Case Reports in Women's Health 29 (2021) e00272

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Coombs-negative haemolytic anaemia in pregnancy: A case report

Holly George *, E. Haslett, Mac Macheta

Blackpool Victoria Hospital, Whinney Heys Road, FY3 8NR, UK

ARTICLE INFO

Article history:
Received 29 October 2020
Received in revised form 11 November 2020
Accepted 16 November 2020
Available online xxxx

Keywords:
Case report
Obstetrics
Haematology
Anaemia
Maternal medicine

ABSTRACT

We present a rare case of Coombs-negative autoimmune haemolytic anaemia in a multiparous woman in secondary care. There were no known underlying medical or obstetric risk factors for haemolytic anaemia. Following extensive investigation and a therapeutic trial of oral corticosteroids, a diagnosis was made. Autoimmune haemolytic anaemia is potentially fatal, and prompt diagnosis with haematology input is essential to ensure maternal and fetal safety in pregnancy and the puerperium. With only a small number of cases of Coombs-negative autoimmune haemolytic anaemia reported in the literature, we present this rare case for discussion. We highlight the importance of thorough investigation of refractory anaemia in pregnancy and consider the associated challenges.

1. Introduction

Anaemia, predominantly iron deficiency anaemia, affects up to 30–40% of pregnant women [1]. Anaemia in pregnancy can be associated with an increased risk of maternal death. In one paper a haemoglobin level of less than 89 g/L was associated with the highest risk [2]. Autoimmune haemolytic anaemia (AIHA) has an incidence of approximately 0.83 in 100,000[3] in the general population. It is rare in pregnancy, affecting as little as 1 in 140,000 pregnancies [3]. In most cases the diagnosis is straightforward when there is the combination of anaemia, reticulocytosis, a high LDH, low or undetectable haptoglobin and a positive direct Coombs test (DCT). Only 5–10% of all cases of AIHA are Coombs negative. We report a case of Coombs-negative autoimmune haemolytic anaemia in a multiparous woman who presented at 16 weeks of gestation with shortness of breath and epigastric pain.

2. Case report

A 41-year-old woman, gravida 5, para 2, presented with epigastric pain and shortness of breath at 16 weeks of gestation. Her BMI was 33.8 kg/m^2. She was rhesus positive and had a venous thromboembolic (VTE) score of 2 (moderate), not requiring antenatal thromboprophylaxis. Her booking haemoglobin level was 141 g/L. She had had an emergency Caesarean section 16 years previously for a brow presentation, followed by a successful vaginal birth after caesarean (VBAC) 3 years later. Her medical history includes idiopathic intracranial hypertension with no treatment, previous large loop excision of the transformation zone (LLETZ) of the cervix for an abnormal cervical cytology, and previous left nephrectomy as she was an organ donor. There were no obstetric or haematological complications in any previous pregnancies.

In the index pregnancy the patient was taking 400μg folic acid; there was no other drug history to note. Antenatally she was commenced on 150 mg aspirin, as she was high risk for developing pre-eclampsia (age, > 10-year pregnancy interval). A glucose tolerance test was arranged as she was at high risk for developing gestational diabetes (age, BMI). Cervical length scan screening was arranged in view of previous LLETZ. Serial growth scans were planned for 30,34 and 38 weeks of gestation (for maternal age). There was no relevant family history of note.

On first presentation at 16 weeks of gestation she complained of shortness of breath and epigastric pain. Initial blood results revealed a haemoglobin level of 79 g/L, with a raised bilirubin level of 23 umol/L, raised reticulocyte count of 5% and undetectable haptoglobin. Ferritin, B12 and folate levels were also normal. All other blood results were within normal range for gestation and common causes of abdominal pain in pregnancy were excluded, such as urinary tract infection, pancreatitis and appendicitis. In view of the raised bilirubin level, a referral was made to haematology. An ultrasound scan of the abdomen revealed a normal liver, no gall stones, no evidence of splenic or hepatic venous thrombosis, but evidence of splenomegaly, with the spleen measuring 16 cm. There was no evidence of preceding infection. Serology and polymerase chain reaction (PCR) were negative for cytomegalovirus, Epstein Barr virus and toxoplasmosis. A connective tissue screen was also negative. The haematology team further investigated the cause of her severe refractory anaemia. The blood test results during the course of investigations can be seen in Fig. 1; the patient had raised LDH and persistent anaemia. Bilirubin and reticulocyte count remained raised

* Corresponding author.
E-mail address: hollyg13@doctors.org.uk (H. George).

https://doi.org/10.1016/j.crwh.2020.e00272

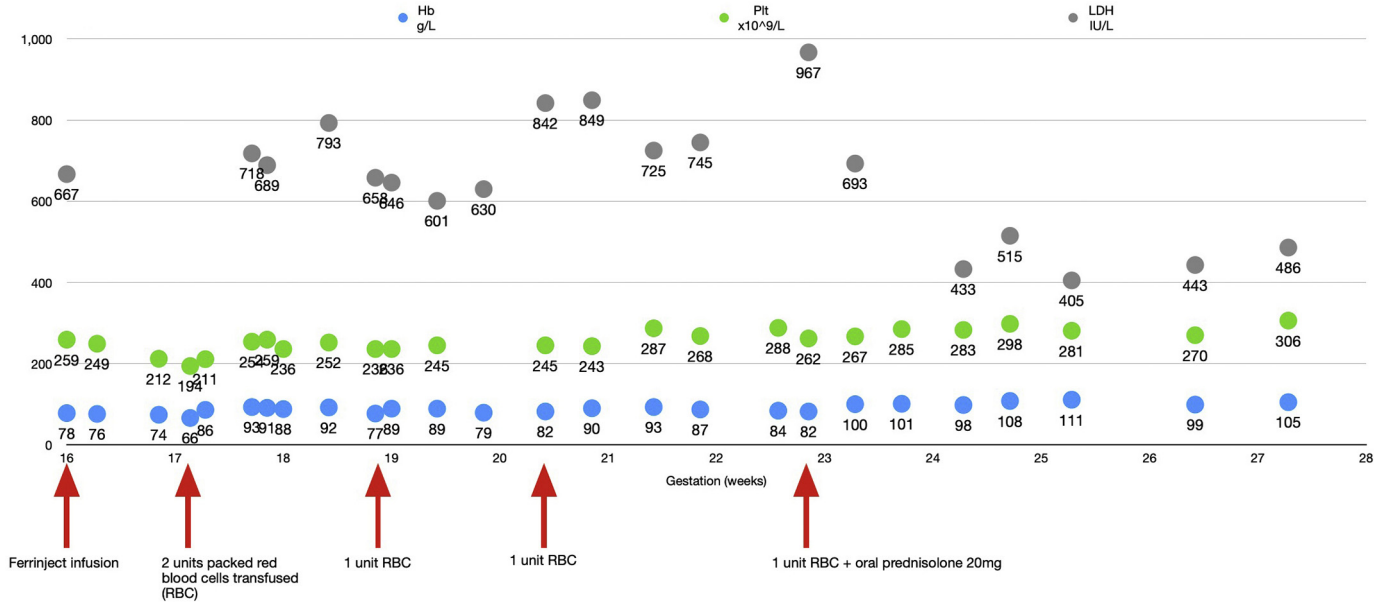

Fig. 1. Blood results.

throughout the antenatal period. Direct Coombs tests were repeatedly negative using anti-IgG and complement antisera and remained negative when repeated with a polyspecific anti-immunoglobulin anti-sera. The findings were in keeping with the rare diagnosis of Coombs-negative haemolytic anaemia. The patient was discharged and had haematology day-unit follow-up, having her first blood transfusion on at 17 + 1/40 weeks of gestation, after tests revealed a haemoglobin level of 66 g/L (Fig. 1). During the course of her investigations, she received a total of five blood transfusions antenatally. Screening for paroxysmal nocturnal haemoglobinuria (PNH) was negative, urine haemosiderin negative with no evidence of PNH clone on flow cytometry. Blood results as seen in Fig. 1 revealed ongoing haemolysis.

The patient was commenced on 20 mg prednisolone as per haematology plan at 22 + 6/40 weeks of gestation, with resolution of symptoms seen within days. As seen in Fig. 1, haemoglobin and LDH improved following the initiation the therapeutic oral corticosteroid therapy. Reticulocyte count and bilirubin also returned to normal within three days of treatment. A satisfactory Hb was maintained when the prednisolone was reduced to 10 mg daily. Subsequently, this patient went on to develop gestational diabetes, potentially secondary to steroid treatment, with additional underlying risk factors such as age and BMI. She was managed by the obstetric diabetes team.

Antenatally, fetal wellbeing was monitored. A growth scan performed at 28 weeks of gestation showed normal growth on the 90th centile, normal liquor volume and end diastolic flow/umbilical artery doppler. A plan for delivery was made, for an induction of labour at 37 weeks, and the patient had weekly haematology follow-up.

A live female infant was born by normal vaginal delivery at 37+ 3 weeks of gestation. Blood results for the neonate where all normal: Hb 193 g/L, WCC 10.8 × 10^9/L, Plat 386 × 10^9/L, Cord bilirubin 41 umol/L, DCT - negative. Postnatally the patient was weaned off oral corticosteroid treatment, and maintained a normal haemaglobin level of 144 g/L. Follow-up tests also revealed normal bilirubin and reticulocyte count. The potential for recurrence of this condition is unknown, due to its rarity. The patient was counselled regarding postnatal contraception.

3. Discussion

AIHA is caused by a host immune system creating immunoglobulin auto-antibodies against red cell membrane antigens, leading to their premature destruction by the spleen and reticuloendothelial system. The DCT uses an antibody against immunoglobulins to detect these on the red cell surface but when the level of antibody coating is very low, the test may be negative, as in this case [4]. The autoimmune mechanism of haemolysis in this case is confirmed by the prompt response to immunosuppression with cortiosteroids.

As IgG antibodies can cross the placenta, the fetus is subsequently at risk of developing haemolytic disease of the newborn (HDN). Testing of umbilical cord DCT, haemoglobin and bilirubin are required, and monitoring for symptoms essential [5]. Treatment recommendations for maternal autoimmune haemolysis are initially oral corticosteroids with IV immunoglobulins in refractory patients. Occasionally, additional immunosuppression with azathioprine or rituximab is required and rarely splenectomy may be indicated.

4. Conclusion

Conditions such as haemolytic anaemia can be fatal and require multidisciplinary input to ensure safe and effective treatment of the patient. With no preceding history or risk factors, this is a rare case of acquired auto-immune haemolytic anaemia in pregnancy. The case highlights the importance of thorough investigation for what may appear to be simple anaemia in pregnancy, especially when refractory to treatment.

Contributors

Dr Holly George drafted the paper and performed the literature search and review.

Dr. E Haslett contributed to revision of the paper.

Dr. M Macheta provided haematology expertise and contributed to revision of the paper.

Conflict of Interest

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

Funding

No funding from an external source supported the publication of this case report.

Patient consent

Obtained.

Provenance and peer review

This case report was peer reviewed.

References

[1] WHO, Iron Deficiency Anaemia: Assessment, Prevention and Control, 2001 WHO/NHD/01.3, Geneva 2001.
[2] B. Brabin, M. Hakimi, D. Pelletier, An analysis of anemia and pregnancy- related maternal mortality, J. Nutr. (2001) 604S–615S.
[3] R. Sokol, S. Hewitt, B. Stamps, Erythrocyte autoantibodies, autoimmune hemolysis and pregnancy, Vox Sang. (1982) 169–176.
[4] Stamps Hill, Massey. The diagnosis and management of primary autoimmune haemolytic anaemia, Br. J. Haematol. 176 (2017) 395–411, https://doi.org/10.1111/bjh.14478BJH Guideline.
[5] S. Issaragrisil, M. Kruatrachue, An asso- ciation of pregnancy and autoimmune haemoly- tic anaemia, Scand. J. Haematol. 31 (1983) 63–68.