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Hydrops Fetalis Secondary to Noonan Syndrome: A Case Report and Literature Review

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Background

Hydrops fetalis is a rare condition with a range of pathophysiological causes. Our aim is to present a case of hydrops fetalis caused by a de novo variant associated with Noonan syndrome, and review the literature regarding diagnosis and investigation.

Case Description

A 26-year-old primipara was referred to the Feto-Maternal Unit at 13-weeks gestation following findings on a combined first trimester screen of an 11.9mm cystic hygroma. She underwent investigation for early onset hydrops including a CVS. The PCR and microarray were normal, along with other investigations for hydrops. However, genetic hydrops panel/WES trio testing through Clinical Genetics demonstrated a de novo variation in the BRAF gene (c. 1447A>G), associated with multiple genetic syndromes including Noonan Syndrome. Serial ultrasounds showed progressing cystic hygroma, jugular lymphatic sacs, micrognathia and a developing right pleural effusion.

The couple elected to continue the pregnancy after extensive counselling regarding the poor prognosis. She presented at 22+4 weeks gestation in extreme preterm labour and proceeded to deliver a live male infant who passed away three hours later. Appearance was consistent with ultrasound findings with a large cystic hygroma anteriorly and a hydropic and oedematous placenta. No further genetic testing was performed given the confirmed diagnosis antenatally.

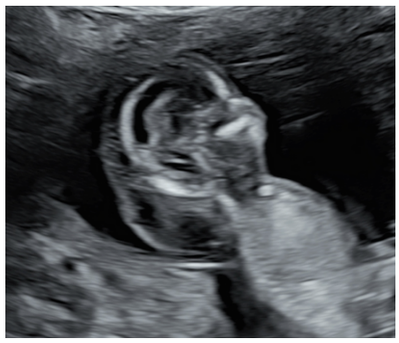
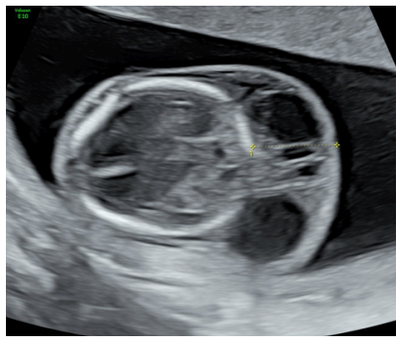
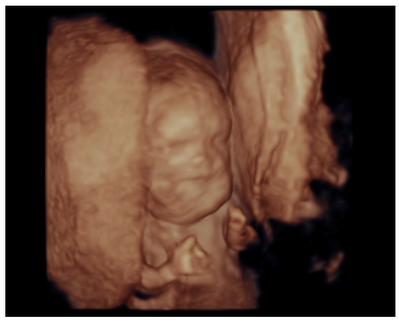
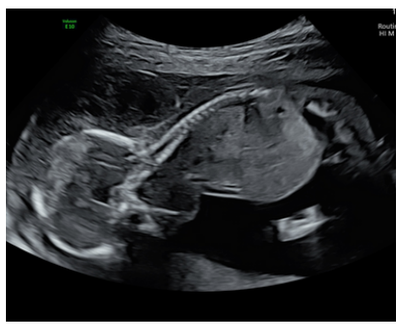

Figure 1: Large cystic hygroma at 14+0 weeks
Figure 2: Large jugular lymphatic sacs at 17+0 weeks
Figure 3: Significant skin oedema at 19+0 weeks
Figure 4: 3D image with significant fetal hydrops at 19+0 weeks
(Clockwise from top left)

Discussion

Hydrops fetalis is the accumulation of excess pathological extracellular fluid in a fetus. It is defined by the presence of two or more fluid collections seen on ultrasound imaging. This includes ascites, pleural or pericardial effusions, and skin oedema. [1]

Hydrops fetalis is categorised into immune and non-immune causes. Due to the decreasing cases of allo-immunisation which causes immune hydrops fetalis, non-immune hydrops fetalis now accounts for up to 90% of cases. [2]

Evaluation of the cause of fetal hydrops includes maternal and fetal testing [3]. Detailed maternal history, laboratory testing and serology should be taken to identify any inherited diseases, infections, drug exposures, or possible allo-immunisation. Fetal investigation begins with thorough ultrasonography, including a fetal echocardiogram. Amniocentesis should be offered for karyotyping and chromosomal microarray. Further testing including whole exome sequencing and testing of amniotic fluid for metabolic storage disorders and enzymopathies should be offered if all else remains negative.

Antenatal management of hydrops fetalis is varied depending on the cause identified. In all circumstances, careful monitoring is required for maternal complications such as mirror syndrome and preeclampsia [4].

Noonan syndrome is an autosomal-dominant, multi-system disorder with an estimated incidence of 1 in 1000–2500 live births [5]. Most cases are due to a de novo pathogenic variant, however an affected parent has been identified in up to 40% of patients. Diagnosis can be difficult as the phenotype varies from severely affected neonates with life-threatening conditions to largely asymptomatic adults [5]. Prenatal features in fetuses with Noonan syndrome can include increased nuchal translucency, cystic hygroma, distended jugular lymphatic sacs, hydrops fetalis, pleural or pericardial effusion and cardiac and renal anomalies. [6]

Conclusion

Hydrops fetalis is a condition of excess fluid accumulation in the fetus, associated with high risk of neonatal morbidity and mortality. Causes include immune and non-immune mechanisms and are often diagnosed antenatally. Evaluation of causes includes ultrasonography and maternal laboratory testing. Genetic testing including an extended hydrops panel/WES trio testing should be offered where the PCR and microarray are normal.

References

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