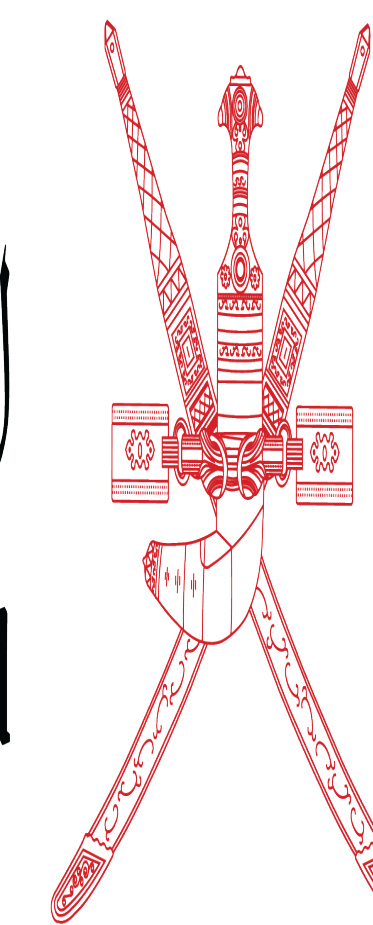


A NON-IMMUNE HYDROPS FETALIS WITH AN UNDERLYING AARS2 GENE MUTATION WITH COMBINED OXIDATIVE PHOSPHORYLATION DEFICIENCY 8: CASE REPORT AND LITERATURES REVIEW

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INTRODUCTION

Hydrops fetalis is defined as abnormal accumulation of fluid in more than two compartments such as ascites , pleural effusion , pericardial effusion and skin edema.

In this report , we present a 39 years old pregnant lady at 28 weeks of gestation, with 5 alive healthy children and 1 pregnancy with intrauterine fetal death due to non-immune hydrops fetalis , Referred to fetal medicine unit in a tertiary hospital for scan which revealed abnormal findings suggestive of hydrops fetalis . Moreover, further investigations including whole exome sequences done reported a homozygous variant of uncertain significance identified in the AARS2 gene and autosomal recessive combined oxidative phosphorylation deficiency 8. However the pregnancy ended up with intrauterine fetal death at 34 weeks of gestation. In conclusion , early initiation of treatment in the form early referral to a high-risk center, multidisciplinary counselling and close coordination between obstetric and neonatal specialists or early invasive fetal treatment could contribute to a better outcome.

CASE PRESENTATION

A 39 years old lady, G7P6 , having 5 alive healthy children, last one IUFD affected with NIHF (non immune hydrops fetalis) products of a consanguineous marriage with a positive family history of recurrent IUFD from paternal side . presented to fetal medicine unit at 28 week of gestations , anomaly scan done which revealed abnormal accumulation of serous fluid in skin /edema and of body cavities including pericardial effusions, pleural ascites (figure 1) , increased NF 10.9 mm, Stomach not visible ,Abnormal extremities, clenched hands (Figure 2) . Case of hydrops fetalis . the above findings were explained to the patient and the prognosis is poor including the risk of IUFD. Patient informed that it could be chromosomal or genetic defects. Anti D was given as patient is blood group O -ve and dexamethasone given at 28 weeks .

WORKUP RESULTS



Figure 1:

TORCH screening was sent to rule out infectious cause which reported negative . After 4 weeks , Patient came for re-evaluation and scan repeated at 32 weeks of gestation which revealed same findings with normal umbilical artery doppler pulsatility index and estimated fetal weight of 2805g and deepest pocket pool of 3.7 cm . Rapid aneuploidy test using the QF-PCR technique shows normal bi-allelic profiles for chromosomes 13,15,16,18,21 and 22 with no evidence of trisomy in male profile was detected by QF-PCR test . Array CGH was inconclusive . WES (whole exome sequences) reported a homozygous variant of uncertain significance identified in the AARS2 gene . Autosomal recessive combined oxidative phosphorylation deficiency 8 .

couple came for appointment for counselling which was done by genetics counsellor and primary physician enclosing the current status , fetal outcome and future pregnancies and all their concerns were addressed and agreed with the plan for next pregnancy that chorionic villous sampling to be done at 11 weeks of gestation or as alternative amniocentesis at 15 weeks of gestation.

DISCUSSION AND CONCLUSION

This case highlights a rare but increasingly recognized presentation of **AARS2-related Combined Oxidative Phosphorylation Deficiency 8 (COXPD8)** manifesting as **non-immune hydrops fetalis (NIHF)**. The identification of biallelic pathogenic variants in *AARS2* underscores the importance of considering mitochondrial disorders in the differential diagnosis of unexplained fetal hydrops, particularly when associated with cardiomyopathy or a family history of early neonatal loss. As molecular diagnostic techniques become more accessible, early recognition of mitochondrial translation defects such as AARS2 mutations can improve diagnostic accuracy, guide reproductive counseling, and potentially inform prenatal decision-making. Further case accumulation is essential to better delineate the prenatal phenotype and establish genotype–phenotype correlations in this ultra-rare but clinically significant disorder.



Figure 2: