

Mesenchymal Tumors of the Urinary Bladder

Benign smooth-muscle tumors · true sarcomas · diagnostic mimics

A morphology-centered pathology lecture

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Learning objectives

- Distinguish benign bladder mesenchymal tumors from true sarcomas and spindle-cell mimics.
- Recognize the gross and microscopic features of leiomyoma, leiomyosarcoma, and embryonal rhabdomyosarcoma.
- Use architecture, cytology, lineage markers, and sampling context together.
- Explain why sarcomatoid carcinoma and inflammatory myofibroblastic tumor enter the differential.

A practical map of bladder mesenchymal lesions

Benign tumors

Leiomyoma predominates among uncommon benign mesenchymal bladder tumors.

True sarcomas

Embryonal rhabdomyosarcoma in children; Leiomyosarcoma in adults.

Diagnostic mimics

Sarcomatoid carcinoma and inflammatory myofibroblastic tumor may resemble sarcoma.

Where a mesenchymal tumor arises

Lumen
Urothelium
Lamina propria
Muscularis propria (detrusor)
Perivesical tissue

The principal lineages:

Surface epithelium →
epithelial lesions

Subepithelial & muscle
compartments →
mesenchymal lesions

Layer relationships are simplified; Not drawn to scale.

“Mesenchymal” is a lineage concept

- A mesenchymal tumor shows differentiation toward connective tissue, smooth muscle, or skeletal muscle.
- Gross configuration alone cannot prove the lineage of a bladder mass.
- Spindle-cell morphology is shared by neoplastic and non-neoplastic processes.
- Tissue architecture and differentiation are assessed together.

How common are these bladder tumors?

These comparisons are qualitative: Robbins gives no exact proportions here.

Benign mesenchymal

Uncommon even when all benign types are considered together.

True sarcoma

Distinctly uncommon within primary bladder neoplasia.

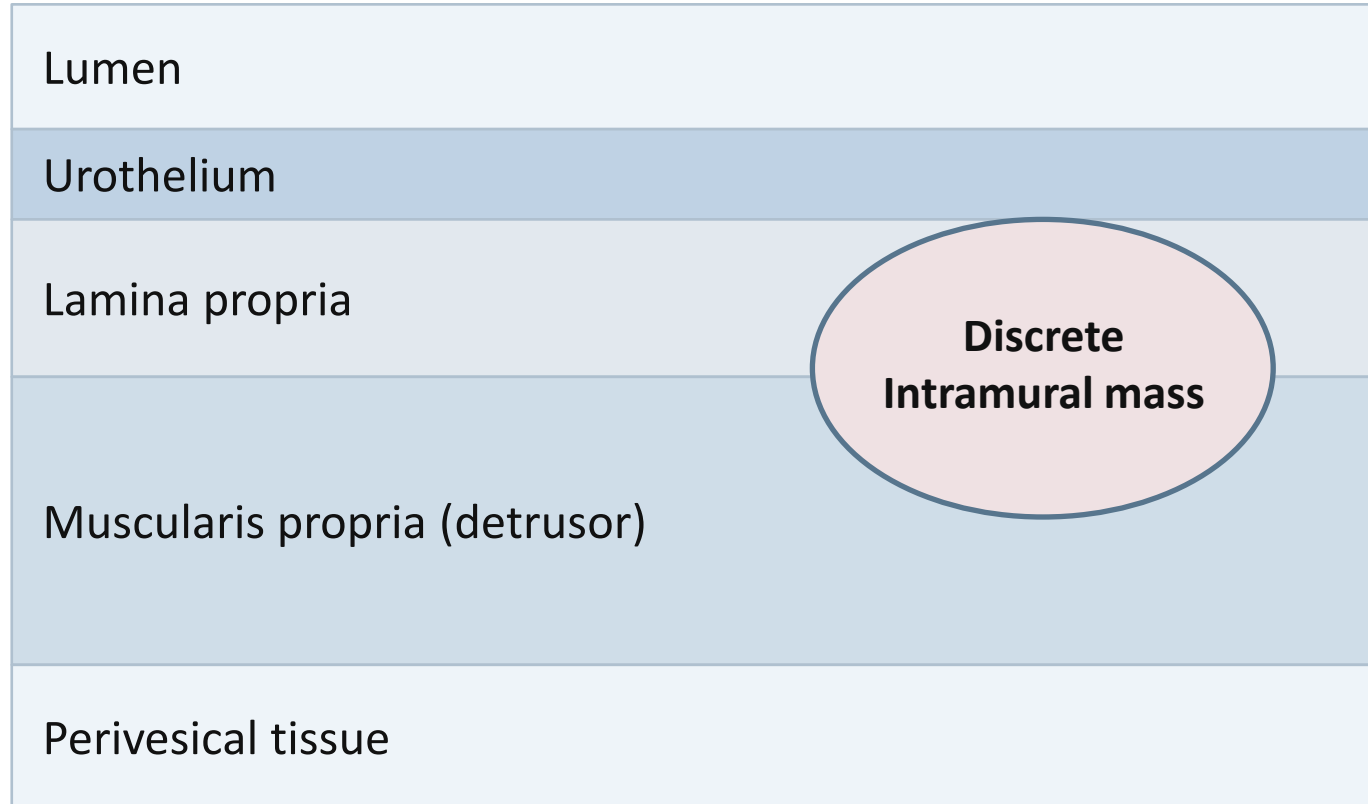
Other spindle-cell lesions

Inflammatory myofibroblastic tumors and sarcomatoid carcinomas exceed true sarcomas.

First diagnostic distinction

Category	What is established	Central question
Leiomyoma	Benign smooth muscle	Is the mass bland and circumscribed?
Leiomyosarcoma	Malignant smooth muscle	Are atypia, mitoses, necrosis and infiltration present?
Embryonal RMS	Malignant skeletal-muscle differentiation	Is primitive myogenic differentiation demonstrated?
IMT / sarcomatoid carcinoma	Potential sarcoma mimics	What is the true lineage?

Intramural (submucosal) location matters



Leiomyoma:

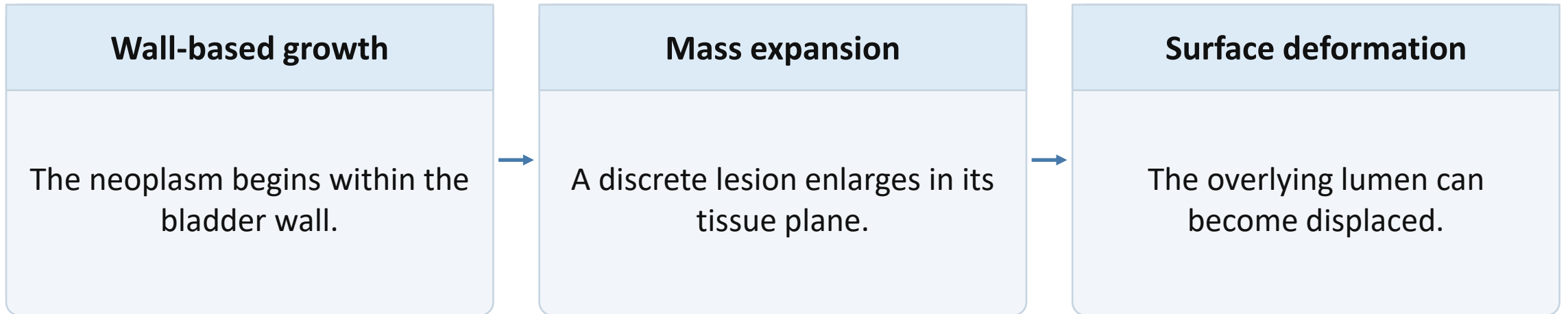
Usually
intramural/submucosal

Circumscribed and
encapsulated grossly

Layer relationships are simplified; Not drawn to scale.

Why a bladder wall lesion may protrude

Topographic interpretation of the gross description; Not a measured growth trajectory.



Two gross patterns: Benign versus malignant

Feature	Leiomyoma	True sarcoma
Typical boundary	Encapsulated / discrete	May form a bulky mass
Shape	Oval to spherical	Large protruding lesion
Texture	Smooth-muscle mass	Soft, fleshy, gray-white
Diagnostic value	Raises suspicion for benignity	Raises suspicion for malignancy

Benign mesenchymal tumors: The core statement

- Many benign mesenchymal tumor types can occur in the bladder.
- Their microscopic appearances resemble the same tumor types elsewhere.
- Collectively these benign bladder tumors are rare.
- Leiomyoma is the most common benign mesenchymal tumor of the bladder.

Leiomyoma: Concise diagnostic profile

Lineage

Benign neoplasm showing smooth-muscle differentiation.

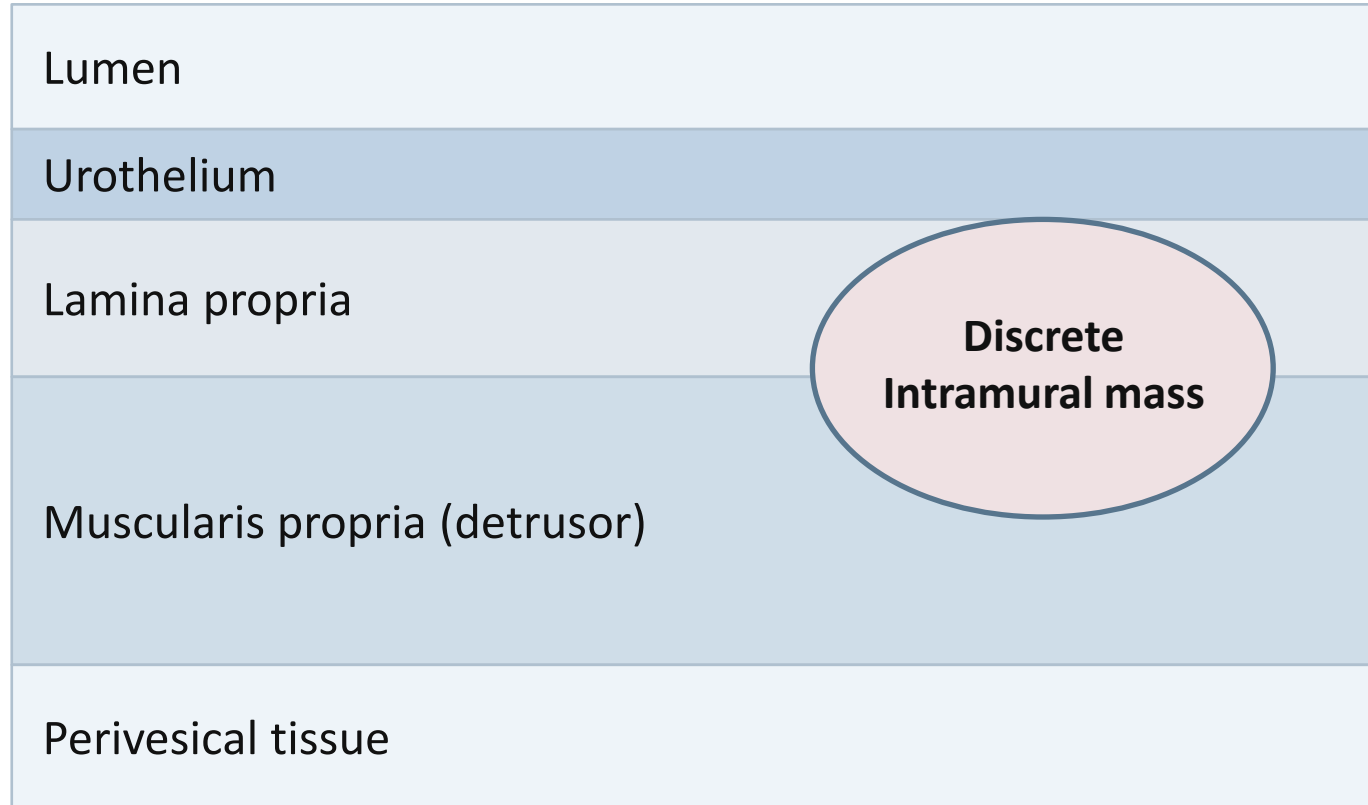
Gross pattern

Typically solitary, intramural, encapsulated and rounded.

Microscopy

Bland intersecting smooth-muscle fascicles with low mitotic activity.

Leiomyoma: Growth within the bladder wall



Leiomyoma:

Usually
intramural/submucosal

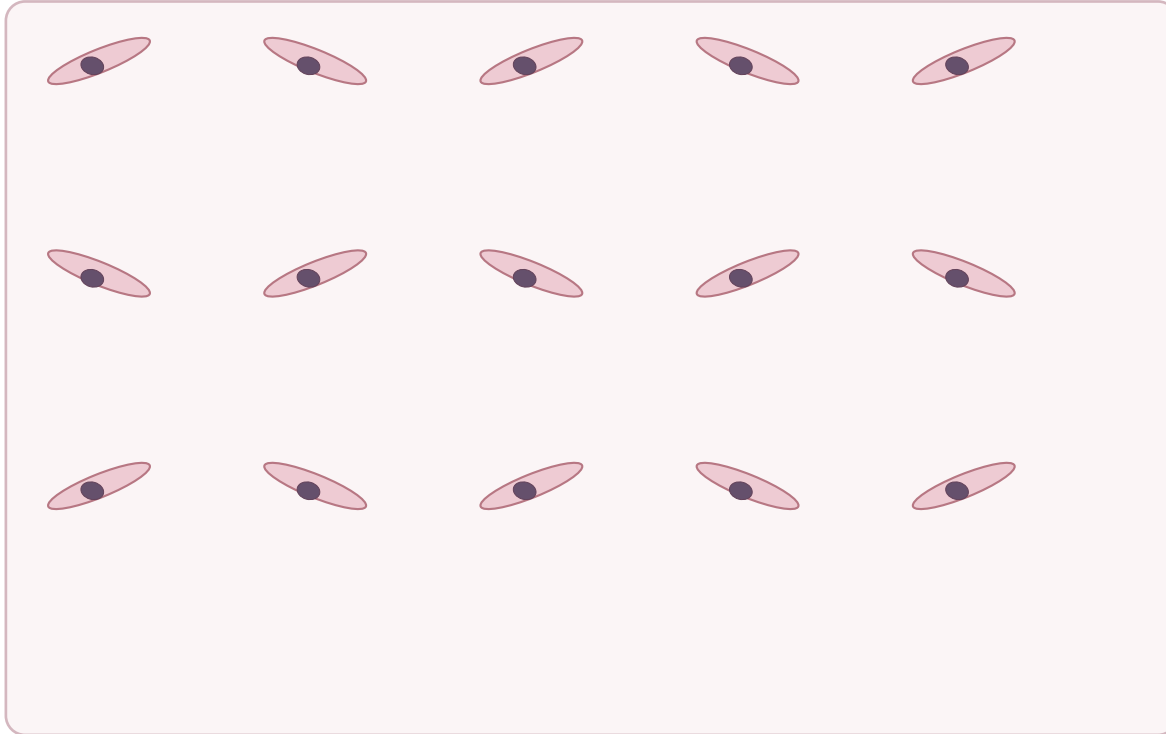
Circumscribed and
encapsulated grossly

Layer relationships are simplified; Not drawn to scale.

Leiomyoma: Gross characterization

- Bladder examples often appear as isolated masses.
- They occupy an intramural or submucosal position.
- Their contour is oval to spherical, with a distinct capsule.
- The size may reach several centimeters.

Leiomyoma: Intersecting fascicles



Schematic: Bland intersecting fascicles

Fascicles

Intersecting bundles of smooth muscle cells

Nuclei

Elongated, blunt-ended, relatively uniform

Cell behavior

Minimal atypia; Few mitoses

Leiomyoma: Microscopic cytology

- Cells have densely eosinophilic spindle-shaped cytoplasm.
- Nuclei are elongated and blunt-ended, with minimal atypia.
- Intersecting bundles create a smooth-muscle architectural pattern.
- Mitoses are few in the general soft-tissue leiomyoma description.

Leiomyoma: A three-part evidence pattern

A synthesis of morphology, not a validated numerical scoring system.

Architecture

Intersecting bundles of smooth-muscle cells.

Cytology

Relatively uniform elongated nuclei.

Proliferation

Few mitoses; No strong malignant morphologic pattern.

Tumor versus background detrusor

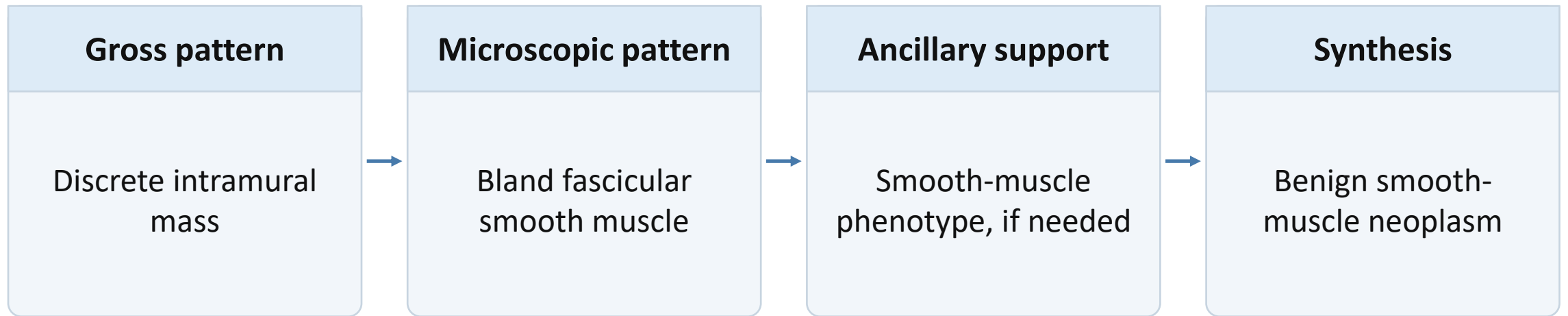
Observation	Why it matters
Mass-forming architecture	A neoplasm must be distinguished from native bladder smooth muscle.
Circumscribed border	Supports recognition of a discrete tumor.
Tumor cells resemble smooth muscle	Phenotypic resemblance does not alone establish benign behavior.
Adequate sampling	Required to assess the entire lesion for adverse features.

Leiomyoma: Immunophenotype is supportive

The markers are described for smooth-muscle tumors in Ch26; The interpretive limitations are an educational inference.

- Smooth-muscle markers document differentiation, not inherently benign behavior.
- Smooth muscle actin, desmin, and caldesmon are useful markers in smooth-muscle tumor evaluation.
- A positive smooth-muscle stain must be integrated with morphology.
- No single immunostain substitutes for assessing mitotic activity and atypia.

Leiomyoma: Diagnostic reasoning



Case A — an intramural bladder mass

An adult has a well-circumscribed intramural bladder mass. Resection shows interlacing fascicles of bland spindle cells, elongated blunt-ended nuclei, and few mitoses.

Interpretation questions

- What lineage do the microscopic findings support?
- Which features favor leiomyoma over leiomyosarcoma?
- What limitation would a small superficial biopsy create?

Case A — morphology-based interpretation

- Smooth-muscle differentiation is suggested by eosinophilic fascicular spindle cells.
- Circumscription, nuclear blandness, and low mitotic activity support leiomyoma.
- A limited biopsy can underrepresent heterogeneity or the lesion boundary.
- A final diagnosis depends on the full observed specimen, not the vignette alone.

Sarcomas: A rare but important category

- True primary sarcomas are distinctly uncommon in the bladder.
- A sarcoma is a malignant mesenchymal neoplasm, not simply a spindle-cell mass.
- Sarcomatoid carcinoma and inflammatory myofibroblastic tumor are more frequent imitators.
- Correct lineage assignment precedes tumor-specific interpretation.

Rarity does not imply a single morphology

Smooth-muscle malignancy

Leiomyosarcoma is the most common bladder sarcoma in adults.

Skeletal-muscle malignancy

Embryonal rhabdomyosarcoma is the most common in infancy and childhood.

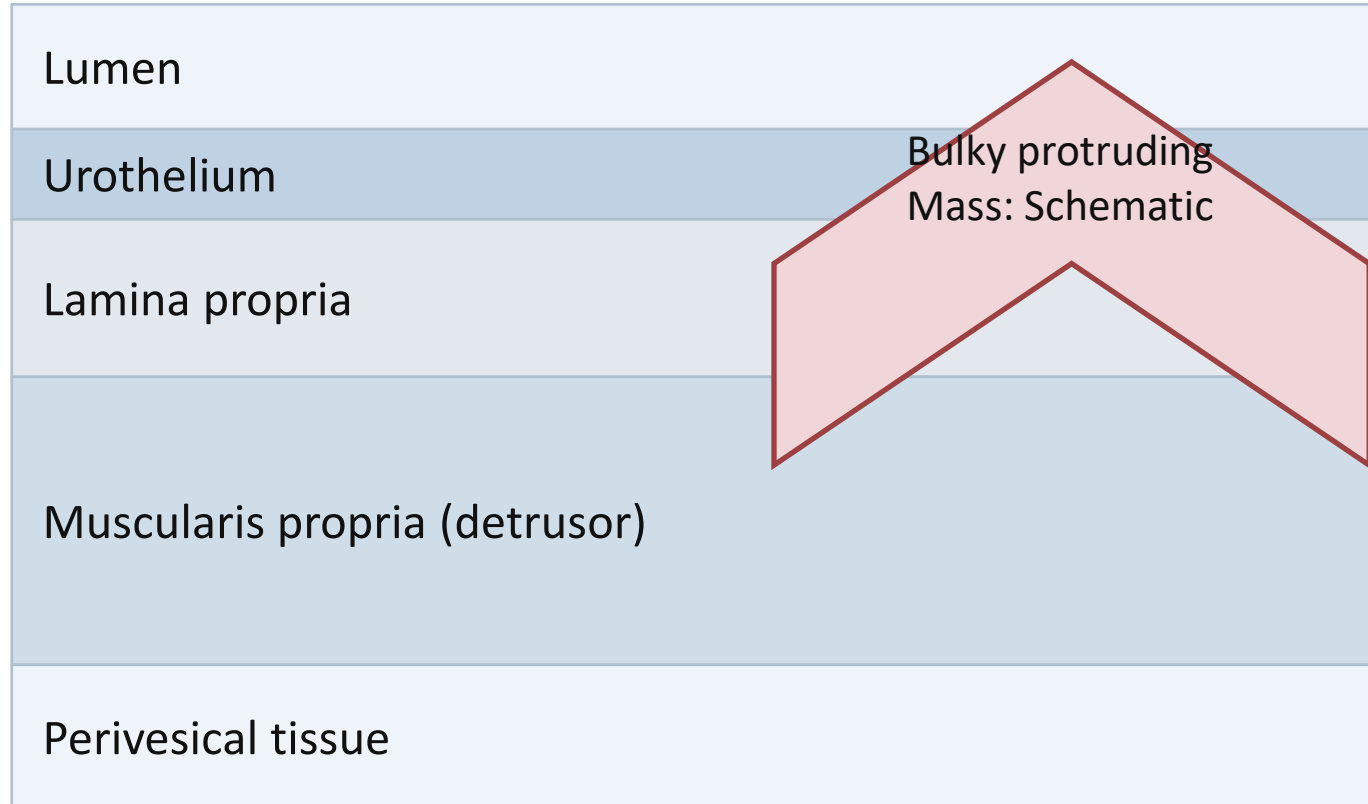
Mimics

Sarcomatoid epithelium and myofibroblastic proliferations demand distinction.

Bladder sarcomas: Gross morphology

- They often present as large masses protruding into the vesical lumen.
- Examples as large as 15 cm.
- Soft, fleshy, gray-white tissue suggests a mesenchymal tumor.
- Gross appearance cannot resolve sarcoma subtype or exclude carcinoma.

A bulky sarcoma may project into the lumen



Sarcomas may project into the bladder lumen as large bulky masses.

Exact site/depth needs tissue assessment.

Layer relationships are simplified; Not drawn to scale.

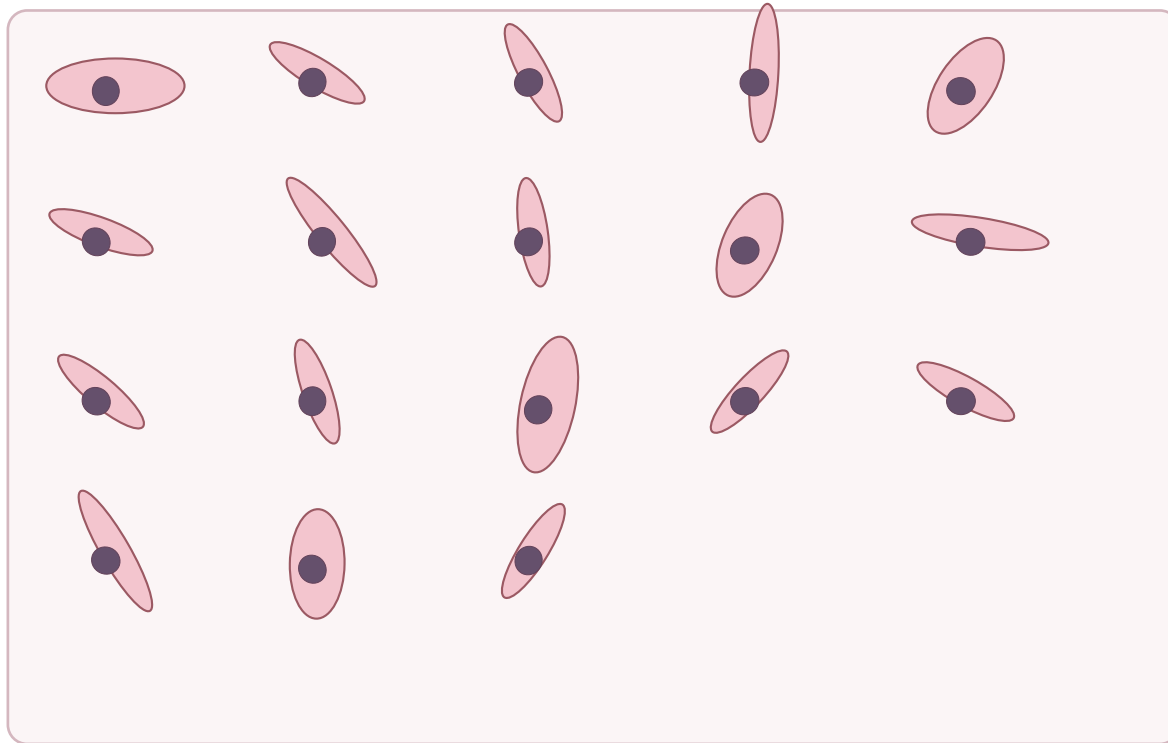
What the cut surface can tell us

Finding	Interpretation / limitation
Large, soft, fleshy mass	Consistent with a sarcomatous gross phenotype.
Gray-white color	A nonspecific tissue appearance, not a lineage marker.
Luminal projection	Describes the growth configuration rather than histogenesis.
Heterogeneity on sectioning	Calls for representative sampling; it is not itself a subtype diagnosis.

Adult bladder sarcoma: Leiomyosarcoma

- Leiomyosarcoma is a malignant smooth-muscle tumor.
- It is the most common bladder sarcoma in adults.
- The soft-tissue counterpart usually shows interweaving fascicles of malignant spindle cells.
- Definitive diagnosis integrates malignant morphology and myogenic differentiation.

Leiomyosarcoma: Malignant spindle-cell pattern



Schematic: Atypia and architectural disorder

Pleomorphism

Variation in nuclear size and shape

Mitotic activity

Brisk proliferation may be evident

Necrosis

Supports malignant behavior in context

Leiomyosarcoma: Cellular features

- Eosinophilic spindle cells form interweaving bundles.
- Nuclei tend to be blunt-ended but are hyperchromatic.
- Cytologic atypia distinguishes malignant cells from bland leiomyoma.
- Brisk mitotic activity and necrosis are common in deep soft-tissue examples.

Leiomyosarcoma: An integrated pattern

Cell identity

Interweaving, eosinophilic smooth-muscle spindle cells.

Malignant cytology

Nuclear atypia and hyperchromasia.

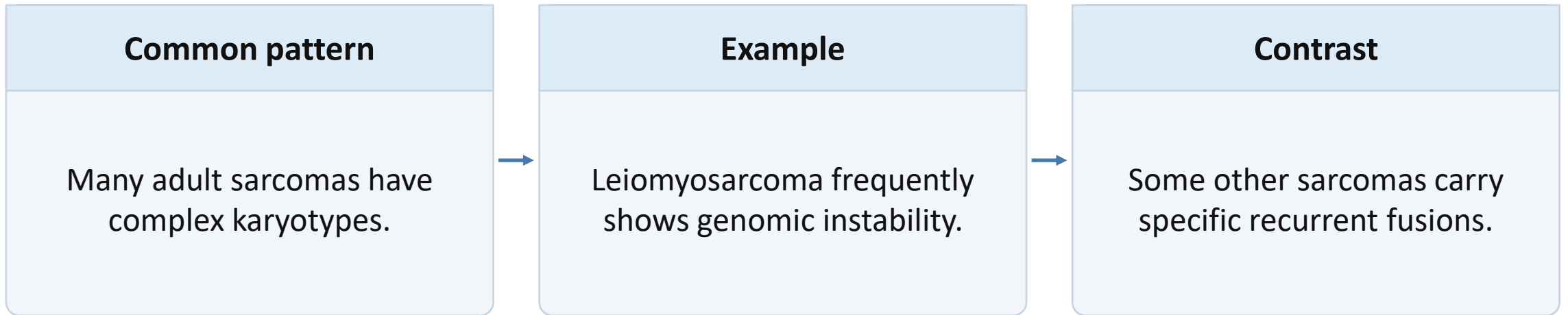
Aggressive behavior

Brisk mitotic activity or necrosis strengthens concern.

Leiomyosarcoma: Ancillary stains

- Smooth muscle actin supports smooth-muscle differentiation.
- Desmin may support a myogenic tumor phenotype.
- Caldesmon can further support mature smooth-muscle differentiation.
- These markers do not independently establish malignant grade or exclude all mimics.

Why complex genomics does not define every sarcoma



Leiomyoma versus leiomyosarcoma

Feature	Leiomyoma	Leiomyosarcoma
Cellular organization	Bland intersecting fascicles	Interweaving malignant spindle cells
Nuclei	Blunt-ended, minimal atypia	Hyperchromatic; atypia may be conspicuous
Mitoses	Few	Often brisk
Necrosis	Not a typical benign feature	Common in deep soft-tissue cases
Stains	Smooth-muscle lineage	Smooth-muscle lineage

Do not use one finding as a shortcut

- An IHC marker establishes lineage more readily than biological behavior.
- Gross circumscription is reassuring but not alone sufficient.
- High-grade nuclear features may be heterogeneous within a mass.
- Sampling, architecture, mitotic activity, and necrosis must be reviewed together.

Pediatric bladder sarcoma: The key entity

- In infancy and childhood, embryonal rhabdomyosarcoma is the leading bladder sarcoma.
- This malignancy demonstrates skeletal-muscle differentiation.
- It may present in a botryoid configuration.
- Anatomic site and age markedly alter the pretest diagnostic possibilities.

Rhabdomyosarcoma and the urinary bladder

Cellular lineage

Skeletal-muscle differentiation even at sites with little normal skeletal muscle.

Relevant subtype

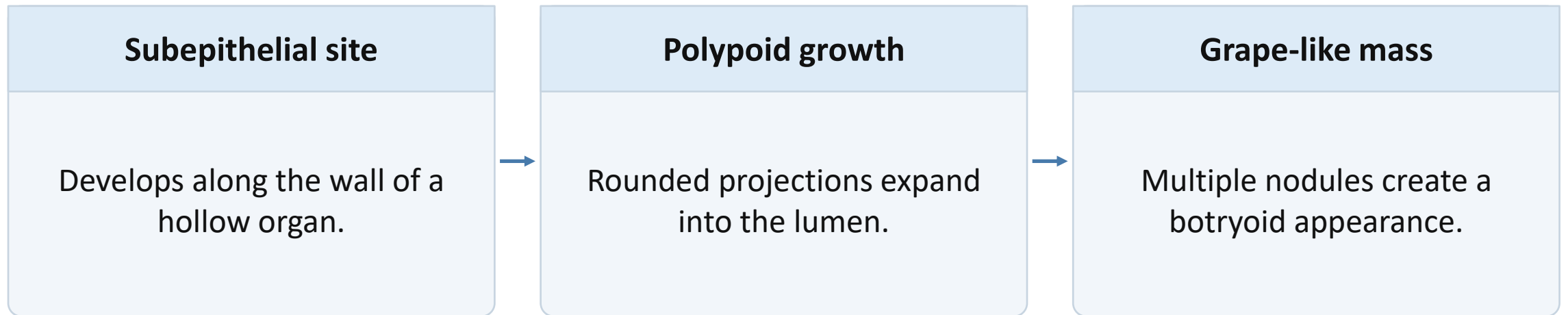
Embryonal rhabdomyosarcoma is important in the pediatric genitourinary tract.

Special pattern

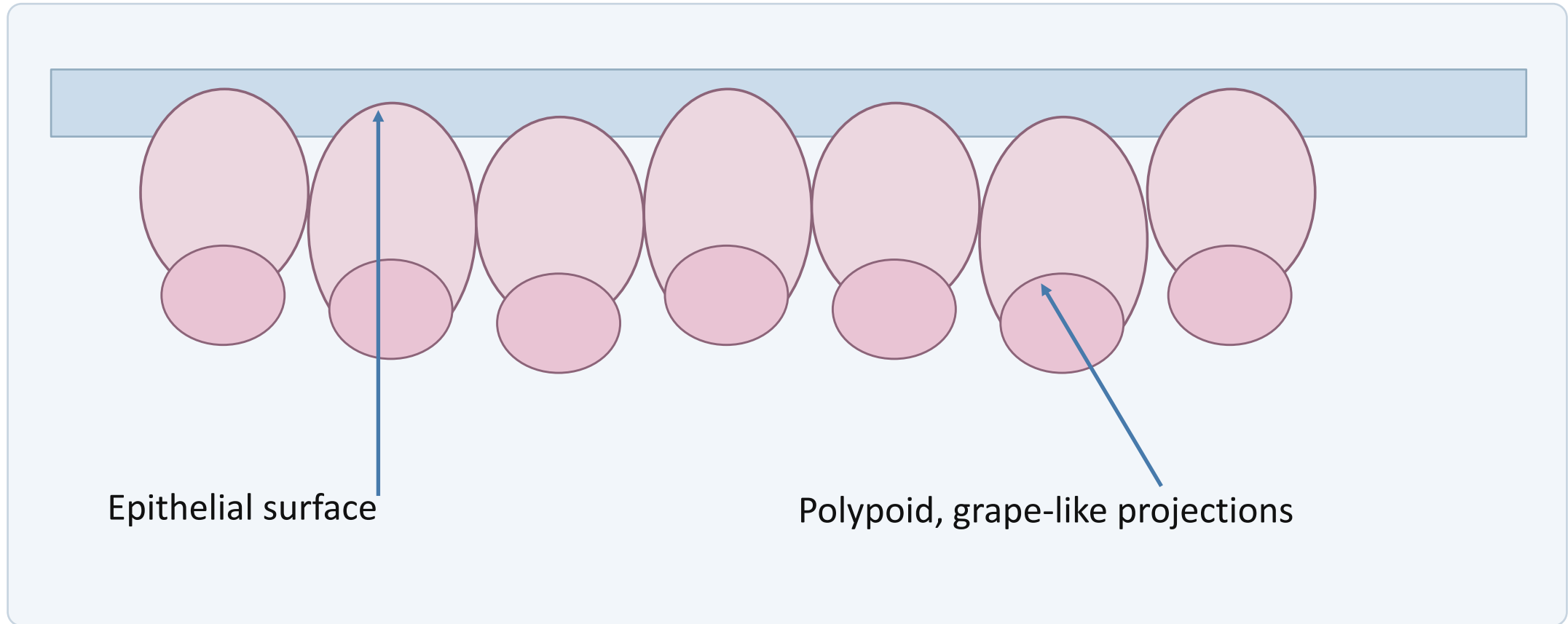
The botryoid pattern is associated with a polypoid mass in a hollow viscus.

Sarcoma botryoides: The gross configuration

A conceptual sequence explaining topology; Not a claim of a fixed time course.



Sarcoma botryoides: Spatial anatomy



Schematic of the “botryoid” gross pattern; Not a patient specimen.

Botryoid does not specify every tumor detail

- “Botryoid” denotes a gross grape-like growth pattern.
- The conventional designation is associated with embryonal rhabdomyosarcoma.
- A polypoid lesion alone is not proof of rhabdomyosarcoma.
- Microscopic lineage confirmation is still required.

Embryonal rhabdomyosarcoma: Morphology

Primitive cells

Round and spindle-shaped malignant cells in a myxoid background.

Differentiating cells

Some tumor cells show rhabdomyoblastic cytoplasm or cross-striations.

Growth pattern

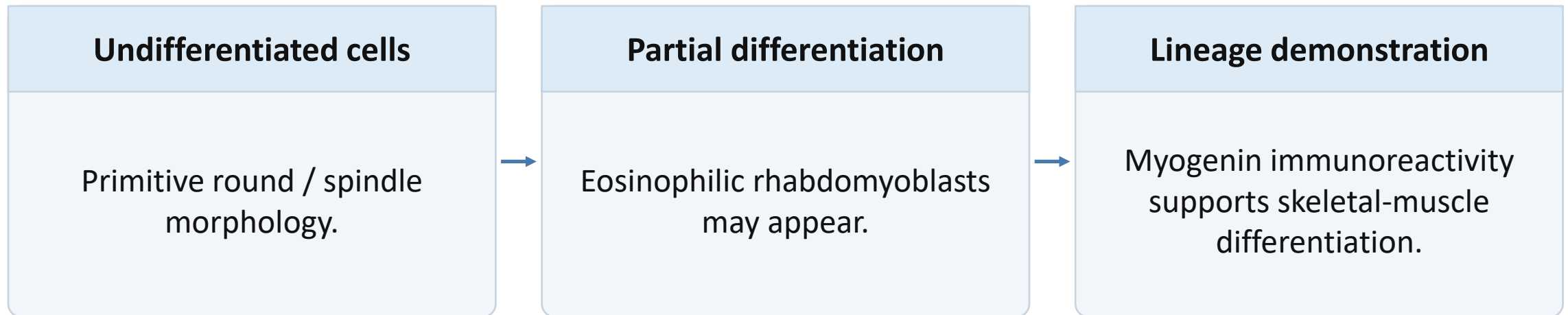
Botryoid examples arise beneath epithelial surfaces of hollow viscera.

The cambium layer: An architectural clue

- Botryoid embryonal rhabdomyosarcoma may show dense subepithelial cellularity.
- This concentrated band is termed the cambium layer.
- Deeper tumor regions may contain a looser myxoid stroma.
- The finding helps explain why a superficial polyp can mask malignant tissue.

From primitive mesenchyme to myogenic phenotype

Conceptual differentiation continuum, not a documented clonal progression sequence.



Rhabdomyoblast morphology

- Cells may vary from primitive round forms to more differentiated eosinophilic forms.
- Some rhabdomyoblasts display cross-striations.
- Cross-striations are not required in every diagnostic sample.
- Myogenic immunohistochemistry is important when morphologic differentiation is limited.

Myogenin: A meaningful lineage marker

- Myogenin is a skeletal-muscle-associated differentiation protein.
- It is useful when confirming rhabdomyoblastic differentiation.
- Nuclear myogenin staining supports skeletal-muscle lineage in the right context.
- Marker interpretation follows morphology; It is not a substitute for tumor classification.

Rhabdomyosarcoma is a heterogeneous family

Subtype	Robbins morphologic / molecular description
Embryonal	Primitive cells in myxoid stroma; RAS pathway changes are frequent.
Alveolar	Fibrous septa, dyscohesive cells; PAX3/7::FOXO1 fusions often present.
Spindle cell / sclerosing	Fusiform morphology; subset with MYOD1 alterations.
Pleomorphic	Large bizarre cells; heterogeneous genetics, generally adult.

Embryonal versus alveolar: A molecular distinction

- Embryonal rhabdomyosarcoma frequently has alterations activating RAS signaling.
- Alveolar rhabdomyosarcoma frequently carries PAX3::FOXO1 or PAX7::FOXO1 fusions.
- These are subtype-level findings, not universal bladder-tumor markers.
- A fusion found in one subtype must not be assigned to every embryonal lesion.

Pediatric pathology: Integrating site and differentiation

Age

Childhood makes embryonal rhabdomyosarcoma particularly relevant.

Site

Genitourinary tract is a recognized pediatric presentation site.

Diagnosis

Architecture plus rhabdomyoblastic differentiation guides classification.

Case B — a polypoid pediatric lesion

A young child has a large, grape-like bladder mass. Histology demonstrates primitive round and spindle cells in myxoid stroma with a dense subepithelial tumor layer.

Interpretation questions

- Which sarcoma subtype is most strongly suggested?
- What does the subepithelial cellular band represent?
- Which stain may confirm skeletal-muscle differentiation?

Case B — diagnosis and reasoning

- The combination favors botryoid embryonal rhabdomyosarcoma.
- Dense subepithelial cellularity is the cambium-layer pattern.
- Myogenin can provide evidence of skeletal-muscle differentiation.
- The polypoid appearance alone is insufficient without diagnostic tissue.

Inflammatory myofibroblastic tumor: A key mimic

- Robbins explicitly highlights inflammatory myofibroblastic tumor among bladder sarcoma mimics.
- A myofibroblastic spindle-cell proliferation may occur with a conspicuous inflammatory infiltrate.
- Inflammatory cells do not by themselves prove a reactive or benign process.
- Careful morphologic and phenotypic classification prevents overcalling true sarcoma.

Inflammatory myofibroblastic tumor: Useful clues

Component	Pathologic finding
Spindle cells	Fibroblastic / myofibroblastic proliferation
Background	Lymphocytes and plasma cells may be conspicuous
Stroma	Variable fibrosis and myxoid change
Molecular support	ALK rearrangement is present in a subset of IMTs

ALK is supportive, not a universal requirement

- A subset of inflammatory myofibroblastic tumors harbors activating ALK rearrangements.
- ALK immunohistochemistry or molecular evidence may support an IMT diagnosis.
- An ALK-negative result cannot, on its own, exclude every IMT.
- Lineage and morphology remain necessary in the differential diagnosis.

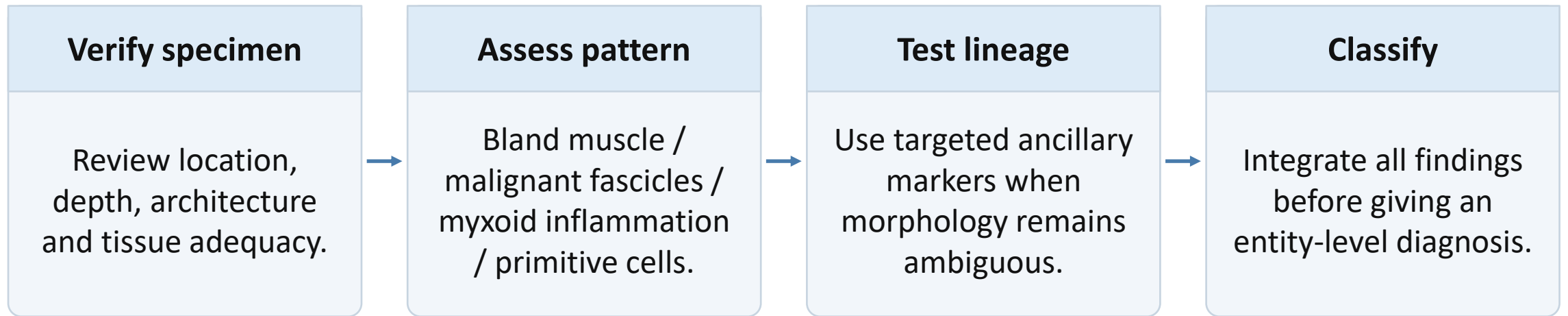
Sarcomatoid carcinoma: Avoid a lineage error

- Some bladder carcinomas assume a sarcomatoid growth pattern.
- A sarcoma-like spindle-cell morphology does not prove primary mesenchymal malignancy.
- The possibility of an epithelial neoplasm must be considered before calling a primary sarcoma.
- A spindle-cell lesion may require expanded evaluation for epithelial differentiation.

True sarcoma versus sarcomatoid carcinoma

Decision point	True mesenchymal sarcoma	Sarcomatoid carcinoma
Conceptual origin	Mesenchymal neoplasm	Carcinoma with sarcoma-like phenotype
Routine morphology	May be spindle-cell or pleomorphic	Can mimic a spindle-cell sarcoma
Primary challenge	Assign differentiation and subtype	Seek evidence of epithelial lineage
Interpretive rule	Do not classify by shape alone	Do not classify by shape alone

Spindle-cell bladder mass: Conceptual work-up



Three different biological questions

Question	What primarily answers it?
What lineage is present?	Morphology plus lineage immunostaining, when indicated.
Is the lesion benign or malignant?	Architectural and cytologic behavior across adequate tissue.
What specific entity is it?	Lineage, age, site, morphology and subtype-defining evidence.
How far does it extend?	Depth, local interface and available sampling.

Adequate specimen assessment is critical

- Small biopsies may fail to represent the full perimeter of a mass.
- Mitotic hot spots, necrosis, and focal differentiation may be unevenly distributed.
- Apparent urothelial coverage is not evidence of urothelial tumor origin.
- Statements about complete removal or extension require an appropriately sampled specimen.

Bladder mesenchymal tumor: Integrated comparison

Entity	Most useful clue	Key pitfall
Leiomyoma	Bland, circumscribed smooth-muscle fascicles	Do not diagnose solely by smooth-muscle marker positivity
Leiomyosarcoma	Atypical smooth-muscle cells + malignant features	Do not infer subtype from gross color
Embryonal RMS	Primitive myogenic cells; possible botryoid growth	Do not equate any polyp with RMS
IMT	Myofibroblastic cells + inflammation; ALK in some	Do not label every spindle-cell lesion sarcoma
Sarcomatoid carcinoma	Carcinoma with sarcoma-like growth	Do not overlook epithelial lineage

What a pathology report should resolve

Teaching-oriented report checklist, not a formal prescribed synoptic template or staging standard.

- Most defensible entity and lineage based on available material.
- Presence of relevant malignant histologic features, where assessable.
- Anatomic extent and margin status, only when the specimen supports assessment.
- Any material limitations or unresolved differential diagnoses.

Case C — a spindle-cell bladder lesion

A bladder mass shows spindle-shaped cells admixed with lymphocytes and plasma cells. No convincing myogenic rhabdomyoblasts are identified; Ancillary testing is being considered.

Interpretation questions

- Which important sarcoma mimic must be considered?
- Why would inflammation alone be insufficient for classification?
- What could ALK testing contribute, and what could it not establish?

Case C — managing diagnostic uncertainty

- Inflammatory myofibroblastic tumor is a relevant differential diagnosis.
- Inflammatory infiltrates can accompany neoplastic growth; Pattern recognition remains essential.
- Positive ALK findings may support IMT in the appropriate context.
- Negative ALK alone does not eliminate other spindle-cell differential diagnoses.

Case D — a malignant adult spindle-cell mass

An adult bladder tumor is large, soft, fleshy and gray-white. The tissue contains atypical eosinophilic spindle cells in fascicles, with brisk mitoses and necrosis.

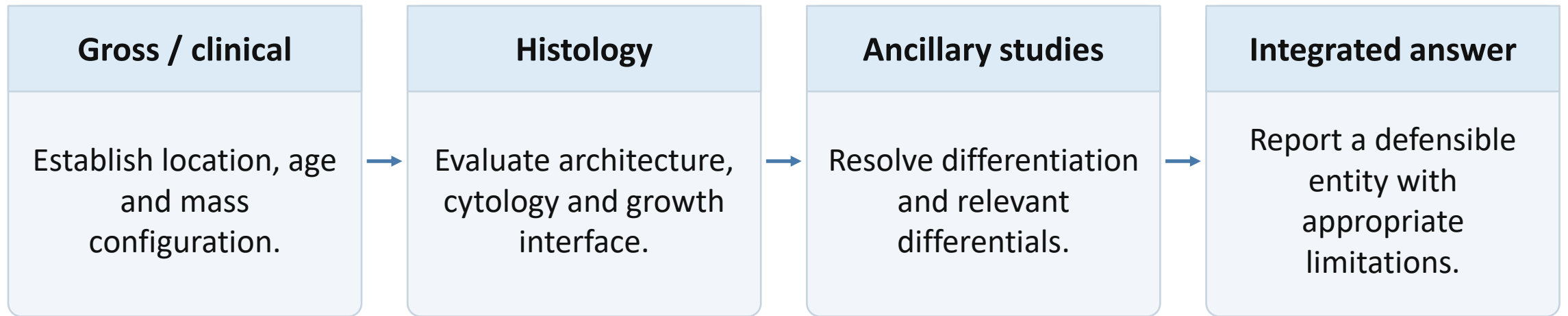
Interpretation questions

- Which primary sarcoma is favored by the differentiation?
- Which features provide evidence of malignancy?
- Which bladder tumor mimic still requires exclusion?

Case D — synthesis of the differential

- Leiomyosarcoma is favored by malignant smooth-muscle morphology.
- Atypia, mitoses and necrosis indicate an aggressive morphologic pattern.
- Smooth-muscle lineage stains may support differentiation, but not behavior alone.
- Sarcomatoid carcinoma remains a critical competing diagnosis.

One diagnostic principle across all four cases



Ten points worth retaining

- Bladder mesenchymal tumors are rare; Leiomyoma is the leading benign example.
- True sarcoma is uncommon; Adult leiomyosarcoma and childhood embryonal RMS are key types.
- Botryoid morphology is a polypoid pattern that needs myogenic confirmation.
- Spindle-cell mimics, especially sarcomatoid carcinoma and IMT, demand consideration.

Evidence boundaries for this lecture

Established bladder facts

The dominant benign and malignant entities and their characteristic gross patterns.

Transferable principles

Comparable smooth-muscle, skeletal-muscle and inflammatory myofibroblastic morphology.

Important limits

No bladder-specific prevalence tables, molecular frequencies, staging cutoffs or treatment protocols are asserted.

References and further reading

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 21, p. 875.
- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 26, pp. 1102–1103.
- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 22, p. 904; Chapter 15, IMT section.
- Source mapping, cross-organ limitations and visual provenance are recorded in speaker notes.