Massive acute thymic haemorrhage and cerebral haemorrhage in an intrauterine fetal death

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Abstract

Massive acute thymic haemorrhage in the neonate occurs extremely rarely and is associated with haemorrhagic disease of the newborn. A 30 year old woman with an unremarkable previous obstetric history presenting at 37 weeks and 4 days gestation with the complaint of loss of fetal movement was found to have a male fetus with findings at necropsy of massive acute thymic haemorrhage, acute intracranial haemorrhage, and hydrops fetalis. This is the first report of massive acute thymic haemorrhage in utero. Massive thymic haemorrhage should be added to the reported causes of lethal non-immunological hydrops.

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A 30 year old woman, gravida 4, para 2012, presented at 37 weeks and 4 days gestation by dates with the complaint of loss of fetal movement. Physical examination showed a gravid uterus consistent with the gestational age. Laboratory values, including fibrinogen, prothrombin time, and partial thromboplastin time values, were all within normal limits. An ultrasound detected no fetal heart movement and the diagnosis of intrauterine fetal death was made. The patient was admitted for induction of labour and delivery. A male fetus was delivered without complication and consent for a complete necropsy was obtained.

The patient's previous medical and surgical history was notable for peptic ulcer disease, previous foot surgery, and aspirin allergy. Her past obstetric history is notable for one voluntary termination of pregnancy, one normal spontaneous vaginal delivery at term, and one vaginal delivery induced for oligohydramnios at term. During the pregnancy in question, the

patient presented at 9 weeks gestation by dates with complaints of nausea and upper respiratory tract symptoms. A vaginal ultrasound performed at that time revealed placenta previa. A subsequent ultrasound study performed at 20 weeks gestation indicated that the placenta previa had resolved. Fetal measurements were appropriate for gestational age and no anomalies were detected at that time.

At 33 weeks gestation she presented with lower abdominal pain. Membranes were found to be intact and active fetal movement was present. The patient was reassured and sent home. An additional ultrasound study performed at 36 weeks gestation again showed a fetus with measurements appropriate for gestational age and no congenital anomaly. Ten days later the patient presented with absence of fetal movement.

Pathological findings

Necropsy examination revealed a macerated male fetus, weighing 3550 g with normal growth and development, skin slippage involving over 50% of the body surface, and diffusely oedematous soft tissue. The head was normally formed and facies were normal. There was no cleft lip or palate and ears were normally positioned. Extremities were normal in position and number. The back was unremarkable. Normal male genitalia were noted and the anus was patent. Crown-rump, crown-heel, and toe-heel measurements were all compatible with the gestational age.

Internally, there were bilateral pleural effusions of approximately 20 ml total and a pericardial effusion of approximately 5 ml. Internal organs were normally formed and positioned, but were uniformly extremely pale. The thymus was almost entirely replaced by 55 ml of acute haemorrhage (fig 1). Light microscopic examination of paraffin wax embedded sections of the thymus confirmed the presence of acute haemorrhage (fig 2).

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Figure 1 Massive haemorrhage (55 ml) obliterating the thymus. The haemorrhage did not enter the pericardial sac and the underlying heart was normal.

Figure 2 Haematoxylin and eosin stained section of thymus showing acute haemorrhage extending into thymic cortex and medulla and residual thymocytes.

Immunohistochemical stains for CD34, factor VIII, and Ulex were all negative, confirming that no vascular tumour was present. The residual thymus showed severe thymic fetal stress involution. The brain weighed 410 g and the cerebral hemispheres, brainstem, and cerebellum were consistent with the gestational age. Approximately 50 ml of acute haemorrhage was present in the subarachnoid space and cerebral parenchyma, involving the frontal, temporal, and parietal lobes, bilaterally. The placenta was hydropic and the chorionic villous parenchyma was pale.

Discussion

In her classic 1962 text, Potter states: "... among the 10,000 autopsies on infants under one year of age that I have been fortunate enough to observe, the thymus has never shown any abnormality that might have led to death."¹ Neonatal massive thymic haemorrhage has since been reported only six times.²⁻⁴ Although two patients underwent surgical removal of a massively enlarged haemorrhagic thymus and survived, in general, the condition has been fatal in the neonatal period and is believed to be associated with haemorrhagic disease of the newborn. The possibility of trauma to the thymus during delivery complicated by shoulder dystocia has been considered, although this possibility seems unlikely, because the thymus is protected by the rigid sternum.⁴ This is the first report of massive thymic haemorrhage in an intrauterine fetal death.

Massive thymic haemorrhage may lead to hydrops fetalis through two mechanisms. First, a profound anaemia is caused by the considerable red blood cell loss, manifest in this case by the extreme pallor of the internal organs and placental chorionic villous parenchyma. Loss of blood has previously been implicated as a cause of non-immunological hydrops in at least four settings: twin to twin transfusion,⁵ fetomaternal haemorrhage,⁶ in utero intracranial haemorrhage,⁷ and Kasabach-Merritt syndrome.⁸ Second, the large haemorrhage distorting the thymus and filling the mediastinum may interfere with cardiac output. Both mechanisms may have contributed to cardiac collapse and the ensuing hydrops fetalis in this case.

Fetal intracranial haemorrhage, unlike the other types of haemorrhage previously known to cause hydrops, represents fetal blood loss into a closed space which can precipitate the events leading to hydrops. Fetal thymic haemorrhage appears to be a second type of closed space haemorrhage that can precipitate hydrops, which has not been reported previously. Intracranial haemorrhage did not occur together with neonatal massive thymic haemorrhage in previous reports.

The absence of organisation of the thymic and cerebral haemorrhages suggests that the hydrops fetalis and ensuing death were acute events. In other cases of hydrops caused by haemorrhage, such as twin to twin transfusion and fetomaternal haemorrhage, blood loss probably occurs over a prolonged period of time and the onset of hydrops may be more gradual. The normal sonogram 10 days before the patient's presentation with loss of fetal movement suggests that both the large intracranial and thymic haemorrhages were extremely rapid. Although the patient presented 10 days after her last normal sonogram, the death may have occurred earlier. Judging from the extent of fetal maceration and skin slippage, in addition to the loss of nuclear basophilia in several tissues microscopically, even taking into account that these changes are accelerated by hydrops, the interval between fetal death and delivery is probably about two days. Given this death to delivery interval, the death occurred approximately eight days after the patient's previous sonogram and the haemorrhages approximately six to seven days after she was last examined.

The presence of two massive haemorrhages implies a haemorrhagic disease of the newborn-like syndrome occurring in utero. No coagulopathy is present in the mother and her previous pregnancies were not complicated by fetal haemorrhages. The size of the acute haemorrhages, especially the thymic haemorrhage, suggests that a substantial amount of fetal blood can be lost in a very short period of time, even in the case of "closed space" haemorrhage. The normal sonogram at 36 weeks implies that there are no warning signs in the days preceding the onset of massive haemorrhages. Massive thymic haemorrhage should be added to the reported causes of lethal non-immunological hydrops.

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