



Myomatous erythrocytosis syndrome: A case series

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ARTICLE INFO

Article history:

Received 25 July 2019

Received in revised form 18 August 2019

Accepted 19 August 2019

Keywords:

Myoma
Erythrocytosis
Uterine fibroids

ABSTRACT

Uterine leiomyomas are tumor-associated causes of secondary erythrocytosis. Ectopic erythropoietin production by fibroid smooth muscles has been proposed and demonstrated in the literature. Here, we present three cases of large leiomyomas with an incidental finding of isolated erythrocytosis on preoperative workup. Two patients underwent total abdominal hysterectomy while one patient underwent a myomectomy. Both histologic examination confirming the diagnosis of leiomyoma and serial complete blood counts showing normalization of post-operative hemoglobin levels together with isolated erythrocytosis constitute the criteria to fulfill a diagnosis of myomatous erythrocytosis syndrome. All three criteria were observed in the three cases described. To date, fewer than 40 cases have been reported worldwide. These are the first reported cases of myomatous erythrocytosis syndrome in the Philippines.

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1. Introduction

Leiomyomas or uterine fibroids are the most common solid tumors in women. Women over 45 years of age have an estimated 60% lifetime risk of having fibroids, based on recent longitudinal studies. Associated risk factors include family history, race, age, menopausal status, obesity, and consumption of food additives [1,2]. Although 40–60% of those affected remain asymptomatic, some present with abnormal uterine bleeding, pelvic pain or pressure symptoms, reproductive dysfunction, and a pelvic mass [3]. Rarely, hemoglobin and hematocrit levels are elevated, owing to ectopic production of erythropoietin.

Thomson and Marson were the first to describe this condition, in 1953. Since then, three criteria have been used to diagnose myomatous erythrocytosis syndrome: isolated erythrocytosis, myomatous uterus, and restoration of normal hematologic values after a myomectomy or hysterectomy [4]. According to a review by LevGur and Levie, fewer than 40 cases of myomatous erythrocytosis syndrome have been reported in literature over the past six decades [5].

1.1. Case series

1.1.1. Case 1

A 46-year-old nulliparous postmenopausal woman consulted with a one-year history of a gradually enlarging hypogastric mass associated with intermittent hypogastric pain. She had congestive heart failure (functional class I) from hypertensive heart disease. She noted

occasional exertional dyspnea. Her family medical history was unremarkable. She had had her menarche at 13 years old and subsequent menses had been regular and monthly until the age of 45.

The patient was overweight, with a body mass index (BMI) of 26.3 kg/m². She was not plethoric, and systemic physical examination findings were normal. On pelvic examination, the cervix was flushed and deviated anteriorly, and the corpus was enlarged to 26 weeks' size. Abdominopelvic ultrasound showed an enlarged uterus with a large subserous myoma with intramural component (FIGO Grade 5) which measured 28.2 × 22.0 × 6.3 cm at the posterior corpus. Color flow of the mass showed absent vascularity. A complete blood count showed isolated erythrocytosis, with a hemoglobin level of 197 g/L and hematocrit of 0.58. Serum erythropoietin was elevated at 29.53 (normal range: 2.59–18.5). 2D echocardiography showed concentric remodeling of the left ventricle with mildly depressed systolic function and Grade I diastolic dysfunction from chronic hypertension.

The patient was referred to the hematology service to rule out any blood dyscrasia and for preoperative clearance. Jak-2 mutation assay was negative; hence, polycythemia vera was ruled out. She was started on hydroxyurea 500 mg once daily. Venesection was done twice. She was cleared for exploratory laparotomy, and total hysterectomy with bilateral salpingectomy.

On admission, repeat hemoglobin and hematocrit were 213 g/L and 0.62, respectively. Venesection was done every other day to obtain a hematocrit of 0.55. Pelvic magnetic resonance imaging (MRI) showed a well-defined, slightly enhancing mass with smooth margins measuring 20.7 × 20.4 × 12.4 cm (Fig. 1) and color flow of the mass showed absent vascularity. The mass exhibited good planes of differentiation from the adjacent structures. The primary consideration was a leiomyoma. The patient underwent surgery on the 7th hospital day.

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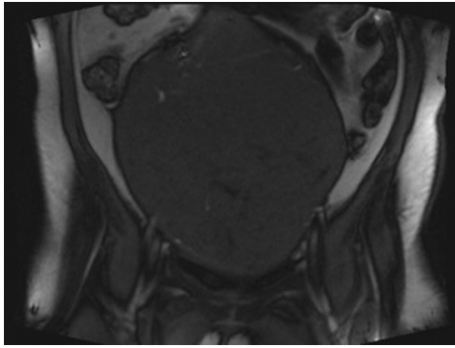


Fig. 1. Magnetic resonance imaging shows a well-defined, slightly enhancing mass with good planes of differentiation from adjacent pelvic structures.

Intraoperatively, the uterus measured $22.5 \times 23.5 \times 17.0$ cm and had a smooth serosal surface. There was a well-circumscribed mass at the cervicocorporeal junction measuring $18.0 \times 18.5 \times 12.0$ cm (Fig. 2). This mass displaced the uterine corpus superiorly. It had a whorled pattern on cut section, with no areas of hemorrhage or necrosis. The endometrium was 0.2 cm thick. The rest of the abdominopelvic organs were grossly normal.

The patient tolerated the procedure well and had an unremarkable postoperative course. She was discharged with normalized values of hemoglobin and hematocrit, at 144 g/L and 0.44.

1.1.2. Case 2

A 45-year-old nulliparous postmenopausal woman had a two-year history of a gradually enlarging abdominopelvic mass associated with pelvic pain. She had a 15-year history of uninvestigated primary infertility. Family medical history was unremarkable. Menarche had been at 12 years of age, and subsequent menses were regular and monthly until the age of 44. There was no history of increase in menstrual flow or duration.

On pelvic examination, the corpus was enlarged to 24 weeks' size. The rest of the findings on systemic physical examination were essentially normal. Pelvic ultrasound showed a $22.7 \times 21.3 \times 20.2$ cm

well-circumscribed heterogeneous mass at the fundal portion of the uterus, subserous with <50% intramural component (FIGO Grade 6). Color flow mapping of the mass showed absent vascularity. Hemoglobin was shown to be elevated at 184 g/L with a hematocrit of 0.55. Serum erythropoietin was increased to 24.63 (normal range: 2.59–18.5). She was cleared for surgery by the hematology service.

The patient underwent exploratory laparotomy and total hysterectomy with bilateral salpingo-oophorectomy with an unremarkable operative course. Intraoperatively, there was a subserous, lobulated mass at the fundal area measuring $28.0 \times 21.5 \times 19.0$ cm (Fig. 3a). The rest of the abdominopelvic structures were smooth and grossly normal. Cut section of the mass showed a trabecular pattern with no necrosis (Fig. 3b).

1.1.3. Case 3

A 27-year-old nulliparous premenopausal woman presented with a three-year history of gradually enlarging abdominopelvic mass associated with pelvic pain. There were no associated menstrual disturbances or bowel movement changes.

She had a BMI of 22.1 kg/m². On pelvic examination, the cervix was deviated to the right and posteriorly. The corpus was enlarged to 24–26 weeks' size. Pelvic ultrasound (Fig. 4a) showed a well-circumscribed, lobulated heterogeneous mass measuring $34.5 \times 14.9 \times 8.6$ cm at the left anterolateral uterine wall, intramural with subserous component (FIGO Grade 6). Baseline hemoglobin was 174 g/L while the hematocrit was 0.53. She was cleared by the hematology service for surgery. She was given three doses of GnRH agonist monthly to induce amenorrhea while awaiting elective surgery. The patient was offered ulipristal acetate but had no funds to procure the medication.

The patient underwent open myomectomy. There was a $30.0 \times 25.5 \times 9.0$ cm well-circumscribed mass at the left lateral uterine wall, with a subserous intraligamentary component (Fig. 4b). No compromise to the endometrium was noted. Cut section showed a whorled pattern with no areas of necrosis or hemorrhage. Both adnexa were grossly normal. The patient tolerated the procedure well.

1.1.4. Informed Consent

Informed consent was obtained from all three patients.



Fig. 2. There was a well-circumscribed mass at the posterior isthmic area, displacing the corpus superiorly. Cut section showed a whorled pattern.

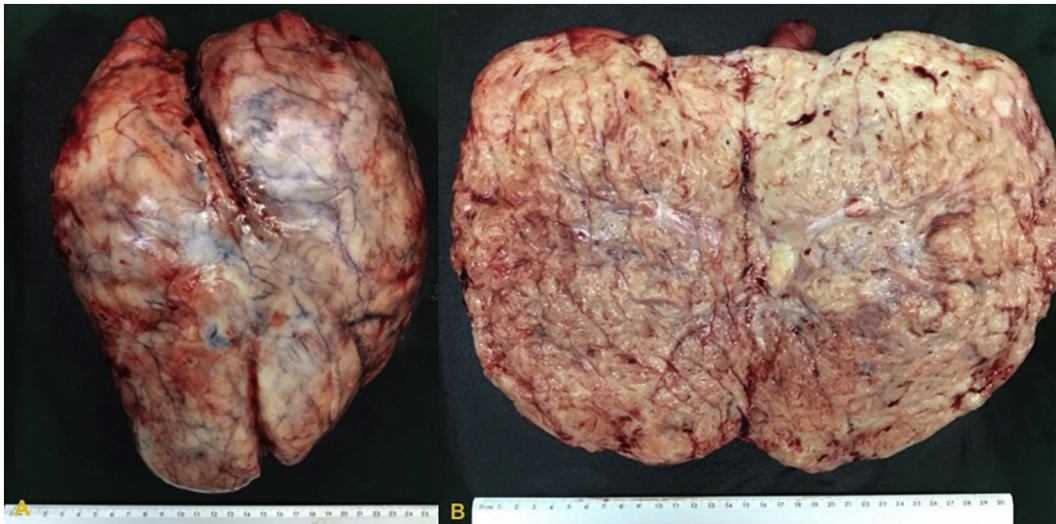


Fig. 3. A 28.0 × 21.5 × 19.0 cm firm, well-circumscribed mass at the fundal area, subserous. Cut section showed a trabeculated surface with no areas of hemorrhage or necrosis.

2. Results

All three cases had histopathologic confirmation of myoma uteri with postoperative normalization of hemoglobin and hematocrit levels. Serum erythropoietin levels returned to normal as well. These cases fulfilled the criteria for the diagnosis of myomatous erythrocytosis syndrome.

3. Discussion

3.1. Myomatous Erythrocytosis Syndrome

Isolated erythrocytosis has been shown to result from ectopic production of erythropoietin (Epo) in various malignancies, including renal cell and hepatocellular carcinoma. It has been found to occur in benign tumors such as cerebellar hemangioblastoma and adenomas. It is less commonly associated with uterine leiomyoma [4].

Various mechanisms have been proposed to explain this occurrence. One hypothesis is the autonomous production of erythropoietin by the leiomyoma, which is not subjected to any negative feedback mechanism [4]. Suzuki and colleagues documented this through radio-immunoassay studies in 2001 [6]. Epo mRNA expression in the tissue

samples was confirmed through reverse transcription polymerase chain reaction. Ectopic erythropoietin production accounts for the large sizes of leiomyoma encountered in this syndrome through its mediation of angiogenesis, mitogenesis, and inhibition of apoptosis [7].

3.2. Preoperative Management

The etiology of isolated erythrocytosis must be identified and secondary causes identified in collaboration with hematology services. Secondary causes include chronic respiratory disease and polycythemia vera. The possibility of polycythemia vera or a myeloproliferative disorder should be confirmed through Jak2 mutation testing. Serum erythropoietin levels may likewise be checked with considerations of EPO-mediated entities [8].

Risks for thrombosis, embolizations, and other cardiovascular complications should be considered prior to surgery. Preoperative planning should be undertaken to minimize or avoid these complications and may involve venesection, as was undertaken in case 1. This may be done once or twice weekly to reduce hematocrit levels to below 0.60 [9,10]. Hemoglobin levels returned to normal immediately after surgery and were maintained on subsequent outpatient visits.

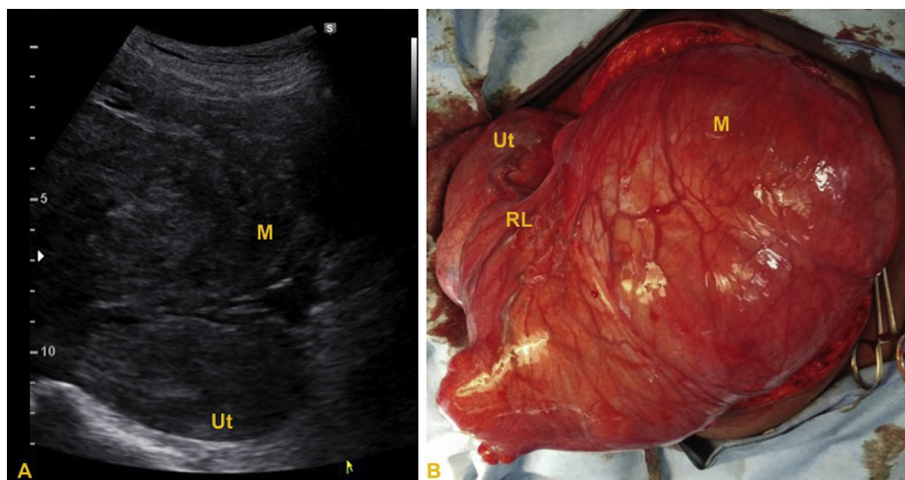


Fig. 4. A: Pelvic ultrasound shows a well-circumscribed, lobulated heterogeneous mass at the left anterolateral uterine wall, intramural with subserous component; B: Intraligamentary myoma stretching the round ligament at the left uterine wall. Ut = uterus, M = myoma, RL = round ligament.

4. Conclusion

All reported gynecologic tumors associated with erythrocytosis have been shown to be benign. Awareness of the association between uterine leiomyoma and erythrocytosis is important for patient counseling and appropriate preoperative planning. Various hormonal mechanisms involved in this condition must be explored to guide workup and treatment strategies. To date, these are the first reported cases of myomatous erythrocytosis syndrome in the Philippines.

Contributors

The two authors co-managed the patients and co-wrote the article.

Funding

No funding was received from an external source.

Patient consent

Obtained.

Provenance and peer review

This case report was peer reviewed.

Declaration of Competing Interest

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

References

- [1] E.A. Stewart, C. Cookson, et al., Epidemiology of uterine fibroids: a systematic review, *BJOG Int. J. Obstet. Gynaecol.* 124 (10) (2017) 1501–1512.
- [2] V. Tanos, K.E. Berry, Benign and malignant pathology of the uterus, *Best Pract. Res. Clin. Obstet.* 46 (2018) 12–30.
- [3] S.S. Singh, L. Belland, Contemporary management of uterine fibroids: focus on emerging medical treatments, *Curr. Med. Res. Opin.* 31 (1) (2015) 1–2.
- [4] O. Yosuke, T. Hidaka, K. Fukuta, et al., A case of myomatous erythrocytosis syndrome associated with a large uterine leiomyoma, *Case Rep. Obstet. Gynecol.* (2014) <https://doi.org/10.1155/2014/602139> Available at.
- [5] M. LevGur, M.D. Levie, The myomatous erythrocytosis syndrome: a review, *Obstet. Gynecol.* 86 (1995) 1026–1030.
- [6] M. Suzuki, S. Takamizawa, K. Nomaguchi, et al., Erythropoietin synthesis by tumour tissues in a patient with uterine myoma and erythrocytosis, *Br. J. Haematol.* 113 (1) (2001) 49–51.
- [7] F. Pollio, S. Staibano, G. Mansueto, et al., Erythropoietin and erythropoietin receptor system in a large uterine myoma of a patient with myomatous erythrocytosis syndrome: possible relationship with the pathogenesis of unusual tumor size, *Hum. Pathol.* 36 (2005) 120–127.
- [8] M.F. McMullin, Idiopathic erythrocytosis: a disappearing entity, *Hematology* (1) (2009) 629–635.
- [9] J. Shibata, J. Hasegawa, H. Siemens, et al., Hemostasis and coagulation at a hematocrit of 0.85: functional consequences of erythrocytosis, *Blood* (2003) <https://doi.org/10.1182/blood-2002-09-2814>.
- [10] F.A. Khan, R.A. Khan, M. Iqbal, Polycythemia vera: Essential management protocols, *Anesth. Pain Intensive Care* 16 (1) (2012) 91–97.