GA came in early labour with ultrasound features of hydrops. Postnatal Cord Blood was collected. WES showed a **heterozygous autosomal dominant VOUS in Exon 12 of gene EPHB4 responsible for Lymphatic malformation-7 and reported to cause NIHF**



3a



3b

Image 3a&b Fetal hydrops and Increased MCA PSV MoM

CONCLUSION

Genetic investigations are crucial for prognostication and determining the risk of recurrence in NIHF cases

Proper genetic counselling and segregation analysis of variants specially VOUS are essential for managing such cases