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Abnormal heart rate pattern in fetal anaemia secondary to transient abnormal myelopoeisis in a fetus without trisomy 21: A case report

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ABSTRACT

Decreased fetal movements (DFM) are a non-specific and common symptom in the third trimester of pregnancy that hold an association with fetal compromise. A 28-year-old woman at 31 weeks and 3 days of gestation presented with DFM and was found to have a pathological fetal heart rate trace. Following emergency Caesarean section the fetus was diagnosed with transient abnormal myelopoeisis (TAM). Timely treatment was initiated and the neonatal outcome was good. Transient myeloproliferative disorders are almost uniquely found in infants with trisomy 21 (T21). This is the first case report of TAM in the absence of T21 wherein the diagnostic process was commenced antenatally due to non-reassuring fetal status and highlights the importance of antenatal heart rate abnormalities.

1. Introduction

Transient abnormal myelopoeisis (TAM) is a myeloproliferative condition almost exclusively found in infants with trisomy 21 (T21), usually diagnosed in the first days to weeks of life [1]. Myeloproliferative conditions are among the least common causes of fetal anaemia and antenatal diagnosis is infrequent and associated with significant perinatal morbidity and mortality [2]. The clinical presentation of fetal anaemia is dependent on cause, but there is an association with subjectively decreased fetal movements (DFM) as well as abnormal fetal heart rate (FHR) patterns on computer tocography (CTG) [3].

This report describes a rare case of fetal anaemia secondary to TAM without chromosomal T21, diagnosed following an emergent delivery at 31 weeks for non-reassuring fetal status on CTG which was attended due to DFM. In this case, timely investigation of DFM resulted in rapid management and diagnosis, leading to a positive outcome in a condition which otherwise has significant perinatal morbidity and mortality.

2. Case Presentation

A nulliparous 28-year-old woman presented initially to her local private hospital at 31 weeks and 3 days with DFM and irregular mild uterine tightenings consistent with threatened preterm labour. She was managed with two 11.4 g doses of intramuscular betamethasone 24 h apart to reduce the risk of neonatal respiratory distress syndrome, intracranial haemorrhage and necrotising enterocolitis associated with prematurity should she progress to preterm labour, and inpatient monitoring was commenced. Two days later she was transferred to a quaternary obstetric unit due to a newly abnormal FHR pattern. Her antenatal history included Rhesus-positive blood group, normal antenatal serology, a low-risk aneuploidy screen and a normal fetal morphology scan with a low-lying anterior placenta and a short cervix (15 mm at 29 weeks and 5 days of gestation) for which she was using progesterone pessaries daily. She had no medical or surgical history and her BMI was normal.

Examination at time of presentation to the quaternary unit showed normal observations, a soft abdomen without palpable uterine activity, a long cervix, and small volume active per vaginal bleeding with no evidence of rupture of membrane on speculum examination.

A bedside ultrasound scan showed an anterior placenta, raised amniotic fluid index (AFI) with a deepest pocket of 8 cm and normal umbilical artery pulsatile index of 1.03. Fetal fibronectin (FFN) was 335 ng/mL and quantitative fetomaternal haemorrhage (qFMH) was negative. CTG showed a normal baseline of 140BPM with reduced variability, no reactivity and recurrent decelerations (Fig. 1). The CTG did not improve with interventions, including intravenous fluids and repositioning, so an emergency lower-segment Caesarean section was called 90 min following her transfer for non-reassuring FHR (Fig. 2). The operation was uncomplicated with no evidence of placental abruption or uterine abnormalities and minimal blood loss.

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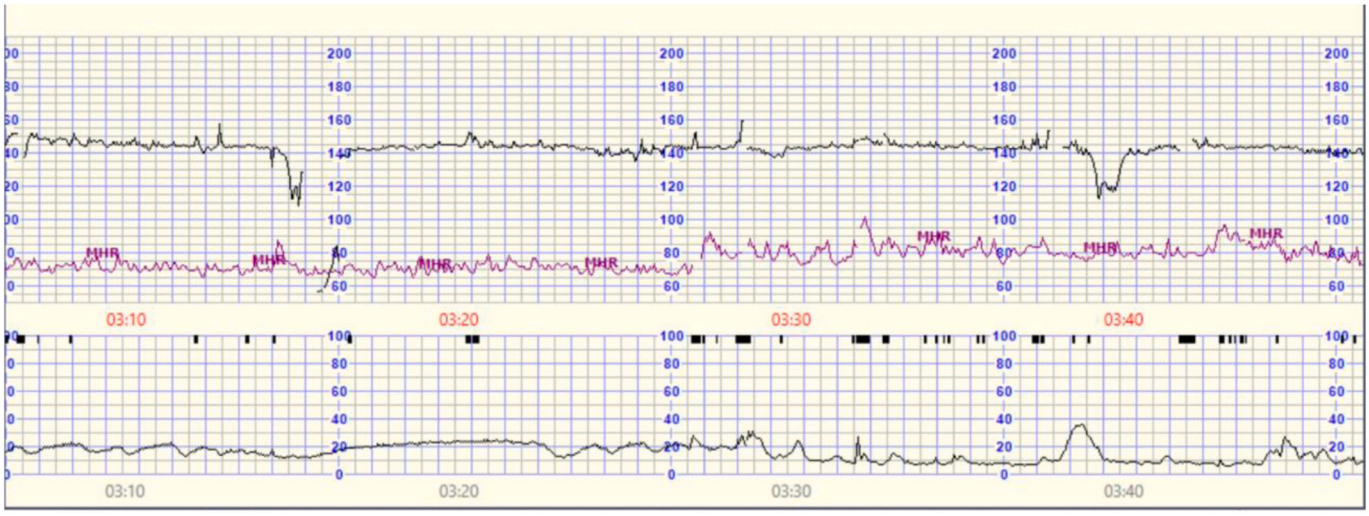

Fig. 1. Cardiotocography before interventions (including intravenous fluids and repositioning).

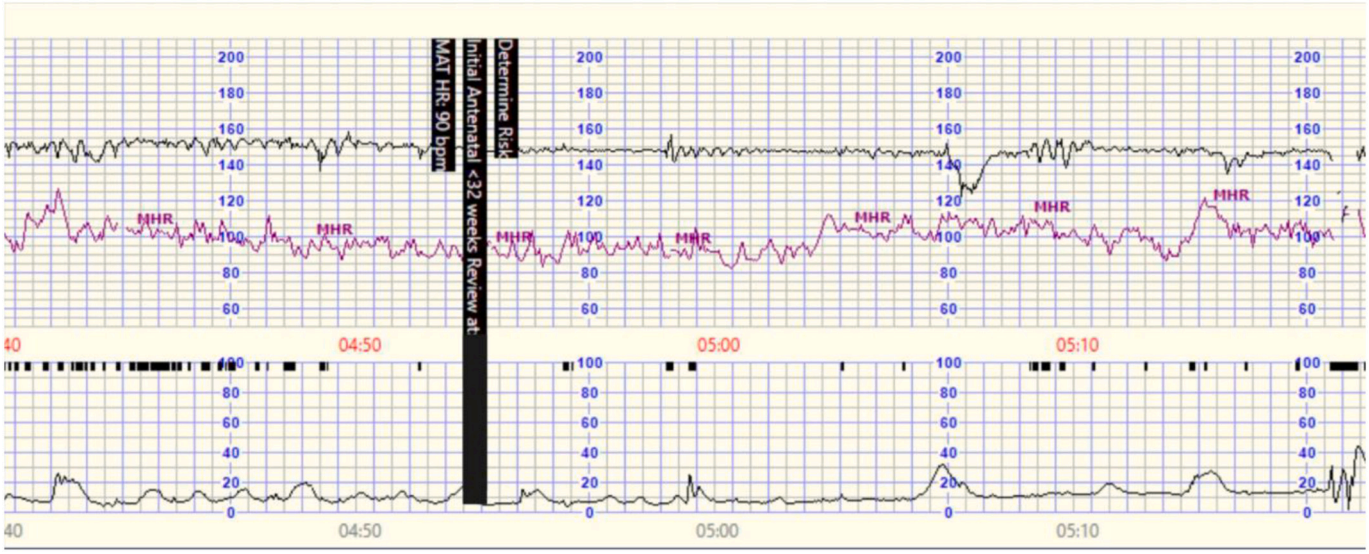

Fig. 2. Cardiotocography after interventions.

A male newborn was delivered, weighing 1713 g with Apgar scores of 2, 6, and 7. The umbilical artery pH was 7.1, with a lactate of 6.8 and base excess of −7. Clinically, he was flat and mildly hydropic with pitting oedema on the chest and palpable hepatomegaly. He required intermittent positive-pressure ventilation (IPPV) and subsequently continuous positive airway pressure (CPAP) on transfer to the neonatal intensive care unit (NICU).

The infant was anaemic with a haemoglobin (Hb) level of 48 g/L (ref. 102–130 g/L) at birth, and leukocytotic with white cells of 54 $\times$ 10^9/L (ref. 6.4–12.1 $\times$ 10^9/L), prominent blasts and a film suggestive of acute leukaemia. He was initially treated with 20 mL/kg of packed red blood cells (PRBC) and then transferred to a specialised paediatric haematology service. Further investigations included peripheral blood flow cytometry, cytogenetics, and comparative genomic hybridisation (CGH) and he was treated with low-dose course of cytarabine while awaiting results given the suspicion of acute myeloid leukaemia (AML). Peripheral blood flow cytometry demonstrated a significant myeloblast population and cytogenetics revealed T21 in the myelocytes as well as a positive GATA mutation - findings consistent with TAM despite a normal karyotype. The infant required a further 3 transfusions of PRBC to correct his severe anaemia and remained an inpatient until 6 weeks and 5 days of age, by which time he was clinically stable, on full suck feeds and not requiring respiratory support. He initially required weekly full blood counts (FBC) on discharge, which were gradually extended to 3-monthly with specialist paediatric haematology follow-up. He required no further active treatment and remained well at 18 months of age.

3. Discussion

DFM is a non-specific and common presentation, reported by 16% of pregnant people in their third trimester [4]. Though no robust evidence defines an objective reference range for normal fetal movement counts, maternal reports of decreased movements compared with their own baseline has a known association with poor perinatal outcomes, including growth restriction, placental insufficiency, and stillbirth [5]. A proposed mechanism for this involves the fetus' attempt to reduce oxygen consumption and prioritise major organ function in the context of fetal compromise [6]. Given this, DFM has become a target of national and global campaigns to reduce preventable stillbirths [4]. Several large-scale randomised trials in recent years have assessed education packages to encourage prompt presentation and review of DFM, including the AFFIRM and My Baby's Movements trial, though these

both failed to show a significant reduction of stillbirth rates [7]. Despite this, standard consensus-based guidelines support monitoring and investigation of subjectively reported DFM [4,5].

Fetal anaemia is rare but can be lethal if not diagnosed and managed promptly. Its clinical presentation depends strongly on aetiology and can be non-specific [3]. The most common cause is isoimmunisation, followed by non-immune conditions including congenital infections, feto-maternal haemorrhage, haemoglobinopathies and, rarely, haematological malignancies and myeloproliferative disorders [8,9]. TAM is almost exclusively associated with T21 and progresses to AML in 10–20% of cases within the first 5 years of life [1]. The clinical severity varies and the majority of cases will spontaneously resolve, though some require interventions for anaemia caused by suppression of other haematopoeitic cell lines, organomegaly and sepsis [10]. The overall perinatal mortality has been reported to be between 27% and 60%, with worse outcomes reported in those infants requiring treatment [1]. Antenatal diagnosis of TAM is very rare and is associated with significant mortality - a review of 39 cases reported a stillbirth rate of 30.8% and neonatal death rate of 17.9% [2].

TAM in a neonate without a T21 phenotype or karyotype is a rare and poorly understood phenomenon, with a 2014 review citing only 14 published cases in the preceding 20 years [11]. Among these, most cases displayed T21 mosaicism or isolated T21 in the myeloid cell line as well as a specific mutation in the GATA-1 gene involved in myeloid cell differentiation, causing the premature arrest of that process and myeloproliferation as seen in TAM. The rate of transformation to AML is at least as high in these infants as in those with T21, and similar surveillance should be performed [11].

In investigating DFM, ultrasound assesses growth and well-being, and in the context of anaemia hydrops and polyhydramnios can be present [3]. Increased cardiac output and reduced blood viscosity secondary to anaemia result in increased flow in the form of raised middle cerebral artery peak systolic velocity (MCA-PSV) [8]. Studies have shown an MCA-PSV of >1.5 multiplications of the median (MoM) in a population with risk factors for isoimmunisation to have high sensitivity and acceptable specificity for fetal anaemia [9].

Like ultrasound, CTG is a crucial investigation of DFM. It reflects acute fetal status and has a strong positive predictive value relating to fetal oxygenation in utero [12]. Abnormal FHR patterns, including reduced variability, absent reactivity and decelerations, can provide suspicion of fetal hypoxia and prompt further investigations, though they give limited information regarding aetiology of fetal compromise [12]. Fetal anaemia is associated with a pathognomonic CTG finding known as a sinusoidal pattern, characterised by a stable baseline between 120 and 160BPM with minimal variability and a smooth oscillation of 5–15 amplitude about 2–5 cycles per minute without reactivity [13]. Like many cardinal findings, however, sinusoidal CTGs are uncommon. Instead, fetal anaemia is often associated with the non-specific CTG abnormalities as described above, specifically reduced variability, no accelerations and recurrent complex decelerations.

This case seems to be the first to report severe fetal anaemia secondary to TAM in a non-T21 infant diagnosed perinatally in the course of emergent preterm delivery for non-reassuring FHR. Antenatal diagnosis of fetal anaemia is difficult, due to varied aetiology and non-specific clinical findings, including but not limited to those present in this case: DFM, polyhydramnios and abnormal FHR pattern. DFM is common and large-scale data has not yet proven the appropriate intervention to prevent DFM-associated stillbirth. However, this case presents a scenario wherein timely presentation and clinical evaluation of this mother's reported DFM potentially prevented an adverse outcome and supports the recommendation that pregnant people who notice a subjective decrease in frequency or number of fetal movements should present to a maternity service for review without delay.

Contributors

Meredith Grey gained consent from the patient for the report to be published, drafted the manuscript, undertook a literature review, revised the article critically for important intellectual content and compiled the final manuscript for submission.

Rahul Chatterjee contributed to patient care and revised the article critically for important intellectual content.

Sumathi Rajendran contributed to patient care and revised the article critically for important intellectual content.

All authors approved the final submitted manuscript.

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Patient consent

The patient gave written consent for the case report to be published.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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