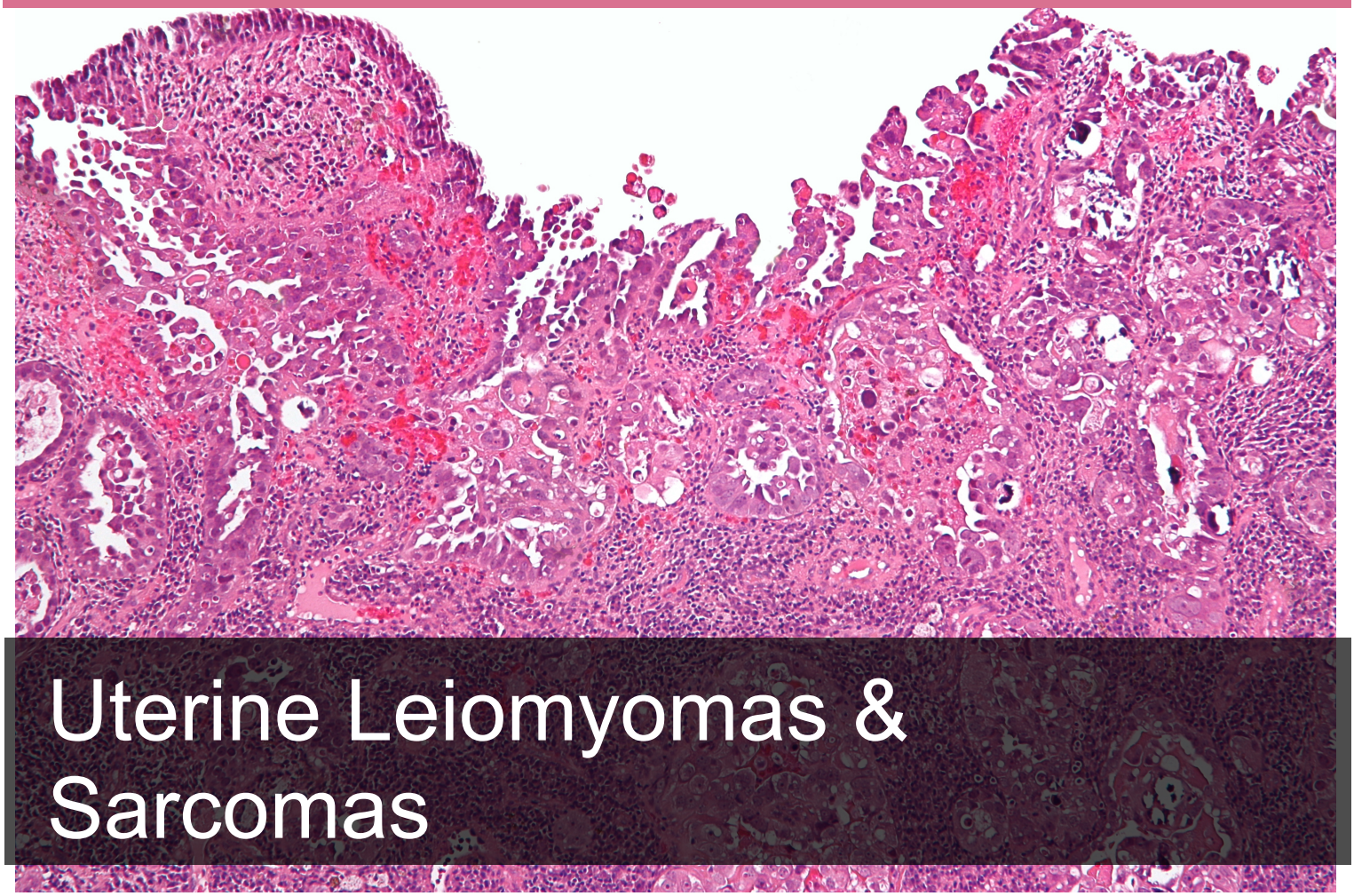

Uterine Leiomyomas & Sarcomas

429 OB/GYN Team

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UTERINE LEIOMYOMA

INTRODUCTION

- Uterine leiomyomas ("fibroids") are benign tumors derived from the smooth muscle cells of the myometrium
- They are the **MOST COMMON NEOPLASM OF THE UTERUS**
- Estimates are that **> 45%** of women have leiomyomas by the 5th decade of life
- Most are **asymptomatic**
    - If symptomatic: can cause excessive **uterine bleeding**, **pelvic pressure** and **pain**, as well as **infertility**
- They can grow to impressive sizes, but their malignant potential is <0.1%
- Risk factors for developing leiomyomas include:
    - **Increasing age during the reproductive years**
    - Ethnicity (**african-american**)
    - **Nulliparity**
    - **Family** history
    - Oral contraceptive pills and depot medroxyprogesterone acetate (dmpa) injections may be associated with **reduced risk**

PATHOGENESIS

- Factors that initiate leiomyomata are not known
- **Ovarian sex steroids are important for their growth**
    - **Regress after menopause** (unless stimulated by exogenous hormones)
    - Can also **enlarge during pregnancy**
    - Have increased levels of estrogen and progesterone receptors
    - Leiomyomas also have higher levels of **growth factors** that stimulate the production of **fibronectin** and **collagen** (major components of the extracellular matrix that characterizes these lesions)

CHARACTERISTICS

PATHOLOGY

- Spherical, **well-circumscribed**, white, firm lesions with a whorled appearance on cut section. Usually <15 cm in size.
- Does not have a true cellular capsule
- Few blood vessels and lymphatics traverse the pseudocapsule → ***degenerative*** changes as the tumors enlarge
- The most commonly observed degenerative change is: **HYALINE ACELLULARITY**
    - Fibrous and muscle tissues are replaced with hyaline tissue

- **Cystic degeneration** may occur when the hyaline substance breaks down from a further reduction in blood supply
- **Calcification** may occur in degenerated fibroids, particularly after the menopause.
- **Fatty degeneration** (rare)
- During **pregnancy** 5-10% of women with fibroids undergo a **painful** **RED DEGENERATION** caused by **hemorrhage** into the tumor

SITES

- **Leiomyomas arise within the myometrium (intramural)**, but some **migrate** toward the serosal surface (**subserosal**) or toward the endometrium (**submucosal**)
- *Tumors may develop large pedicles*
  - The **submucosal** leiomyomas can extend through the cervical os
    - Aborting leiomyomata cause significant **bleeding & cramping pain**
  - A **subserosal** leiomyoma on a long pedicle can present as a **mass**
    - Pedunculated subserosal myomata attach to the blood supply of the omentum/bowel mesentery and become **parasitic** leiomyomas
- Leiomyomas can also arise in the cervix, in the broad ligament (intraligamentous), and in the supporting ligaments (round or uterosacral)

SYMPTOMS

- The majority of uterine leiomyomas cause **NO SYMPTOMS**
- Develops insidiously
- Lower abdominal **mass** if it protrudes above the pelvis
- Pelvic pressure, congestion, bloating, a feeling of heaviness in the lower abdomen, or **lower back pain**
- **Frequency, constipation**
- **Urinary retention** and hydronephrosis (**rare**)
- **Menorrhagia** (w/intramural or submucosal tumor)
  - Excessive bleeding → **Anemia**, weakness, dyspnea, and CHF
- **Metrorrhagia** (w/submucous myomas ulcerating through the endometrial lining)
- **Dysmenorrhea**
- **Dyspareunia** (common with incarceration)
- ↑ incidence of **infertility, 2nd trimester abortions**

Fibroids are not generally painful, but severe pain may be associated with red degeneration (acute infarction) within a fibroid. This most commonly occurs during pregnancy.

Most common symptom is: Abnormal uterine bleeding

SIGNS

- On bimanual pelvic examination: a **firm**, **irregularly enlarged uterus** with smoothly rounded protrusions may be felt if subserosal or intramural
- **Nontender** – unless red degeneration
- **Moves with the cervix**

- Very large fibroids can be palpated abdominally
- Those smaller than a 12-14-week gestational size are confined to the pelvis
- Consistency: rock hard (if calcified/postmenopausal), soft or even cystic
- **Ultrasound** can help distinguish adnexal masses from laterally placed myomas

DIFFERENTIAL DIAGNOSIS

Other uterine pathology e.g. uterine sarcoma or other process: inflammation

1. **Ovarian neoplasm**
2. **Tubo-ovarian inflammatory mass**
3. **Pelvic kidney**
4. **Diverticular or inflammatory bowel mass**
5. **Cancer of the colon**

Imaging:
1. Abdominal or TV U/S
2. For intra-cavitary:
   a. Hysteroscopy
   b. Hysterosalpingogram
   c. Sonohysterography

U/S: visualize the fibroids and identify normal ovaries

Adenomyosis usually results in a **uniformly enlarged uterus** ≠ leiomyoma

MANAGEMENT

- If a small asymptomatic fibroid is detected → repeat U/S within 6 months to rule out **uterine sarcoma**.
- If menorrhagia is the chief complaint → endometrial aspiration/fractional dilatation and curettage (D&C)

MEDICAL MANAGEMENT

- **Menorrhagia** may be managed **hormonally**
  - **Progestin-only therapies** or **combination hormonal contraceptive** methods 1st line
    - The goal:
      - Reduce monthly menstrual blood loss with **cyclic** methods
      - Eliminate menses with extended/**continuous** use
  - **GnRH agonists**: effictive in blocking ovarian steroidogenesis →
    - Stops endometrial proliferation → ↓ volume of myometrium & leiomyomas
    - The effects disappear soon after the drug is stopped
    - Only **SHORT COURSES**, administered in preparation for myomectomy or hysterectomy - because of the intense **vasomotor symptoms** and the deleterious they have on **bone mineral density**
    - Intermittent GnRH-agonist ↓ side effects + achieving therapeutic goals
    - GnRH agonists + hormonal agents may minimize some adverse effects of hypoestrogenism (such as osteoporosis)

- **Selective antiprogesterone receptor antagonist** (mifepristone) to reduce the size of uterine myomas without producing the changes in bone density noted with GnRH agonists

SURGICAL MANAGEMENT

- To treat leiomyoma that is not responsive to medical management.
- Indications:

Clinical Presentation	Nonmedical Options	Comments
Desired fertility	Embolization or myomectomy	Usually used for a limited number of leiomyomata
Desires uterine preservation or poor surgical risk	Endometrial ablation or embolization	Embolization only for a limited number of leiomyomata
No desired fertility or uterine preservation	Endometrial ablation or hysterectomy	Hysterectony is definitive therapy
Rapidly growing uterus (double in size in 6 months)	Exploratory laparotomy, abdominal hysterectomy	More extensive surgery if malignancy discovered

- **Myomectomy is the preferred surgical procedure for women with a limited number of tumors who desire uterine preservation**.
  - Hysteroscopically (for submucous masses) or transabdominally (laparoscopically/laparotomy) for other leiomyomas.
  - Pretreatment for 3 months with GnRH agonists and the use of vasoconstrictive agents intraoperatively may improve surgical outcomes
  - Not all the tumors may be removed, and new leiomyomata may grow in the future (25% of women will require a subsequent operation)
  - If the endometrial cavity is entered during myomectomy, future deliveries must be by **cesarean**
- **Hysterectomy** provides **definitive therapy**.
  - **I**f the uterus is large (>12 to 14 cm) → **laparotomy**
  - If the uterus is not bulky and the vagina is not constricted → **vaginal hysterectomy**
    - Laparoscopically assisted vaginal hysterectomy permits excellent visualization of the adnexae and controlled dissection
  - **Rapid growth** of a uterus caused by leiomyoma (doubling in size in <6 months) may be the result of **leiomyosarcoma** → **hysterectomy**
- Other therapies (especially for women who desire uterine preservation)
  - **Embolization of the uterine arteries supplying the leiomyomas**
    - Effective in the short term for controlling bleeding and to shrink the myomas.
  - **Endometrial ablation with hysteroscopic resection, laser ablation**, or roller ball
    - This approach may be appropriate for women who are poor candidates for more extensive surgery

UTERINE SARCOMAS

- 3% of uterine cancers
- They arise from the stromal components of the uterus, either the endometrial stroma or the mesenchymal and myometrial tissues.
- Sarcomas tend to be more advanced at the time of diagnosis, are more likely to disseminate **hematogenously**, and have much lower 2-5 year survival rates

CLASSIFICATION

1. Pure: the only malignant tissue is of mesenchymal origin (majority are leiomyosarcomas and endometrial stromal sarcomas)
2. Mixed: malignant mesenchymal and malignant epithelial tissues are present

Or

1. Homologous: the tissue that is malignant is normally present in the uterus (e.g., endometrial stroma, smooth muscle)
2. Heterologous: the tissue that is malignant is not normally present in the uterus (e.g., bone or cartilage)

LEIOMYOSARCOMA

- The risk of malignant transformation in a benign fibroid is **less than 1%.**
- The histologic criteria for distinguishing leiomyosarcomas from leiomyomas are
  - The **mitotic count** (usually > 10/10 high-power fields)
  - The presence or absence of coagulative necrosis
  - The presence or absence of cellular atypia
- Clinically: the
  - Mean age of patients with leiomyosarcoma is ~55 years.
  - May present with
    - Pelvic **pain**
    - **Abnormal uterine bleeding**
    - Pelvic or lower abdominal **mass**
    - **Pressure** on the bladder or rectum

- The lung is the most frequent site for metastasis
- Must obtain CXR to exclude lung metastases
- IVP to exclude involvement of urinary tract

- Most cases are discovered at the time of exploratory surgery for a probable fibroid.
- Curettings are usually normal.
- If a known fibroid uterus appears to be rapidly enlarging, especially postmenopausally, malignancy should be suspected.
- Treatment:
  - Total abdominal hysterectomy and bilateral salpingo-oophorectomy
  - Adjuvant pelvic radiation ↓ local pelvic recurrence but does not prolong survival because most patients die with distant metastases.
  - Response rates to chemotherapy are very low

ENDOMETRIAL SARCOMA

- The three types of stromal tumors are

1. ENDOMETRIAL STROMAL **NODULE**

- It is rare benign condition
- <3 mitoses/10-high power field
- Hysterectomy is curative

2. ENDOMETRIAL STROMAL **SARCOMA**

- Previously known as endolymphatic stromal myosis
- Low-grade lesion
- Histologically: minimal to no cellular atypia, with <5 mitoses/10 high-power fields
- There is always evidence of **vascular channel invasion**.
- Patients usually present with: **abnormal vaginal bleeding** and **pelvic pain**
- Rx: total abdominal hysterectomy and bilateral salpingo-oophorectomy (usually curative)
    - Local and distant **recurrences** may occur even 10 to 20 years later
    - Prolonged survival is possible after resection of recurrent disease
    - Response to progestins is good
    - Pelvic disease may respond to **radiation** therapy

3. HIGH-GRADE ENDOMETRIAL SARCOMA

- High-grade endometrial sarcoma generally
- Causes **abnormal uterine bleeding**
- > 50% of the patients are **premenopausal**
- Dx: endometrial **biopsy** or uterine **curettage**
- Histologically: >10 mitoses/10 high-power fields, and very poorly differentiated cells
- Aggressive myometrial invasion occurs, and ***hematogenous spread is common at the time of diagnosis***
- Rx: total abdominal hysterectomy and bilateral salpingo-oophorectomy.
    - A thorough exploration of the **peritoneal cavity and retroperitoneum** should be made for evidence of **metastases**
    - Postoperative pelvic irradiation
    - In patients with metastatic disease, **progestogens or chemotherapy** may be offered
    - The best chemotherapeutic agents are cisplatin, doxorubicin, and ifosphamide
    - Prognosis is poor

MIXED MÜLLERIAN TUMORS

- 40% of uterine sarcomas
- Up to 50% of patients with this lesion have evidence of metastatic disease at the time of diagnosis if surgically staged
- Uterine sarcomas are poor because of the propensity for hematogenous dissemination
- The overall 5-year survival rate is about 35%