Patient presents w/ symptoms suggesting leiomyoma or asymptomatic leiomyoma is discovered upon pelvic exam or imaging

2. DIAGNOSIS
   Do pelvic exam & diagnostic tests confirm leiomyoma?

   Yes
   Is patient symptomatic but leiomyomas growing rapidly?

   No
   CLINICAL DECISION
   Is uterine size <16 wk & other causes of pelvic mass have been excluded?

   No
   EXPERT REFERRAL

   Yes
   CLINICAL DECISION
   Should patient be managed medically or surgically?

   No
   MEDICAL MANAGEMENT
   See next page

   Yes
   SURGICAL MANAGEMENT
   See next page

   C
   Patient observation

   ALTERNATIVE DIAGNOSIS

   No
Leiomyomas (2 of 5)

MEDICAL MANAGEMENT OF LEIOMYOMA

Pharmacotherapy
- Gonadotropin releasing hormone (GnRH) analog x up to 6 mth w/ or w/o estrogen-progestogen add-back therapy
- GnRH antagonist

SURGICAL MANAGEMENT OF LEIOMYOMA

Should patient receive pre-surgical pharmacotherapy?

Yes

No

Surgey
- Myomectomy
- Hysterectomy
- Endometrial ablation
- Myolysis
- Magnetic resonance-guided focused ultrasound surgery (MRgFUS)

A178

Leiomyomas
- Benign tumors of the uterus that consist of smooth muscle & extracellular matrix collagen & elastin
- Most common solid pelvic tumors & one of the most frequent clinical condition encountered in gynecologic practice
- Most prevalent & tend to grow during reproductive yr & usually regress during menopause
- Malignant transformation is extremely rare

Signs & Symptoms
- About 50% of fibroids are asymptomatic
- Abnormal uterine bleeding clinically manifests as menorrhagia leading to iron deficiency anemia
- Pelvic mass & pelvic pressure symptoms: Increased abdominal girth, urinary frequency, urinary incontinence, dysuria, hydrenephrosis, constipation, tenesmus
- Non-cyclic pelvic pain, dyspareunia & dysmenorrhea
- Obstetric complications: Rapid growth of the fibroid, red degeneration & pain, reproductive dysfunction, spontaneous miscarriage

DISEASE PRESENTATION

Leiomyomas
- Pelvic exam may reveal a palpable enlarged, firm & irregular uterus
- Myomatous uterus size is reported in menstrual wk as is a pregnant uterus
- Size of >12- to 20-wk may be palpated on abdominal exam
- Diagnosis can be difficult in obese women

DIAGNOSIS

Physical Exam
- Pelvic exam may reveal a palpable enlarged, firm & irregular uterus
- Myomatous uterus size is reported in menstrual wk as is a pregnant uterus
- Size of >12- to 20-wk may be palpated on abdominal exam
- Diagnosis can be difficult in obese women

Diagnostic Tests
- Transvaginal ultrasound (TVS): Accurate in excluding endometrial hyperplasia, but often unable to distinguish submucosal fibroids & polyps
- Transvaginal sono-hysterography (TVSH): Should be considered if submucous fibroids & polyps are suspected
- TVSH may avoid the need for diagnostic hysteroscopy in approximately 47% of women who can then proceed to a planned operative hysteroscopy
- Magnetic resonance imaging (MRI): May be considered in women in whom the location & nature of the fibroids remain unclear after TVS & TVSH
- May also be used in those who wish to avoid discomfort of TVSH

Differential Diagnosis
- Pregnancy, adenomyosis, ovarian neoplasm

Not all products are available or approved for above use in all countries. Specific prescribing information may be found in the latest MIMS.
**PHARMACOTHERAPY**

**Indications for Medical Treatment**
- Preserve fertility in women with large leiomyomas prior to attempting conception
- Treatment of women near menopause in an effort to avoid surgery
- Women with medical contraindications to surgery
- Personal or medical indications for delaying surgery
- Option as stand-alone treatment for temporary symptom relief
- Can be given as a preoperative adjunct to reduce the size of fibroids, control bleeding & improve hemoglobin levels

**Medical Treatment of Leiomyomas**

**Gonadotropin Releasing Hormone (GnRH) Analogs**
- Most established & successful pharmacological management of myomas
- Best suited for women in the perimenopausal or preoperative periods
- **Actions:** Down-regulate GnRH receptors at the pituitary level resulting in significant reductions in follicle stimulating hormone (FSH), luteinizing hormone (LH) & ovarian steroids, thus producing a hypoestrogenic state
- **Effects:**
  - Maximal diminution of uterine & myoma size is achieved within the 1st 12 wk of therapy
  - Menorrhagia or related anemia are controlled after the 1st mth of treatment
  - Pressure symptoms are usually relieved in the 1st 2 mths
  - May induce amenorrhea in some women depending on the duration of use
- Approximately half of the women treated will experience leiomyoma regrowth within a few mths after treatment cessation
- Treatment duration should be no more than 6 mths
- Significant side effects stem from the state of hypoestrogenism manifesting clinically as hot flushes, headaches, vaginal dryness, depression & bone demineralization
- Side effects can be alleviated by add-back therapy using estrogen, progestin, or both. Addition of hormones however may limit the effectiveness in treating myoma
- Add-back therapy has been shown not to compromise the efficacy of GnRH agonists

**Pretreatment to Surgery**
- Pretreatment with GnRH analog for 2-4 mths for uterine fibroids is recommended for patients with large uterus (>18 wk size) or pre-op anemia
- **Effects:** Pre- & post-op Hb & Hct are significantly improved. Studies reported shrinkage of the fibroid w/ a reduction in median uterine volume of 31-39% & myoma volume decrease by 23-27%

**GnRH Antagonists**
- Eg Abarelix, Cetrorelix, Ganirelix
- Recently USFDA approved for clinical use
- Used as injectables, usually at doses of 5 mg twice daily for the initial 2 days followed by 0.8 mg twice daily for at least 3 mths
- **Actions:** Directly compete with endogenous GnRH for pituitary binding sites, suppressing gonadotropin release
- **Effects:** Result in a rapid decrease in myoma & uterine vol w/ minor side effects

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Leiomyomas (4 of 5)

Type of surgery will depend on patient’s age, patient preference, position & number of fibroids & patient’s desire to retain reproduction potential. Asymptomatic leiomyomas do not usually need surgery.

Indications for Surgical Treatment

- Anemia from abnormal uterine bleeding that is unresponsive to hormonal treatment
- Chronic pain (severe dysmenorrhea, dyspareunia or lower abdominal pressure/pain)
- Acute pain (prolapsing submucosal leiomyoma or torsion of pedunculated leiomyoma)
- Infertility w/ fibroids as the only abnormal finding
- Compression symptoms or discomfort from enlarged uterus
- Urinary symptoms (hydronephrosis after complete evaluation)
- Rapidly enlarging fibroids in the premenopausal patient or after menopause, enlarging myoma raises the risk of leiomyosarcoma even though it remains very rare

Hysterectomy

- Treatment of choice when leiomyosarcoma is detected
- May be considered in women w/ severe symptoms uncontrolled by other therapies
- Increases the risk for urinary stress incontinence & pelvic prolapse
- Hormone therapy is needed to prevent premature menopause

Abdominal Hysterectomy

- Associated w/ prolonged hospital stay

Laparoscopic Hysterectomy

- Benefits include less postoperative pain & faster recovery

Myomectomy

- Size & location of fibroids determines the most appropriate approach
- Approx 10% of women treated w/ myomectomy eventually require hysterectomy w/in 5-10 yr
- Exception are women who have had a previous pregnancy w/ complications related to fibroids

Abdominal Myomectomy

- Used to remove large or multiple fibroids that have grown deep into the uterine wall
- Requires the longest hospital stay & recovery time

Laparoscopic Myomectomy

- May be used to remove isolated fibroids ≤8 cm in diameter that have grown on the outside of the uterus
- Preferable over abdominal myomectomy in women who wish to preserve their reproductive potential
- Provides more rapid recovery & less postoperative complications

Hysteroscopic Myomectomy

- 1st-line therapy to remove fibroids that have grown from the uterine wall into the uterine cavity
- Least invasive & has the shortest recovery time

Endometrial Ablation

- Surgical procedure to destroy the entire uterine lining w/ electricity, laser, freezing, microwaves or radiofrequency energy
- May be employed when abnormal uterine bleeding is the main symptom & fertility is no longer desired

Uterine Fibroid Embolization (UFE)

- Percutaneous procedure that involves no general anesthesia or surgical incision
- Option for symptomatic women of reproductive age who are not interested in child-bearing
- Actions: Occlusion of uterine arteries, disrupts the blood supply to fibroids, leading to infarction
- Effects: Improvement in fibroid-associated symptoms, preservation of the uterus & obviation of the potential complications & lengthy recovery associated w/ surgery
- Studies w/ patient follow-up after 5-7 yr have shown that UFE provides durable symptom relief & improves quality of life
Leiomyomas (5 of 5)

SURGERY (CONT’D)

Myolysis & Cryomyolysis
- Considered a uterine-sparing alternative to myomectomy in select patients ≥40 yr who do not desire future fertility
- Myolysis employs a high-frequency electric current while cryomyolysis uses extreme cold to destroy the blood supply to the fibroids
- Cannot be performed if leiomyomas are >10 cm or <3 cm

Magnetic Resonance-Guided Focused Ultrasound Surgery (MRgFUS)
- Uses focused high-energy ultrasound to destroy fibroid tissue
- Volume reduction is less than the mean levels seen after both myomectomy & UFE
- Role has not been established in relation to other treatment modalities

All surgical alternatives to hysterectomy allow the formation of new leiomyomas & rapid growth of preexisting leiomyomas, which may eventually require hysterectomy

PATIENT OBSERVATION
- Record location of palpable leiomyomas
- Re-assess if new symptoms occur
- Periodic repeat exams to ensure tumors are not growing rapidly

Dosage Guidelines

GONADOTROPIN-RELEASING HORMONE ANALOGS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>Goserelin</td>
<td>3.6 mg depot inj SC into the anterior abdominal wall every 28 days</td>
<td>Adverse Reactions:</td>
</tr>
<tr>
<td></td>
<td>Administer w/ Fe supplement, Duration: Up to 3 mth prior to surgery</td>
<td>Hypoestrogenism that manifests as</td>
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<td></td>
<td></td>
<td>(transient vag bleeding, hot flushes, vag dryness, decreased libido, breast tenderness, insomnia, depression, irritability &amp; fatigue, decreased elasticity of the skin, headache, after several wk of treatment: osteoporosis; GI effects (nausea, abdominal discomfort). Other effects (transient increase in menstrual bleeding, reduction in glucose tolerance can develop, changes in serum lipids &amp; hepatic effects, hypersensitivity reactions))</td>
</tr>
<tr>
<td>Leuprorelin</td>
<td>3.75 mg depot inj SC/IM once monthly or 11.25 mg depot inj SC/IM as a single dose every 3 mth</td>
<td>Special Instructions: Add-back strategy w/ estrogen/progesterone can eliminate most of these side effects</td>
</tr>
<tr>
<td></td>
<td>Administer during the 1st 5 days of the menstrual cycle</td>
<td>- In later stages of treatment, pregnancy is unlikely as long as recommended doses are administered</td>
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<tr>
<td></td>
<td>Administer w/ Fe supplement, Duration: Up to 6 mth, may be used up to 3 mth prior to surgery</td>
<td></td>
</tr>
<tr>
<td>Triptorelin</td>
<td>3.75 mg depot inj SC/IM every 28 days or 0.5 mg SC inj/day for 7-10 days, followed by 0.1 mg SC inj/day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Start therapy during the 1st 5 days of the menstrual cycle</td>
<td>Duration: Up to 6 mth</td>
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All dosage recommendations are for non-elderly adults w/ normal renal & hepatic function unless otherwise stated.
Not all products are available or approved for above use in all countries.
Products listed above may not be mentioned in the disease management chart but have been placed here based on indications listed in regional manufacturers’ product information.
Specific prescribing information may be found in the latest MIMS.
Please see the end of this section for reference list.
Leiomyomas


