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Title page

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Keywords

Human Parvovirus B19; Transient Abnormal Myelopoiesis; Trisomy 21; Hydrops Fetalis

Introduction

Non-immune hydrops fetalis (NIFH) is associated with significant perinatal mortality (Norton et al. 2015). Management is dependent upon underlying aetiology with improved prognosis in treatable causes (Norton et al. 2015). Prenatal investigation is offered to identify chromosomal anomalies and fetal infection (Norton et al 2015). A case of NIFH with features of fetal anaemia caused by human parvovirus B19 (HPV19) infection in a fetus with Trisomy 21 is described with management of the pregnancy.

Case Report

A 25 year-old, multiparous woman was referred at 13 weeks and 6 days of gestation with an enlarged nuchal translucency (4.8 millimetres). First trimester anatomy scan demonstrated no anomaly and prenatal chromosomal testing was declined. A fetal echocardiography at 20 weeks was normal. At 24 weeks NIFH was diagnosed with echogenic bowel, ventriculomegaly (ventricular height of atrium measuring 10 millimetres) and cardiomegaly. The middle cerebral artery (MCA) peak systolic velocimetry (PSV) was elevated at 49-50 centimetres/second (cm/s) (more than 1.5 multiples of median (MoM)) and there was a high clinical suspicion of fetal anaemia. Intrauterine transfusion (IUT) was performed by intrahepatic vein puncture with fetal blood sampling demonstrating a haemoglobin of 5.5 gram/decilitre (g/dL). Uneventful IUT with pack cells to a haemoglobin 10g/dL was performed.

Quantitative fluorescence polymerase chain reaction (QF-PCR)/chromosomal microarray testing, and screening for cytomegalovirus, HPV19 and toxoplasmosis were performed. Maternal serology noted HPV19 positive for immunoglobulin M (IgM) antibodies. Fetal karyotype demonstrated Trisomy 21 on QF-PCR (confirmed on full karyotyping). The fetal blood film showed no evidence of transient abnormal myelopoiesis (TAM). A multidisciplinary team discussion concluded that fetal anaemia in this case was secondary to HPV19 infection rather than TAM and resolution of the anaemia was based on high reticulocyte count (more than 15%). MCA PSV was normal during subsequent weekly follow up. Fetal deoxyribonucleic acid (DNA) was stored for *GATA1* mutational analysis.

Discussion

Fetal anaemia from HPV19 infection is a common causes of NIFH (Bascietto et al. 2018). Spontaneous resolution is low (Bascietto et al. 2018) and IUT is a well-established treatment (Lindenburg et al. 2013) evidenced by raised MCA PSV (Moise. 2008). Clinical resolution of anaemia after the first IUT in this case excluded the need for further prenatal transfusions.

Trisomy 21 is associated with TAM in up to 30% of cases. TAM is diagnosed by increased blast cells in neonates with Trisomy 21 and *GATA1* mutation, although there is no internationally defined blast threshold to diagnose TAM. This transient leukaemia may be associated with childhood myeloid leukaemia of Down syndrome (ML-DS) (Zipursky et al. 2003). For TAM to transform into ML-DS, a three-step model is required in fetal Trisomy 21, with a *GATA1* mutation and at least one additional oncogenic mutation occurring before the age of 5 years has been proposed (Bhatnagar et al. 2016).

Prenatal TAM presents most commonly in third trimester, with at least 2 ultrasound features (hepatomegaly +/- splenomegaly, hydrops fetalis, pericardial effusion, aberrant liquor volume, cardiac

abnormalities, ascites, pleural effusion and peripheral oedema) seen in 71.8% of cases (Tamblyn et al. 2015). The presence of NIFH associated with hepatomegaly in TAM has a very poor prognosis (92% mortality rate) (Tamblyn et al. 2015).

This is an interesting case study of NIFH with Trisomy 21 which demonstrates a logical triage of aetiology with multidisciplinary management of a complex case. Rapid investigation of the fetal anaemia was attributed to HPV19 infection, excluding TAM, based on the absence of peripheral blood blast cells. Treatment of the life-threatening fetal anaemia by IUT has successfully reversed the hydrops caused by underlying HPV19 infection.

Conclusion

The diagnosis and management of hydrops fetalis with Trisomy 21 is complex and although TAM is a possible cause, it is important not to miss the more common diagnosis of HPV19 infection which is treatable with IUT.

Disclosure statement

The authors report no conflicts of interest.

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