Non Immune Hydrops Fetalis

Major A J Lyon

MA, MRCP, RAMC

Senior Specialist in Paediatrics

Major J Johnson

MB, MRCPATH, RAMC

Consultant Pathologist

British Military Hospital, Rinteln

SUMMARY: With the decline in the frequency of rhesus isoimmunisation, hydrops fetalis secondary to other factors is becoming increasingly recognised. We describe a case in association with chorioangioma of the placenta. The causes of non immune hydrops are reviewed and the problems of management discussed.

Case Report

A 1880 gm female infant, was born by spontaneous vertex delivery to a 32 year old, para 2 woman. The labour was spontaneous at 31 weeks gestation and delivery, described as precipitant, followed a second stage of only two minutes. Pregnancy had been complicated by a high serum alpha foeto-protein at 16 weeks gestation but the level in the amniotic fluid was normal. Ultra sound scan at this stage revealed no obvious abnormalities in fetus or placenta.

At birth the infant was oedematous but there was no gross ascites or pleural effusion. The placenta weighed 1080 gm and showed hydropic changes. A large polypoid mass was delivered with the placenta. Histologically this was a chorionangioma.

Investigations soon after birth included: Haemoglobin 13.6 gram per cent. Blood groups B rhesus positive (Mother's group B rhesus positive). Direct Coomb's test negative. White cell count 40,000 with a normal differential. Platelets 120,000 per cubic millimeter. Sodium, potassium, urea, bilirubin, pH and blood gases all normal. Blood cultures negative. There was no detectable IgM titre for toxoplasma, rubella, cytomegalovirus or herpes virus. Chest X-ray showed pulmonary oedema.

She required continuous positive airway pressure to maintain adequate ventilation and oxygenation. The fluid intake was restricted and, once stabilised, digoxin and diuretics started. The initial response was good with a significant diuresis, weight loss being 380 gms in the first two days. The blood gases, acid-base state and all biochemistry remained normal. Her haemoglobin dropped to 8.0 gms during the

first twenty-four hours and was corrected by a slow infusion of packed cells.

After forty-eight hours her condition deteriorated; she became hypotensive with a metabolic acidosis and evidence of an intravascular coagulopathy. Infective screen was negative but her CSF was bloody. Despite full supportive therapy she died when four days old.

At post mortem there was a subtentorial haemorrhage with a tentorial tear, and a large area of haemorrhage into the left cerebral hemisphere. The other organs were normal with the exception of the thymus which was small, weighing a few grams. The tentorial tear and subsequent haemorrhage was presumed to have resulted from the rather precipitant delivery in the preterm, stressed infant. The collapse at forty-eight hours after birth was thought to be due to a secondary haemorrhage into the left cerebral hemisphere.

Discussion

The incidence of hydrops fetalis secondary to cause other than isoimmunisation is unknown. Approximately 20% of cases of hydrops in 1970 were estimated to be non immunologic¹ but, with the decline in rhesus isoimmunisation, non immune hydrops may become the predominant form. Macafee et al¹ report on 182 consecutive cases of hydrops of which 33 (17.6%) were due to nonimmune causes. They give an incidence of 1:3538 deliveries for non immune hydrops fetalis. Only six of these cases survived, a mortality rate of 82%, which agrees with other reports². The mortality remains high even if infants

Table I
Conditions associated with Non Immune Hydrops Fetalis

Chronic fetomaternal transfusion	Congenital abnormalities
Twin-twin transfusion	Achondroplasia
Homozygous thalassaemia	Trisomy E
Congenital heart disease	Turner Syndrome
Arteriovenous malformation	Fetal neuroblastoma
Myocarditis	Umbilical vein thrombosis
Pulmonary hypoplasia	Chorioangioma
Renal vein thrombosis	Maternal diabetes mellitus
Intrauterine infections	Maternal toxæmia
Syphilis	Idiopathic
Toxoplasmosis	
Cytomegalovirus	
Congenital hepatitis	

with major congenital abnormalities are excluded. Table I lists the conditions reported in association with non immune hydrops fetalis.

The aetiology of oedema in hydropic infants, whatever the aetiology, is poorly understood. Anaemia, heart failure, decreased colloid osmotic pressures and primary placental abnormalities have all been implicated. Macafee et al¹ had no cases of fetal anaemia or low plasma proteins, while Etches and Lemons², reporting on twenty two infants with non immune hydrops, could find no constant underlying physiological abnormality to account for oedema formation.

Chorioangioma is a common benign placental neoplasm. It is a hamartomatous malformation of primitive mesenchyme and occurs in 1:100 microscopically examined placentas but significant tumours occur in only approximately 1:5000 births. Fox³ reports on 344 cases of chorioangioma and found only 4 cases of fetal oedema. He concludes that the association of chorioangioma and oedema is uncommon. Since then there have been a few other reports of this tumour resulting in hydrops fetalis^{4, 5, 6}.

Tonkin et al describe a case in which the baby was severely anaemic. They postulated that this was due to blood pooling in the physiologic dead space created by the abnormal vessels of the tumour. Abnormal connections between the maternal and fetal circulation may result in anaemia due to fetomaternal transfusion. The infant reported here was anaemic at birth but no Kleihauer was performed on maternal blood. However, Ellis and Kohler⁷ report an association between low thymic weight, as found in this case, and chronic fetomaternal transfusion.

It was postulated by Sweet et al⁸ that the vascular abnormality in the chorioangioma was responsible for protein loss resulting in oedema due to hypoalbuminaemia. A chronic protein loss was inferred

from their finding of hypercholesterolaemia with the hypoalbuminaemia analogous to the findings in the nephrotic syndrome. A more detailed study of protein and cholesterol levels in hydropic infants may help in elucidating the cause of the oedema.

Hydrops fetalis can be detected in utero as there is usually associated hydramnios and ultra sound scans can detect fetal ascites or pleural fluid. The appropriate timing of delivery in these cases is unknown although premature delivery is indicated if there is evidence of progressive hydrops.

The initial management of these infants involves vigorous resuscitation at birth. Immediate abdominal paracentesis and thoracentesis may be needed if excessive fluid is compromising ventilation. Despite the marked increase in total body water and extracellular fluid, the blood volume in these infants is frequently reduced and immediate volume expansion with a plasma expander (e.g. Haemacell 20 mls/Kg) may be required.

The laboratory investigations to be considered in cases of hydrops fetalis are listed in Table II.

After initial stabilization, several problems may be encountered and close monitoring is essential.

Repeated paracentesis and thoracentesis may be needed if ventilation and oxygenation are inadequate. The generalised oedema makes the readings from transcutaneous oxygen monitors unreliable and an intravascular electrode should be used for continuous PO₂ monitoring. Pulmonary oedema is best managed by positive pressure ventilation. Initially high pressures may be needed but, with the careful use of diuretics (e.g. frusemide 1-2 mg/Kg/day) lower pressures may be tolerated. The oedema will respond to moderate fluid restriction (60-80 mls/Kg/day). Spontaneous diuresis usually takes place in the first few days with a maximal weight loss by 7-10 days. Etches and Lemon² found the mean weight loss of the surviving babies in their series to be 28% of birth weight.

Hypovolaemia should be corrected with packed cells. Monitoring of blood volume can be a problem in sick neonates. Blood pressure should be constantly monitored either with a transducer on an umbilical artery catheter or with automatic monitors which use an oscillometric technique. Peripheral vasoconstriction however can keep the blood pressure in the normal range despite hypovolaemia. When perfusion improves e.g. following correction of metabolic acidosis with bicarbonate, the blood pressure may drop rapidly. In the absence of environmental cold stress, a normal core temperature in excess (1.0 C) of the peripheral temperature implies hypovolaemia with a failure to perfuse the skin. Differential temperature measurement therefore is a simple method of detecting hypovolaemia in sick neonates.

More than half the reported cases of non immune hydrops were complicated by disseminated intravascular coagulopathy within the first 24 hours of life. Management is with repeated exchange transfusion using fresh blood. Serum for the investigations detailed in Table II must be taken before beginning an exchange transfusion.

Table II

Investigation of Non Immune Hydrops Fetalis

Full blood count, platelets	Blood gases
Haemoglobin	Total IgM
Electrophoresis	
Kleihauer test on maternal blood	Serology for congenital infections (Torch screen)
Urea and Electrolytes, creatinine	Chromosomes
Liver function tests, albumin, Chloesterol	X rays - chest, abdomen, long bones
Blood group, Coombs test, Maternal blood group	Placental anatomy

Non immune causes of hydrops fetalis are becoming relatively more important. An awareness of this problem and its related causes is important. Hopefully with earlier recognition, close monitoring and active management of this condition, the prognosis will improve for those babies with no other major abnormality. There is little information on the out-

come of future pregnancies after a mother has delivered a baby with non immune hydrops fetalis.

Macafee¹ reported that of twenty three mothers followed to their next pregnancy, twenty two had uncomplicated deliveries of normal infants and the remaining one delivered another hydropic infant which survived as a normal child. It is reasonable to assume therefore that parents can be reassured regarding future pregnancies.

- 1 MACAFEE C A J, FORTUNE D W, REISCHER N A. Non immunological hydrops fetalis. *J Obstet gynaec Brit Cwlth* 1970; **77**: 226-237.
- 2 ETCHES P C, LEMONS J A. Non immune hydrops fetalis: Report of 22 cases including 3 siblings. *Paediatrics* 1979; **64**: 326-332.
- 3 FOX H. Vascular tumours of the placenta. *Obstet gynecol Surv* 1967; **22**: 697-771.
- 4 DANIEL S J AND CASSADY G. Non immunologic hydrops fetalis associated with a large haemangio-endothelioma. *Paediatrics* 1968; **42**: 828-833.
- 5 TONKIN I L, SETZER E S, AND ERMOCILLA R. Placental chorioangioma: A rare cause of congestive heart failure and hydrops fetalis in the newborn. *Am J Radiol* 1980; **134**: 181-183.
- 6 SWEET L, REID W D, AND ROBERTON N R. Hydrops fetalis in association with chorioangioma of the placenta. *J Pediatr* 1973; **82**: 91-94.
- 7 ELLIS J., AND KOHLER H G. Small infant thymus in cases of fatal feto-maternal transfusion. *Br Med J* 1976; **1**: 694.

'COMMUNICABLE DISEASES: NEW FRONTIERS'

A conference will be held in London on 11th April, 1984, 1015 to 1530. Sessions on Trends in sexually transmitted diseases (Professor M W Adler); AIDS (Dr B McEvoy); Haemolytic Uraemic Syndrome (Dr P Gully); Hantaan Virus (Professor D I H Simpson). Further information from Royal Society of Health, 13 Grosvenor Place, London SW1X 7EN. Telephone 01-235 9961.