Imaging in the Diagnosis of Sarcoma Botryoides

Laura Chiel, HMS Year III
Gillian Lieberman, MD

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Objectives:

- To review the imaging studies of choice for pediatric GYN abnormalities.

- To examine the use of these studies in the diagnosis of sarcoma botryoides.

- To give a general overview of the key clinical and pathological features of sarcoma botryoides.
Our Patient: History of Present Illness:

- Mother of 18-month-old girl reports that she saw a growth coming out of her child’s vagina two days ago when changing her diaper.

- Pediatrician appreciated mass but did not know what it was.

- Denies changes in urination or bowel movements.

- Denies vaginal bleeding.

- Denies change in behavior, discomfort, changes in eating.

- Denies unwanted touching or abuse.

- Denies concern for foreign body in the vagina.

(HPI+PE from resident note.)
Our Patient: Physical Exam:

- Tanner stage I.

- The labia majora, clitoris, urethra, and hymen appear normal. The perineum appears normal without any skin lesions.

- 1-2cm round polypoid lesion protruding from the vagina.
  - Portion of the mass protruding from the vagina is red and purplish.
  - Closer to the hymenal ring, the mass appears lighter pink, thought perhaps to be a stalk or a smaller appendage on the larger mass.
  - Origin of mass is not clear.

- No bleeding or vaginal discharge.

(HPI+PE from resident note.)
Partial Differential Diagnosis for Interlabial Mass in All Ages:

• Urological
  – Prolapsed urethra
  – Urethral polyp

• Gynecological
  – Hemato(metro)colpos (imperforate hymen, vaginal atresia, vaginal septum)
  – Paraurethral cyst
  – Genital prolapse

• Malignant
  – Rhabdomyosarcoma of the vagina (sarcoma botryoides)
  – Clear cell adenocarcinoma
  – Germ cell tumor
Let’s continue to view the menu of tests available to distinguish between these diagnoses...
Ultrasound in Pediatric GYN Imaging:

- No ionizing radiation
- Bladder serves as an acoustic window
  - Good visualization of anatomy
- Color/ Doppler allow for further characterization
- Relatively inexpensive
- Peds friendly
- Operator dependent
- Less anatomic visualization in patients with increased body habitus or inability to fill bladder
MRI in Pediatric GYN Imaging:

- No ionizing radiation
- “Problem solver”
  - Allows further characterization of US findings and with greater specificity
- Expensive
Other Pediatric GYN Imaging Studies:

Other
Plain films - sometimes ordered first to assess acute abdominal pain
- Diagnosis of teratoma
- Lack of fine detail
- Radiation

CT
- Surgical planning
- Staging
- Radiation

Fluoroscopy
- Surgical planning
- Additional diagnostic yield
- Radiation
Laura Chiel, HMS III  
Gillian Lieberman, MD

ACR Appropriateness Criteria for GYN Imaging:

In our patient, transabdominal US would be more appropriate than transvaginal US, as our patient’s hymenal ring was in tact.

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<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically Suspected Adnexal Mass</td>
<td>US pelvis transvaginal</td>
<td>9</td>
<td>All three tests (TVS, TAS, and Doppler) may be performed depending on the clinical circumstances.</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>US pelvis with Doppler</td>
<td>9</td>
<td>All three tests (TVS, TAS, and Doppler) may be performed depending on the clinical circumstances. Color or power US is recommended, less so spectral Doppler.</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>US pelvis transabdominal</td>
<td>8</td>
<td>All three tests (TVS, TAS, and Doppler) may be performed depending on the clinical circumstances.</td>
<td>O</td>
</tr>
<tr>
<td>Reproductive age female (not pregnant) Initial evaluation.</td>
<td>MRI pelvis without and with contrast</td>
<td>6</td>
<td>See statement regarding contrast in text under “Anticipated Exceptions.”</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>MRI pelvis without contrast</td>
<td>5</td>
<td></td>
<td>O</td>
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<tr>
<td></td>
<td>CT pelvis without contrast</td>
<td>2</td>
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<td></td>
<td>CT pelvis with contrast</td>
<td>2</td>
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<td></td>
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<tr>
<td></td>
<td>CT pelvis without and with contrast</td>
<td>2</td>
<td></td>
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<tr>
<td></td>
<td>Image-guided aspiration or biopsy adnexal mass</td>
<td>2</td>
<td></td>
<td>Varies</td>
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<tr>
<td></td>
<td>FDG-PET/CT whole body</td>
<td>1</td>
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</tr>
</tbody>
</table>

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level
Let’s continue to view how these tests were used to help establish a diagnosis...
Partial Differential Diagnosis for Interlabial Mass in All Ages:

• **Urological**
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  – Urethral polyp

• **Gynecological**
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  – Paraurethral cyst
  – Genital prolapse

• **Malignant**
  – Rhabdomyosarcoma of the vagina (sarcoma botryoides)
  – Clear cell adenocarcinoma
  – Germ cell tumor
Our Patient: Sagittal Ultrasound:

Try to correlate our patient’s ultrasound with the anatomical drawing and see if you notice any abnormalities. Continue to the next slide for findings.
Our Patient: **Heteroechoic Lesion Expanding the Vaginal Vault on Sagittal Ultrasound:**

- **Bladder**
- **Uterus**
- **Endometrial stripe**

*Increased through transmission*
Our Patient: Heteroechoic Lesion Expanding the Vaginal Vault on Transverse Ultrasound
Our Patient: **Normal Appearing Ovary(*)** on Transverse Ultrasound:

The normal appearance of the **uterus and ovary** on US confirms that the disease process does not extend beyond the vaginal vault.
Partial Differential Diagnosis for Interlabial Mass in All Ages:

- **Urological**
  - Prolapsed urethra
  - Urethral polyp
  
- **Gynecological**
  - Hematómetrocolpos (imperforate hymen, vaginal atresia, vaginal septum)
  - Paraurethral cyst
  - Genital prolapse
  
- **Malignant**
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  - Germ cell tumor
Our Patient: **Pulsatile, Low Resistance Flow** on Transverse Ultrasound:

FR 6Hz
P1
2D
80%
C 62
P Med
Gen
CF
94%
500Hz
WF 52Hz
Med

PW
40%
WF 100Hz
SV2.0mm
M3
6.0MHz
3.3cm

Transverse US

CHB PACS
Partial Differential Diagnosis for Interlabial Mass in All Ages:

- **Urological**
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  - Germ cell tumor

Would not have flow in collection of blood → off ddx

Would not have blood flow in cyst → off ddx

Mann, et al. *Imaging of Gynecologic Disorders in Infants and Children*
Our Patient: Normal **Distal Urethra** on Ultrasound:

- Pubic symphysis
- Urethra
- Vaginal wall

**Heteroechoic mass in vaginal vault**

**Transverse US**

*FR 37Hz, RS Z 1.1, 2D, 64%, C 62, Pen, age: 58 of 51*
Partial Differential Diagnosis for Interlabial Mass in All Ages:

- **Urological**
  - Prolapsed urethra
  - Urethral polyp
- **Gynecological**
  - Hemato(metro)colpos (imperforate hymen, vaginal atresia, vaginal septum)
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  - Germ cell tumor

Anterior urethra normal in appearance on US

Mann, et al. *Imaging of Gynecologic Disorders in Infants and Children*
Our Patient: **Hyperintense Lesion with an Equivocal Stalk (*)** that Distends the Vaginal Vault on STIR MR:

Fluid is bright.  
Fat is dark.
Our Patient: **Septations and Loculations within the Vaginal Mass on MRI:**

Fluid is bright. Fat is dark.

This appearance could be consistent with myxoid tissue.
Our Patient: **Heterointense, “Spoke-Wheel” Enhancement of Vaginal Mass on MRI**

T1 Fat Saturated Axial MRI
CHB PACS
Our patient went for biopsy.
We’ll see how the MRI findings correspond with the biopsy findings in just a moment...
Our Patient: Operative Report:

“PRE-OPERATIVE DIAGNOSIS: 1. Intravaginal mass. 2. Need for venous access.

POST-OPERATIVE DIAGNOSIS: 1. Intravaginal mass. 2. Need for venous access.

PROCEDURES PERFORMED:
1. Perineal examination under anesthesia.
2. Anoscopy.
3. Cystourethroscopy
4. Vaginoscopy.
5. Resection of vaginal mass 7 x 6 x 5.5 centimeters.
6. Bilateral bone marrow biopsies performed by the oncology service.
7. Placement of #6 French PowerPort via modified Seldinger technique in the left subclavian vein using intraoperative fluoroscopy.

ANESTHESIA: General endotracheal with placement of a single-shot caudal and 10 milliliters of Marcaine 0.25% locally at the placement of the Port-A-Cath site.

COMPLICATIONS: None.

ESTIMATED BLOOD LOSS: 5 milliliters.

BLOOD ADMINISTERED: None.

PATHOLOGY SPECIMENS:
1. Intravaginal mass for frozen section consistent with rhabdomyosarcoma.
2. Intravaginal mass for permanent evaluation.”

(From the medical record)
Our Patient: Pathology Report:

1. Vaginal mass, #1, excision:
   - Embryonal rhabdomyosarcoma (sarcoma botryoides).
   - Abundant hemorrhage and necrosis.

2. Vaginal mass, #2, excision:
   - Embryonal rhabdomyosarcoma (sarcoma botryoides).
   - Sections show a population of tumor cells with a high N:C ratio, irregular nuclear contours, and patchy prominent eosinophilic cytoplasm. A submucosal zone of marked increased tumor cellularity (cambium layer) is seen with remaining tumor cells percolating through abundant watery/myxoid stroma. Scattered karyorrhectic debris and mitotic figures (11 per 10 high power fields) are seen.”
Sarcoma Botryoides: MRI Findings in Two Patients
Mariya Kobi, MD, Gaurav Khatri, MD, Morris Edelman, MD, and John

HISTORADIOLOGIC CORRELATION:
“Cystic” spaces: Solid myxoid stroma
Hyperintense on T2, Hypointense on T1

Septations: Infoldings of epithelial lining and cambium layer of tumor

Cambium layer: “hypercellular submucosal band of spindle-shaped tumor cells . . .
which lies just below the overlying usually intact epithelium of the involved viscus.”
Sarcoma Botryoides vs. Clear Cell:

Table 3
Key clinical and imaging features of uterine/vaginal neoplasms

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Key Clinical Features</th>
<th>Key Imaging Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhabdomyosarcoma</td>
<td>Cluster of grapes, central necrosis, locally aggressive</td>
<td>Central areas of decreased echogenicity due to necrosis</td>
</tr>
<tr>
<td>Clear cell</td>
<td>Maternal diethylstilbestrol use</td>
<td>Nonspecific imaging findings</td>
</tr>
</tbody>
</table>

Shah, et al. Imaging of Pediatric Pelvic Neoplasms
Our Patient: **Botryoid Appearance within Vaginal Mass on MR:**
Classification of Rhabdomyosarcoma:

Rhabdomyosarcoma

- Embryonal: 60-70%
- Botryoid
- Spindle
- Alveolar
- Anaplastic/Pleomorphic

Male:Female : 1.5:1

- Often present in the vagina/GU system
- Infants/children: vaginal
- Adolescence/reproductive: cervical
- Postmenopause: uterine
Rhabdomyosarcoma: Some Facts:

- Rhabdomyosarcomas originate from cells that turn into skeletal muscle cells under normal circumstance in places that normally do not have skeletal muscle.

- Rhabdomyosarcoma is the most common soft-tissue cancer in children; 3-4% of all childhood cancer.

- Rhabdomyosarcomas present in the head/neck (35-40%), GU tract (25%), and extremities (20%).
Different types of RMS may develop due to mutations at various points on this pathway.
Diagnosis and Work-Up:

Diagnostic biopsy

Staging Evaluation:
• Radiologic imaging
• Metastatic work-up
  • Bilateral bone marrow aspiration and biopsy
  • Chest CT
  • Radionuclide bone scan
• Lab Studies
  • Baseline CBC, electrolytes, BUN, LFTs, phosphorus, magnesium, uric acid, calcium
• Lymph node assessment
**International Rhabdomyosarcoma clinical classification in groups**

I
Localized disease, completely resected, no regional nodes involved

Ia
Confined to organ or muscle of origin

Ib
Infiltration outside organ or muscle of origin

II
Regional disease

IIa
Microscopic residual disease, no regional nodes involved

IIb
Regional disease, completely resected, nodes may be involved and/or extension of tumor into adjacent organ

IIc
Regional disease with involved nodes, grossly resected, but with evidence of microscopic residues

III
Incomplete resection or biopsy with gross residual disease

IV
Distant metastases present at onset

TNM Staging is used as well
Rhabdomyosarcoma: Prognosis and Treatment

Treatment is multi-modal and involves radiation, chemotherapy, and surgery. Recent initiatives are trying to reduce the amount of radiation exposure to children in order to diminish future risk of cancer, infertility, and other complications.

<table>
<thead>
<tr>
<th>Prognosis, (%)</th>
<th>Stage</th>
<th>Clinical group</th>
<th>Site</th>
<th>Size</th>
<th>Age</th>
<th>Histology</th>
<th>Mets</th>
<th>Nodes</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent (&gt;85)</td>
<td>1</td>
<td>I</td>
<td>Favorable</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0</td>
<td>VA + XRT</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>II</td>
<td>Favorable</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0</td>
<td>VA + XRT</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>III</td>
<td>Orbit only</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0</td>
<td>VA + XRT or XRT + VAC</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>I</td>
<td>Unfavorable</td>
<td>a</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or NX</td>
<td>VA</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>II</td>
<td>Favorable</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N1</td>
<td>VAC + XRT</td>
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<tr>
<td></td>
<td>1</td>
<td>III</td>
<td>Orbit only</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N1</td>
<td>VAC + XRT</td>
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<tr>
<td></td>
<td>1</td>
<td>III</td>
<td>Favorable, excluding orbit</td>
<td>a or b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or N1 or NX</td>
<td>VAC + XRT</td>
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<tr>
<td></td>
<td>2</td>
<td>II</td>
<td>Unfavorable</td>
<td>a</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or NX</td>
<td>VAC + XRT</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>I or II</td>
<td>Unfavorable</td>
<td>a</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N1</td>
<td>VAC + (XRT, 60 Gy)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>I or II</td>
<td>Unfavorable</td>
<td>b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or N1 or NX</td>
<td>VAC + XRT</td>
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<tr>
<td></td>
<td>2</td>
<td>III</td>
<td>Unfavorable</td>
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<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or NX</td>
<td>VAC + XRT</td>
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<td>Unfavorable</td>
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<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N1</td>
<td>VAC + XRT</td>
</tr>
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<td></td>
<td>3</td>
<td>III</td>
<td>Unfavorable</td>
<td>b</td>
<td>&lt;21</td>
<td>EMB</td>
<td>M0</td>
<td>N0 or N1 or NX</td>
<td>VAC + XRT</td>
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<td></td>
<td>1,2,3</td>
<td>I, II, III</td>
<td>Favorable or unfavorable</td>
<td>a or b</td>
<td>&lt;21</td>
<td>ALV/UDS</td>
<td>M0</td>
<td>N0 or N1 or NX</td>
<td>VAC + XRT</td>
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<td>4</td>
<td>I, II, III or IV</td>
<td>Favorable or unfavorable</td>
<td>a or b</td>
<td>&lt;10</td>
<td>EMB</td>
<td>M1</td>
<td>N0 or N1 or NX</td>
<td>VAC + XRT</td>
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<td></td>
<td>4</td>
<td>IV</td>
<td>Favorable or unfavorable</td>
<td>a or b</td>
<td>&lt;10</td>
<td>EMB</td>
<td>M1</td>
<td>N0 or N1 or NX</td>
<td>See text</td>
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<tr>
<td></td>
<td>4</td>
<td>IV</td>
<td>Favorable or unfavorable</td>
<td>a or b</td>
<td>&lt;21</td>
<td>ALV/UDS</td>
<td>M1</td>
<td>N0 or N1 or NX</td>
<td>See text</td>
</tr>
</tbody>
</table>

Favorable: orbit/ocular, head and neck (excluding parameningeal), genitourinary (not bladder or prostate), and biliary tract; Unfavorable: bladder, prostate, extremity, parameningeal, trunk, retroperitoneal, pelvis, other; a: tumor size 5 cm in diameter; b: tumor size >5 cm in diameter. EMB: embryonal, botryoid, or spindle-cell rhabdomyosarcomas or alveolar sarcomas with embryonal RMS; N0: regional nodes clinically not involved; N1: regional nodes clinically involved; N0: nodes status unknown. VAC: vincristine, actinomycin D, cyclophosphamide; XRT: radiotherapy; Topo: topotecan; Go: group; ALV/UDS: alveolar or undifferentiated sarcoma; EFS: event-free survival. Adapted with permission from: Raney RL, Anderson Jr, Barr FG, et al. Rhabdomyosarcoma and undifferentiated sarcoma in the first two decades of life: A selective review of Intergroup Rhabdomyosarcoma Study Group Experience and rationale for Intergroup Rhabdomyosarcoma Study V. J Pediatr Hematol Oncol 2001; 23:213. Copyright © 2001 Lippincott Williams & Wilkins.
Our Patient: Prognosis and Treatment

- Our patient had no metastasis at presentation and was found to be stage 1, group III.

- Mass was resected.

- 1 week later, chemotherapy with actinomycin, vincristine, and cyclophosphamide was initiated.

- At week 13, radiologic restaging will be performed.

- Despite aggressive treatment, our patient continues to develop and grow without complication.
Summary:

- The first line imaging study for pediatric GYN mass is US, followed by MRI.

- Imaging can help point towards and away from specific diagnoses.

- Sarcoma botryoides is a subtype of embryonal rhabdomyosarcoma that often presents in the GU tract.
References:

- Okcu MF, Hicks J, Horowitz M. Rhabdomyosarcoma and undifferentiated sarcoma in Childhood and adolescence: Clinical presentation, diagnostic evaluation, and staging. *UptoDate 7/12.*
- Okcu MF, Hicks J, Horowitz M. Rhabdomyosarcoma and undifferentiated sarcoma in Childhood and adolescence: Treatment. *UptoDate 7/13.*
- www.netterimages.com
Acknowledgements:

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