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Polycythemia in a Patient with a Large Retroperitoneal Leiomyoma

AUTHORS:
Lilley EJ[a]; Yu W[b]; Roland CL[a]

CORRESPONDING AUTHOR:
Christina L. Roland, MD, MS, FACS
Department of Surgical Oncology
The University of Texas MD Anderson Cancer Center
1400 Pressler Street
Unit 1484
Houston, TX 77030
Email: clroland@mdanderson.org

AUTHOR AFFILIATIONS:
a. Department of Surgical Oncology
The University of Texas MD Anderson Cancer Center
Houston, TX 77030

b. Department of Pathology/Laboratory Medicine The University of Texas MD Anderson Cancer Center
Houston, TX 77030

Background	A 41-year-old female presented with a new diagnosis of polycythemia vera accompanied by the incidental finding of a large retroperitoneal mass.
Summary	A 41-year-old woman presented with fatigue and increasing abdominal fullness. Initial workup with her primary care physician revealed severe anemia (hemoglobin 21 gm/dL), a 40 cm left retroperitoneal mass abutting and displacing the left kidney, and elevated serum erythropoietin. Imaging suggested retroperitoneal sarcoma, but preoperative biopsies indicated a well-differentiated smooth muscle neoplasm. The patient underwent surgical resection with en bloc partial nephrectomy, and final pathology confirmed the diagnosis of retroperitoneal leiomyoma of Müllerian origin. Postoperatively, her hemoglobin and erythropoietin levels normalized. This case highlights the potential for erythropoietin secretion from extrauterine leiomyomas, mirroring a mechanism observed in some uterine fibroids and likely contributing to tumorigenesis.
Conclusion	We present a case of polycythemia and elevated serum erythropoietin levels in a patient with a large retroperitoneal leiomyoma. This finding suggests a potential role for erythropoietin in the pathogenesis of this tumor type.
Key Words	leiomyoma; retroperitoneal tumor; myomatous erythrocytosis syndrome

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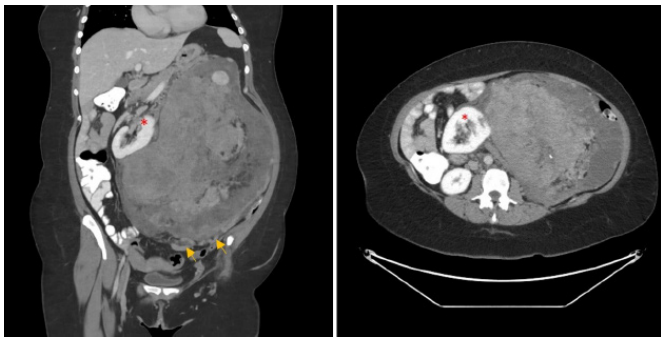
Case Description

Benign retroperitoneal smooth muscle tumors (BRSMTs), most often leiomyomas, are rare. They share histological similarities with uterine leiomyomas, including ER and PR positivity, suggesting a related pathogenesis that remains poorly understood. In approximately 60 reported cases, large uterine fibroids in women have been associated with erythrocytosis, likely due to erythropoietin production within these hormonally sensitive tumors.[1–5] A similar presentation was recently documented in a patient with an extrauterine, intraperitoneal mass.[6] Here, we describe a rare case of polycythemia in a patient with a large retroperitoneal leiomyoma.

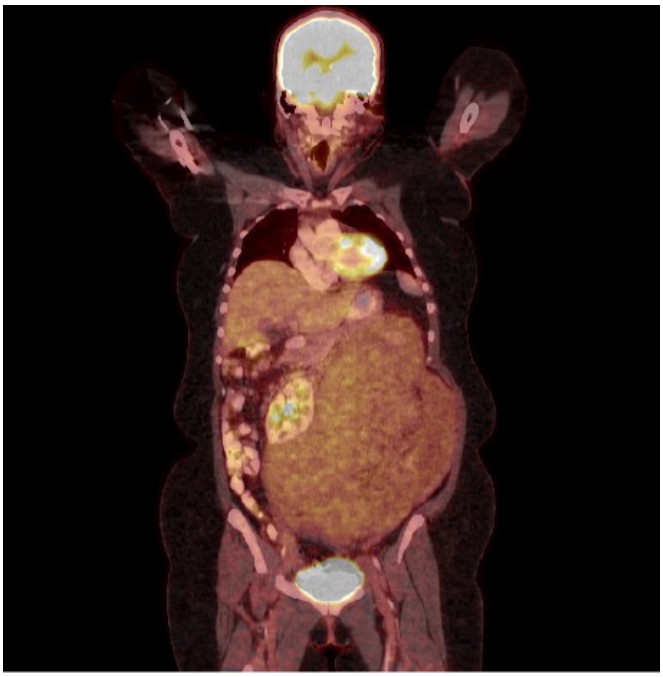
A healthy 41-year-old woman presented to her primary care physician with symptoms of fatigue, abdominal fullness, and early satiety. Initial workup revealed polycythemia (hemoglobin of 21 gm/dL). Abdominopelvic CT scan shown in Figure 1 demonstrated a large (32 × 27 cm), heterogeneously enhancing left retroperitoneal mass with significant mass effect on surrounding organs (left kidney, pancreas, spleen, and bowel). The patient's uterus appeared normal in size (11 × 5 cm) and morphology. PET-CT shown in Figure 2 showed diffuse heterogeneous activity (SUV up to 4.3). Core biopsy indicated a well-differentiated smooth muscle tumor with low mitotic activity, lacking nuclear atypia or necrosis. Immunohistochemical staining was positive for desmin, WT1, and PR (with patchy ER positivity) and negative for HMB45 (Figure 3). Fluorescence in situ hybridization (FISH) analysis ruled out MDM2 amplification. These findings strongly suggested a benign leiomyoma of Müllerian origin.

Figure 1. Coronal and Axial Abdominopelvic CT Images. Published with Permission



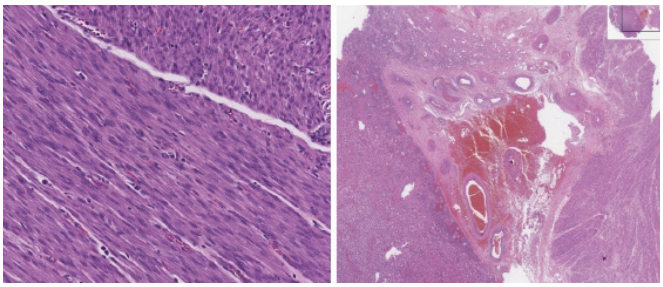
Large, complex left retroperitoneal mass with predominant solid components, peripheral cystic lesions, and interspersed foci of macroscopic fat and calcifications, demonstrating heterogeneous enhancement, displacement of the left kidney (*), and prominent peripheral vessels (arrows).

Figure 2. PET-CT Scan. Published with Permission



Large, predominantly retroperitoneal mass with heterogeneous FDG activity. The mass extends from the left upper quadrant to the superior pelvis, exhibiting concerning features for malignancy/sarcoma.

Figure 3. Histopathology of Well-differentiated Smooth Muscle Tumor. Published with Permission



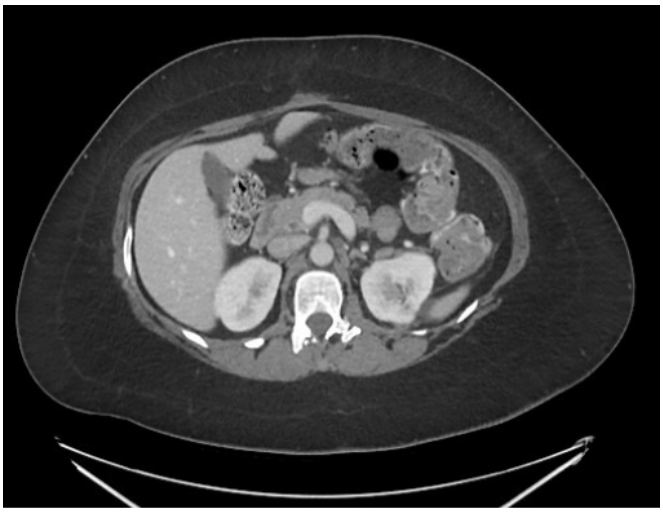
Immunohistochemical profile positive for desmin, WT1, PR (ER patchy); negative for HMB45, pan-melanoma, MDM2 amplification

The patient was referred to sarcoma surgical oncology due to a suspected retroperitoneal mass. Despite the patient's polycythemia, serum erythropoietin levels were elevated (22.0 mIU/mL, normal: 2.6–18.5 mIU/mL), suggesting a potential occult malignancy and prompting the decision for surgical resection. Preoperatively, the patient began aspirin 81 mg for prophylaxis against polycythemia-associated venous thromboembolism risk, also receiving

prophylactic heparin. Intraoperatively, the tumor was found beneath attenuated colonic mesentery (Figure 4), which was meticulously dissected off the tumor capsule. The descending colon was mobilized for retroperitoneal exposure, revealing numerous large vessels (up to 1 cm diameter) on the tumor capsule. Partial nephrectomy was required due to focal adherence to the kidney's upper pole. The 46 × 31 × 15 cm specimen was confirmed as a retroperitoneal leiomyoma upon pathologic evaluation.

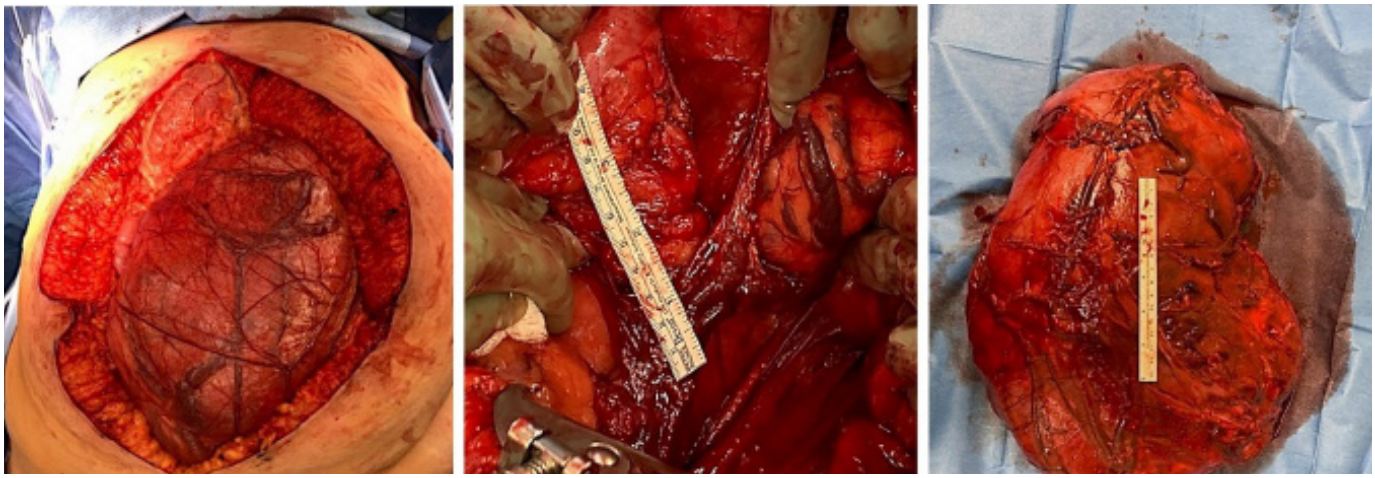
The postoperative course was uneventful, and the patient was discharged home on the fourth hospital day. Two months later, follow-up laboratory tests confirmed a return to normal values, with a hemoglobin level of 12.7 gm/dL and erythropoietin at 11.4 mIU/mL. A CT scan performed eight months after the resection demonstrated no signs of disease recurrence (Figure 5).

Figure 5. Postoperative CT Scan (axial view), 8 Months Status Post-resection. Published with Permission



Abdominal viscera have returned to normal position. No evidence of tumor recurrence.

Figure 4. Intraoperative Visualization of Retroperitoneal Tumor. Published with Permission



From left to right: Well-encapsulated, attenuated colonic mesentery; prominent vessels around the periphery of the tumor (up to 1 cm diameter); final specimen dimensions: 46 × 31 × 15 cm

Discussion

We present a case where a patient exhibited new-onset polycythemia and was concurrently diagnosed with a large retroperitoneal leiomyoma. Although the patient's hemoglobin was elevated, serum erythropoietin levels were also high. Surgical resection led to the normalization of both values. Erythropoietin production by large uterine fibroids resulting in erythrocytosis is a rare but well-documented phenomenon;[2–5] similar cases exist in canine leiomyosarcomas.[7] Wang and colleagues recently reported on a patient with an extrauterine broad ligament leiomyoma causing polycythemia.[6] This case appears to be the first documented instance of polycythemia associated with a myomatous tumor specifically located within the retroperitoneum.

Retroperitoneal smooth muscle tumors can derive from somatic soft tissue (including vessels) or Müllerian/gynecologic tissue. While the majority possess somatic origins and are often malignant, Müllerian-derived retroperitoneal leiomyomas are extremely rare and pose diagnostic challenges. These leiomyomas typically occur in perimenopausal women, with 40% of patients presenting with concurrent uterine fibroids (or a history of hysterectomy due to fibroids).[8] Their development is likely from embryonal remnants of Müllerian or Wolffian ducts or hormonally responsive smooth muscle.[9] While capable of significant growth (2-37 cm, mean 12 cm),[10,11] symptoms may be subtle, with 31% of cases solely presenting with abdominal fullness and 89% having a palpable mass at diagnosis.[11]

Confirming a diagnosis of retroperitoneal leiomyoma necessitates comprehensive tumor sampling and meticulous histological analysis. These tumors closely resemble uterine fibroids, exhibiting smooth muscle cells with eosinophilic cytoplasm, minimally atypical cigar-shaped nuclei, absent necrosis, and extremely limited mitotic activity (usually <3 per 50 high-power fields).[12] They lack vascular association and are often paucicellular; larger tumors may demonstrate hyalinization, fibrosis, calcification, and other degenerative changes.[10,12] Tumor cells almost always express estrogen and progesterone receptors, supporting their Müllerian origin, while positive SMA, desmin, and h-caldesmin staining reaffirms smooth muscle differentiation. Importantly, they lack CD117, DOG1, S-100 protein, and HMB45 expression, helping to exclude other potential diagnoses that may show similar morphology, such as gastrointestinal stromal tumor (GIST), peripheral nerve sheath tumor or perivascular epithelioid cell neoplasms (PEComa).[9,10,12] Surgical resection is usually curative.

The present case is remarkable due to the large tumor size and the concurrent diagnosis of polycythemia. This raises the possibility of erythropoietin playing a role in both pathologies. Myomatous erythrocytosis syndrome (MES), first described in 1953,[13] is a rare condition where erythrocytosis occurs in women with uterine fibroids and resolves after hysterectomy.[4,14] Only around 60 cases are reported in English literature.[2,4] Large fibroid size appears correlated with MES development, with one series indicating an average size of 22.6 cm and weight of 4.9 kg.[4] Estrogen and progesterone potentially regulate erythropoietin production in endometrial cells, which promotes angiogenesis[15] and acts on myoblasts to promote cell proliferation and prevent apoptosis.[1] In patients with MES, fibroid tissues have been shown to produce erythropoietin and expression of the erythropoietin receptor (EPOR), suggesting an autocrine/paracrine role for erythropoietin in tumor development.[3]

Our findings suggest a potential link between EPOR expression and tumor progression. This aligns with prior research identifying EPOR in malignant breast tumors[16,17] and those of the female reproductive system.[18] Though we did not analyze the patient's leiomyoma tissue for erythropoietin/EPOR, the swift and persistent resolution of polycythemia and the normalization of serum erythropoietin levels post-resection endorses the likelihood that ectopic tumor secretion of erythropoietin drove the development of polycythemia. Moreover, erythropoietin's angiogenic and mitogenic properties could explain this tumor's exceptional vascularity and size. Autocrine/paracrine effects on smooth muscle tumor cells expressing both EPOR and erythropoietin may have contributed to increased proliferation. The correlation between tumor size and erythrocytosis development in both this patient and others with MES implies that only large tumors generate sufficient erythropoietin to induce systemic effects and drive hematopoiesis. Further study is warranted to confirm these hypotheses and ascertain the role of erythropoietin in smooth muscle tumor development.

Conclusion

Elevated serum erythropoietin levels in individuals with large retroperitoneal leiomyomas can manifest as polycythemia. The mechanism likely involves erythropoietin secretion by hormonally responsive leiomyoma cells, mirroring observations in patients with uterine fibroids. While complete surgical resection resolves polycythemia and carries minimal recurrence risk, further investigation

is required to fully understand the role of erythropoietin in the pathophysiology of retroperitoneal smooth muscle tumors.

Lessons Learned

Polycythemia has been previously observed in the setting of large uterine leiomyomas and is thought to be related to autocrine/paracrine effects of erythropoietin and expression of EPOR. While the tumor's size and imaging characteristics raised concerns about malignancy, multiple biopsies confirmed a benign leiomyoma of Müllerian origin. This extremely rare tumor's preoperative diagnosis significantly aided surgical planning, allowing safe kidney preservation. Further investigation is warranted to explore the potential role of erythropoietin and EPOR in the development of this unusual tumor type.

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