Unusual presentation of more common disease/injury

Acute non-immune hydrops fetalis caused by intrauterine echovirus infection

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Summary

We present a case of non-immune hydrops fetalis presenting acutely in the third trimester caused by echovirus infection. The infant required intensive care for over 2 weeks.

BACKGROUND

In many cases of non-immune hydrops fetalis (NIHF) the cause is not found. There are very few case reports of confirmed enteroviral-associated NIHF. In contrast to previous case reports, the infant in this case was born later in pregnancy and had a good outcome. The extensive rash and abnormal full blood count were prominent features of the case and pointed towards the cause.

CASE PRESENTATION

A healthy, non-smoking 34-year-old pregnant woman was monitored with fetal ultrasound scans at 2 weekly intervals due to a previous intrauterine death at 35 weeks of unknown cause.

A fetal ultrasound at 32 weeks showed a normal singleton pregnancy but at 34 weeks showed severe hydrops with

normal liquor volume. The mother had no associated systemic symptoms. Due to the history of previous intrauterine death a decision was made to perform an emergency caesarean section.

A severely oedematous baby girl was born at 34+5 weeks weighing 2220 g. She cried at birth but then required a brief period of bag mask ventilation due to poor respiratory effort and bradycardia. Apgar scores were 5 at 1 min, 8 at 5 min and 9 at 10 min. Due to increasing respiratory effort and associated hydrops the baby was intubated at 15 min of age.

She received 2 doses of Surfactant within the first 24 h for associated surfactant deficiency but despite this became increasingly difficult to ventilate requiring high pressures (30 mm Hg).

Platelet counts were low from birth (51). On day 5 she developed an extensive ecchymotic rash (figure 1)

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Figure 1 Extensive ecchymotic rash.

associated with a decreasing platelet count (31) and received a single transfusion of platelets. Following this her platelets remained above 150.

On day 7 she was transferred to a tertiary neonatal unit for possible drainage of pleural effusions. Chest ultrasound performed in the tertiary centre revealed only small effusions and no drains were inserted. Following transfer her ventilatory requirements slowly improved and on day 14 she was successfully extubated to continuous positive airway pressure (CPAP) support. She received CPAP for 2 days and low-flow oxygen for a further 7 days.

Following extubation the oedema gradually improved and she was discharged home on day 34 of life.

INVESTIGATIONS

A full infection screen was sent as routine, including blood cultures, serology for congenital viral infections and urine for cytomegalovirus PCR and culture. Urine viral culture on day 1 was positive for echovirus. Initial haemoglobin was 13.0 and blood films showed neutrophilia with toxic granulation but no features of haemolysis. Platelet counts were low initially (see above). C reactive protein was not raised. An ECG of the heart showed a patent foramen ovale and a small muscular ventricular septal defect but otherwise normal structure and function. An ultrasound of the abdomen showed no renal tract abnormality. Chromosome analysis revealed a normal female karyotype. Metabolic investigations were normal. Serology and urine testing for cytomegalovirus, rubella, toxoplasma and parvovirus were negative.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for NIHF is extensive and can include cardiovascular, haematological, chromosomal, lymphatic, metabolic and urinary tract abnormalities, as well as gastrointestinal and thoracic obstructive causes. A recent systematic review found that in 17% of cases the cause is idiopathic.¹

Neonatal ecchymotic rashes are relatively uncommon and are associated with dermal erythropoiesis on histological examination. Common causes include congenital infections (cytomegalovirus, rubella) and malignancies and blood dyscrasias (leukaemia, neuroblastoma, langerhans cell histiocytosis). Other rarer causes include haemolytic disease of the newborn, neonatal alloimmune thrombocytopenia, congenital vascular lesions and neonatal lupus erythematosus.²

TREATMENT

Intravenous pooled immunoglobulin has been shown to decrease viraemia in neonatal enteroviral infection³ but has not been proven to improve clinical outcome.

No other antiviral agent has been shown to be effective in vivo against enteroviruses.

Treatment is supportive.

OUTCOME AND FOLLOW-UP

At follow-up she is growing normally and meeting her developmental milestones.

DISCUSSION

Hydrops fetalis is a non-specific finding of generalised oedema with associated pleural and pericardial effusions and ascites accompanied by placental enlargement.

The pathophysiology of hydrops fetalis remains poorly understood and it appears to be the end result of a number of distinct disease processes. In animal models, the extent of hydrops correlates with the level of the central venous pressure.⁴ Levels of atrial natriuretic peptide (ANP) are higher in hydropic babies and the decline of ANP levels correlates with recovery.⁵ Changes in serum albumin and levels of renin and angiotensin are likely to be secondary events.⁶ It has been suggested that changes in endothelial nitric oxide metabolism and endothelial 'activation' may also play a role.⁷

Since routine immunisation of Rhesus negative mothers, the majority of newborns with hydrops have a 'non-immune' cause.

Congenital infections account for up to 8% of cases of NIHF.⁸

Enteroviruses are associated with meningo-encephalitis and myocarditis in young children. Two cases of enteroviral associated NIHF with no evidence of myocarditis have been described; however, both babies were born extremely pre-term and did not survive.⁹

We describe a case of proven enteroviral-associated NIHF with no evidence of myocarditis at 34 weeks' gestation in a live born infant with a good outcome.

Enteroviral infection can be under-recognised in pregnant mothers¹⁰ and can have serious consequences for the fetus.¹¹

Learning points

- Infection is an important cause of NIHF and should be actively sought as a cause.
- The presence of a rash with toxic neutrophilia and thrombocytopenia strongly suggests congenital infection.
- Enteroviral infection can cause hydrops in the absence of active myocarditis.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Bellini C, Hennekam RC, Fulcheri E, *et al.* Etiology of nonimmune hydrops fetalis: a systematic review. *Am J Med Genet A* 2009;**149A**:844–51.
2. Mehta V, Balachandran C, Lonikar V. Blueberry muffin baby: a pictorial differential diagnosis. *Dermatol Online J* 2008;**14**:8.
3. Abzug MJ, Keyserling HL, Lee ML, *et al.* Neonatal enterovirus infection: virology, serology, and effects of intravenous immune globulin. *Clin Infect Dis* 1995;**20**:1201–6.
4. Brace RA. Effects of outflow pressure on fetal lymph flow. *Am J Obstet Gynecol* 1989;**160**:494–7.
5. Moya FR, Grannum PA, Riddick L, *et al.* Atrial natriuretic factor in hydrops fetalis caused by Rh isoimmunisation. *Arch Dis Child* 1990;**65**:683–6.
6. Pasman SA, Meerman RH, Vandenbussche FP, *et al.* Hypoalbuminemia: a cause of fetal hydrops? *Am J Obstet Gynecol* 2006;**194**:972–5.
7. De Groot CJ, Oepkes D, Egberts J, *et al.* Evidence of endothelium involvement in the pathophysiology of hydrops fetalis? *Early Hum Dev* 2000;**57**:205–9.

8. **Barron SD**, Pass RF. Infectious causes of hydrops fetalis. *Semin Perinatol* 1995;**19**:493–501.
9. **Bachmaier N**, Fusch C, Stenger RD, *et al*. Nonimmune hydrops fetalis due to enterovirus infection. *Eur J Obstet Gynecol Reprod Biol* 2009;**142**:83–4.
10. **Van den Veyver IB**, Ni J, Bowles N, *et al*. Detection of intrauterine viral infection using the polymerase chain reaction. *Mol Genet Metab* 1998;**63**:85–95.
11. **Brady WK**, Purdon A Jr. Intrauterine fetal demise associated with enterovirus infection. *South Med J* 1986;**79**:770–2.

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