The Journal of Obstetrics and Gynecology of India (May-June 2021) 71(3):322–325
https://doi.org/10.1007/s13224-021-01447-4

CASE REPORT

Myomatous Erythrocytosis Syndrome in Pregnancy Managed with Classical Caesarean Section and Myomectomy: A Case Report

Kusumam Vilangot Nhalil[1] · Smitha Dcouth[1] · Rajani Maroli[1] · K. Ambili[1] · K. P. Shana Rahman[1]

Received: 22 May 2020 / Accepted: 12 January 2021 / Published online: 18 February 2021

Introduction

Women over 45 years are having a lifetime risk of 60% to develop leiomyoma, commonly asymptomatic, but can also with varying gynaecological and abdominal symptoms [1]. Rarely, high haemoglobin and haematocrit levels occur due to ectopic erythropoietin synthesis which is termed as myomatous erythrocytosis syndrome (MES). MES was first described by Thompson and Marson, characterized by erythrocytosis, myomatous uterus, and restoration of haematological abnormalities following hysterectomy or myomectomy [2].

Incidence of myomas in pregnancy is only about 2%. To date, 57 cases of MES have been reported worldwide[1], and incidence of MES in pregnancy is rare; one case of MES in gravid uterus was just mentioned by Pollio F et al. in the literature.

The available evidence towards aetiopathogenesis of MES points to the ectopic production of erythropoietin (Epo) or Epo-like substances by the myomas [3]. Epo is a glycoprotein hormone which binds to specific Epo-receptors (Epo-R). Epo-R are seen in kidneys, liver, and in several non-erythroid physiological and pathological compartments. Its expression mainly depends on oxygen concentration. The striking presence of Epo-mRNA and Epo-protein within myoma tissues acting by autocrine and paracrine mechanisms, plays an important role in the large myoma [3, 4] probably in gravid uterus also. Thromboembolic complications can be prevented by pre-operative venesections [4].

Case History

Our patient is 31-year-old G3P1L1A1 with previous uneventful full-term Vaginal delivery, 11 years back, and had a missed abortion in the next 3 years. Then, the patient underwent two myomectomies for leiomyoma uterus at 3-year intervals for secondary infertility. Of late, she was admitted in surgery ward with cellulitis of right lower limb, at 31 weeks of pregnancy. Deep vein thrombosis was ruled out by venous Doppler, and she was managed with antimicrobials. Then, she was referred to obstetrics department at 32 weeks because of elevated blood pressure. She was diagnosed to have pre-eclampsia and was managed with antihypertensives and other supportive measures. The only abnormality detected in the first trimester was leiomyoma uterus.

In the obstetrics ward, she was found to have elevated haemoglobin (Hb), haematocrit (Hct), and erythropoietin levels on several occasions. Haematologist opined myomatous erythrocytosis syndrome as leiomyoma was detected in the early pregnancy sonograms.

Investigations done are shown in the hospital timeline, shown in Table 1.

First trimester Hb was 12.3 g/dl and Hct: 48%. Late second trimester Hb was 14.5 g/dl. At the time of admission, Hb was 17.8 g/dl and Hct was 55.6%. Initial sonogram done at 7 weeks showed two fibroids: one in the left anterior and other one at the lower posterior part of the uterus measuring 8.7×5.9×11 cm and 2×3 cm, respectively. It increased to 20×16x12 cm and 5×3 cm, respectively, at admission. A biweekly repetition of Epo showed a progressive rise (80.4 mIU/ml and 143 mIU/ml). Peripheral smear reported as erythrocytosis with polychromasia.

Dr. Kusumam.V.N, Additional Professor, Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala. She has 24 years of undergraduate and 21 years of postgraduate teaching experience. Speaker at CME programmes and chaired two sessions. Has five publications in indexed journals.

✉ Kusumam Vilangot Nhalil
vnkusumam1234@gmail.com

[1] Department of O&G, IMCH Govt Medical College, Kozhikode, Kerala, India

Table 1 Timeline of investigations

Gestational age (weeks)	Haemoglobin(g/dl)	Haematocrit (%)	Erythropoietin (mIU/ml)	Sonogram report
32	17.8	55.6		Single live intrauterine gestation (SLIUG), 32 weeks. Two fibroids seen: one at the left lateral wall and the other at the lower posterior wall measuring 20×16x12cm and 5×3 cm, respectively
33	18.7	57.7		
34	18.1	57.3		
35	17.9	56.7	80.4	SLIUG, 34 weeks, fibroid findings similar to 32 weeks
36	16.2 g% (after 5 venesections)	49.6% (after 5 venesections)	143	
Post op day2	11.8	39.7		
Post op day3	11	34.1		
Post op day 5	11.6	35.6		
Post op day 7			8.81	

Treatment History

The patient presented with lower limb cellulitis which was managed with antibiotics and regular dressing. Pre-eclampsia was managed with antihypertensives. She was given heparin as there was increased risk of thromboembolism. She underwent phlebotomy on alternate days, five times prior to surgery, and gradually achieved a haematocrit of 49.6% and haemoglobin of 16.2 g%

Termination of Pregnancy

At 36 weeks of gestation, she underwent classical caesarean section, for pre-eclampsia and unfavourable cervix and delivered a healthy baby of 2.9 kg, after obtaining the consent for surgery and publication. Per-operative examination showed a 20×25 cm size fibroid arising from the lower uterine segment extending into broad ligament on the right side (Figs. 1 and 2) for which myomectomy was followed by sterilization. Specimen was sent for histopathology confirmation and reported as leiomyoma uterus. Post-operative period was eventful with Hb falling to 11 g/dl and haematocrit to 34.1% by second post-operative day. She was discharged on 12th post-operative day. At the time of discharge, erythropoietin level fell to 8.81mIU/ml.

Figure1 Classical caesarean section showing placenta in situ after delivery of the baby with myoma in the lower segment

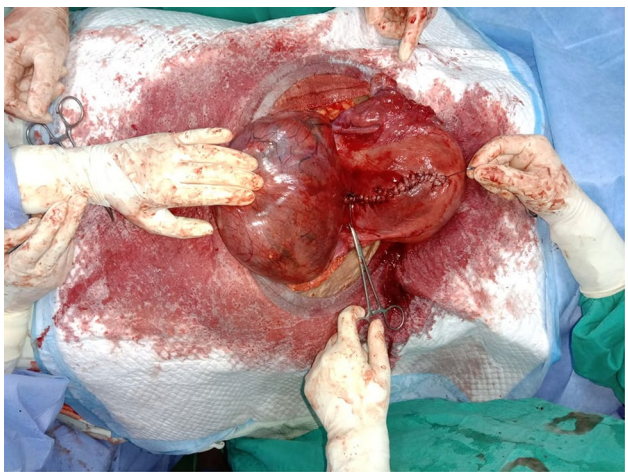

Fig. 2 Myoma in the lower segment with sutured classical caesarean section incision

Discussion

Our case is MES in pregnancy, not much details available in the literature except one case just mentioned by Pollio F et al. MES affects women of wide range of age with abdominopelvic and gynaec symptoms in addition to extra abdominal symptoms[1]. Therefore, screening of haemoglobin, haematocrit, and erythropoietin in a pregnant woman with fibroid may help practitioners make an accurate diagnosis of MES.

Initially, the etiopathogenesis of MES was thought to be the existence of myomatous arteriovenous shunts, interference with pulmonary ventilation or renal blood flow obstruction. These theories became invalid following the observation of erythropoietin production by myoma which is not subjected to any negative feedback mechanism [3]. Ryoko Asano et al. were able to demonstrate Epo immunoexpression in a large myoma [3]. Epo-mRNA was confirmed in tissue samples. Apart from confirming Epo production by myoma smooth muscle cells in MES, a characteristic strong Epo-R expression in myoma endothelial cells and a weak and sporadic Epo-R expression in myoma smooth muscle cells were noticed. Probably, this will explain the progressive rise in Hb and Epo in our case. The role of Epo in MES highlights the potential for targeted molecular therapy like an Epo inhibitor or Epo receptor antagonist that can be given locally into the myoma. This may result in a less invasive and effective therapy for MES.

The present case and others in the literature have shown the association of MES with large-sized fibroids. Although the mechanism is unknown, roles of endogenous growth factors, transforming growth factor beta in extracellular matrix accumulation, and remodelling have been implicated. Epo has other functions which include angiogenesis, mitogenesis, and inhibition of apoptosis by autocrine and paracrine mechanisms. The angiogenic factor of Epo may promote neovascularization to meet increasing demands and facilitate delivery of endogenous growth factors which are necessary for fibroid growth [3].

Polycythaemia is an important risk factor for vaso-occlusive complications. This risk significantly increases with surgical management of MES like myomectomy and hysterectomy. Here comes the importance of pre-operative interventions like venesection and hydration [1, 4].

The most common approach of management in MES is hysterectomy [2]. A recent study by Gordon et al. had successfully treated a case of MES with uterine artery embolization in non-gravid uterus. In our case, we were successful in preserving the uterus by classical caesarean section and myomectomy. The first myomectomy for MES was done by Horwitz and McKelway. Since then, additional 8 cases were successfully treated with myomectomy. This is probably among the first few cases in the literature where MES in pregnancy was successfully treated with myomectomy.

Conclusion

MES is a rare complication of leiomyoma, still more rare during pregnancy. Pregnancy-related prothrombotic state and hyper-viscosity of MES predispose to thromboembolism. Early diagnosis and proper pre-operative management including venesection have a vital role in preventing such complications. A rise in erythropoietin and haemoglobin during pregnancy and fall of both after delivery and myomectomy occurred in this patient. Similar case report is not available in the literature. Even though the exact aetiology for MES remains elusive, the finding of production of erythropoietin and expression of Epo-R by leiomyoma opens scope for new modalities of treatment. The main limitation of the study is that there is no immunohistochemical and genetic proof of the Epo/Epo-R in the resected leiomyoma for want of investigation facility.

Compliance with ethical standards

Informed consent Informed consent was obtained from the patient for surgery and publication of the study. There are no conflicts of interest, and the report do not involve research on animals.

References

1. Mui J, Yang MM, Cohen T, McDonald DI, Hunt H. More than a myoma: a review of myomatous erythrocytosis syndrome. J Obstet Gynaecol Canada. 2020;42(2):198–203.
2. de Guzman GS, Manalo EM. Myomatous erythrocytosis syndrome: a case series. Case Rep Women's Health. 2019;1(24):e00139.
3. Asano R, Asai-Sato M, Miyagi Y, Mizushima T, Koyama-Sato M, Nagashima Y, Taguri M, Sakakibara H, Hirahara F, Miyagi E. Aberrant expression of erythropoietin in uterine leiomyoma: implications in tumor growth. Am J Obstet Gynecol. 2015;213(2):199-e1.
4. Suresh P, Rizk S. Myomatous erythrocytosis syndrome: case report and review of the literature. Cureus. 2020 12(2).

About the Author

Kusumam Vilangot Nhalil Is Additional Professor, Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala. She has 24 years of undergraduate and 21 years of postgraduate teaching experience. She is speaker at CME programmes and chaired two sessions. She has five publications in indexed journals.