Diagnosis of a myeloproliferative disorder in late pregnancy

S Okoli MRCP MRPharm*, **B Wilkins** PhD FRCPATH[†], **S Robinson** MRCP FRCPATH* and **C Harrison** FRACP FRCPATH*

*Department of Haematology; [†]Department of Histopathology, Guy's & St Thomas' Hospital, London SE1 7EH, UK

Summary: A 38-year-old primiparous woman presented with pre-eclampsia at 36 weeks gestation with an abnormal full blood count and leukoerythroblastic blood film. JAK2 V617F was negative and splenomegaly was noted on abdominal ultrasound. Delivery was at 37 weeks gestation by emergency caesarean section due to abnormal cardiotocography. Bone marrow aspirate and trephine confirmed a diagnosis of myelofibrosis. The case highlights a rare presentation of primary myelofibrosis in pregnancy, the difficulties in management, and the UK Obstetric Surveillance System who are collecting epidemiological data on uncommon disorders in pregnancy.

Keywords: haematology, high-risk pregnancy, neoplasm

CASE REPORT

A 38-year-old primiparous Zimbabwean woman with a history of G6PD deficiency presented with pre-eclampsia at 36 weeks gestation. Admission investigations revealed a white cell count of $30 \times 10^9/L$, neutrophil count $25 \times 10^9/L$, haemoglobin 10 g/dL, platelet count $398 \times 10^9/L$, lactate dehydrogenase 2447 IU/L and uric acid 0.60 mmol/L. The blood film showed a leukoerythroblastic picture, 1% myeloblasts (Figure 1). The Val617Phe JAK2 mutation and MPLW515L/K mutations were not detected. Abdominal ultrasound revealed 12 cm splenomegaly. Retrospective review of booking bloods revealed an abnormal full blood count, white cell count $18 \times 10^9/L$, neutrophil count $16 \times 10^9/L$, haemoglobin 8 g/dL and platelet count $598 \times 10^9/L$.

An emergency caesarean section was performed at 37 weeks gestation due to abnormal cardiotocography. Postpartum complications included maternal pneumonia and two haematomas, one in the suprapubic region measuring 9.6×2.4 cm and another in the Pouch of Douglas $6.5 \times 8.3 \times 7.0$ cm. The baby was mildly growth restricted, 2.5 kg, but well, and was discharged with the mother after four days. A bone marrow biopsy was performed day four postpartum. The trephine was hypercellular with marked suppression of the erythroid series and significant expansion of the myeloid series with normal maturation.

The megakaryocytes were dysplastic and held in tight clusters. Collagen and new bone formation were identified (Figure 2), fibrosis score of 3/3 (Figure 3). Chromosomal analysis revealed complex rearrangements to chromosomes 1, 13 and 20, the most important among these were 13q and 20q deletions. A diagnosis of primary myelofibrosis (PMF) was made.

Figure 1 Peripheral blood film – showing features suggestive of myelofibrosis

Figure 2 Bone marrow trephine – Martius Scarlet Blue stain

DISCUSSION

PMF is the least prevalent of all the myeloproliferative disorders in women of child-bearing age affecting 0.02–0.06/100,000.¹

Correspondence to: S Okoli
Email: scokoli@yahoo.com

Figure 3 Bone marrow trephine - reticulin stain. Grade 3 fibrosis

Eight pregnancies in four women with myelofibrosis have been reported to date.^{2,3} These data tentatively suggest that pregnancies in women with myelofibrosis can be successful although potential complications include fetal loss, intrauterine growth restriction, intrauterine death, postpartum haemorrhage and venous thromboembolism.⁴

At present, six weeks postpartum, the patient has total white cell count of $6.4 \times 10^9/L$, neutrophil count $4.5 \times 10^9/L$, haemoglobin 9.2 g/dL and platelet count $449 \times 10^9/L$. Alpha genotyping using multiplex polymerase chain reaction shows the patient to be heterozygous for alpha-plus thalassaemia due to a 3.7 kb deletion. Her Cervantes (2009) score is 2, and DIPSS-plus score of 2, both placing her in the intermediate-2 risk group. These prognostic scoring systems indicate a more aggressive disease course, median survival ~2.9 years.⁵ Patients with PMF with high or intermediate-2 risk disease

can be managed with a variety of treatment modalities. With each one of these options, except allogeneic stem cell transplantation, the primary goal is palliation of symptoms. She is currently being considered for stem cell transplantation.

This case highlights a rare presentation of PMF in pregnancy. Currently the UK Obstetric Surveillance System are collecting prospective data on the epidemiology of myeloproliferative disorders in pregnancy throughout the UK, with a view to gaining further understanding of pregnancy in myeloproliferative disorders, to inform us on how best we can manage this unique group of patients (www.npeu.ox.ac.uk/ukoss).

DECLARATIONS

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