

# Pearls and Pitfalls in Diagnosing Pediatric Urinary Bladder Masses<sup>1</sup>

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**Abbreviations:** IMT = inflammatory myofibroblastic tumor, PUNLMP = papillary urothelial neoplasm of low malignant potential

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## SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- List the common differential diagnoses of bladder masses in children.
- Identify the diverse appearances and locations of various pediatric bladder mass subtypes at different imaging examinations.
- Discuss the potential pitfalls of diagnosing bladder masses in children on the basis of imaging findings.

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Urinary bladder masses are rare in children, and the associated histologic features and prognoses in this population are different from those in adults. Most children with urinary bladder masses present with lower urinary tract symptoms, which may include hematuria, dysuria, frequent urination, and urgency to urinate. However, some of these masses may be identified incidentally or involve generic symptoms such as abdominal distention. In general, pediatric bladder tumors can be divided into those that originate from the bladder epithelium, known as urothelial neoplasms, and mesenchymal bladder neoplasms, which are more prevalent. The most common bladder malignancy in children is a rhabdomyosarcoma, whereas the most common benign bladder lesion in the pediatric population is a papillary urothelial neoplasm of low malignant potential (PUNLMP). The first-line imaging tool for assessing bladder lesions is ultrasonography, which may be followed by a cross-sectional imaging examination such as computed tomography or magnetic resonance imaging if the origin of the mass is unclear or if distant spread is suspected. Although imaging may enable the radiologist to suggest a differential diagnosis based on lesion location and patient age, tissue biopsy generally is required to identify the exact pathologic entity. This is usually performed at cystoscopy and may be curative in cases in which the lesion is small and has low recurrence potential. Knowledge of the clinical, histopathologic, and imaging features of common bladder neoplasms is essential, as it can aid in preventing imaging pitfalls. These may include the misinterpretation of either a pelvic mass as arising from the bladder or a bladder mass as arising from the pelvis, and interpreting an inflammatory mass or bladder detritus as a neoplasm.

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## Introduction

Urinary bladder masses in children are extremely rare. The scarcity of cases of these lesions limits our ability to study them. Even published reviews of institutional experiences with these lesions and national cancer databases spanning up to 30 years include a small number (<200) of cases of these masses in pediatric patients. In general, the frequencies and types of bladder diseases differ between adults and children, although there is some overlap. With the exception of rhabdomyosarcomas, the majority of bladder masses are benign and associated with a favorable clinical outcome.

Bladder lesions may be identified incidentally at imaging performed for assessment of nonurologic symptoms or diseases. However, the majority of patients present with generic symptoms, which may include dysuria, frequent urination, hematuria, incontinence, lower abdominal pain, and/or abdominal distention. In a small number of cases, the presence of a bladder mass combined with

## TEACHING POINTS

- Bladder lesions may be identified incidentally at imaging performed for assessment of nonurologic symptoms or diseases. However, the majority of patients present with generic symptoms, which may include dysuria, frequent urination, hematuria, incontinence, lower abdominal pain, and/or abdominal distention.
- US is the first-line imaging modality for the assessment of bladder lesions in children. It is vital that the patient have a full bladder while being examined, as this will help to prevent a thickened relatively collapsed bladder from being misinterpreted as a mass, or a small soft-tissue lesion from being missed.
- Histologically, the bladder wall comprises four distinct tissue layers (listed here from superficial to deep aspects): the urothelium, lamina propria, muscularis propria, and adventitia.
- Rhabdomyosarcomas are the most common malignant tumors of the urinary bladder in children younger than 10 years and account for 5% of all childhood solid cancers. Although rhabdomyosarcomas can arise from any location in the body where there are primitive muscle cells, they manifest in the bladder and prostate in approximately 20% of cases.
- At imaging, PUNLMPs are difficult to differentiate from noninvasive urothelial carcinomas. They are normally solitary, measure 1–2 cm, and have been described as having a “seaweed in the ocean” appearance.

certain clinical signs and symptoms may be associated with a more specific pathologic process. Examples of such cases include the presence of paragangliomas in association with hypertension, the presence of bladder neurofibromas combined with axillary freckling and skin lesions in the setting of neurofibromatosis type 1, and the presence of bladder hemangioma combined with an enlarged and discolored limb in the setting of a known vascular malformation syndrome.

Imaging strategies include ultrasonography (US) as the first-line examination. In cases in which malignancy is suspected, US may be followed by further cross-sectional imaging such as computed tomography (CT) or magnetic resonance (MR) imaging to clarify the location and extent of disease and the associated complications (eg, regional lymphadenopathy or associated upper urinary tract dilatation). The specific subtype of a tumor usually cannot be determined by using imaging alone, as there are no pathognomonic features for any particular bladder lesion. For further characterization, tissue biopsy is performed—usually by means of cystoscopy.

In this article, the clinical, histopathologic, and imaging features of common bladder neoplasms that affect children are reviewed and illustrated. In addition, the potential differential diagnoses of these lesions, common associated imaging pitfalls, and suggested methods of preventing these pitfalls are outlined.

## Imaging Techniques

US is the first-line imaging modality for the assessment of bladder lesions in children. It is vital that the patient have a full bladder while being examined, as this will help to prevent a thickened relatively collapsed bladder from being misinterpreted as a mass, or a small soft-tissue lesion from being missed. When an abnormality is present, a filled and distended bladder can also aid in determining whether the lesion is adherent to the bladder wall or mobile, because it is a more capacious cavity for assessing changes in movement with patient positioning.

Patients may sometimes undergo micturating, or voiding, cystourethrography, although it is usually not the first-line examination, before US. This protocol may be followed because of scheduling issues or a known urologic problem with which a bladder mass was not considered in the differential diagnosis, such as recurrent urinary tract infections or suspected vesicoureteric reflux. Small bladder lesions are difficult to identify at micturating cystourethrography; however, when they are present, they are best seen on “early filling” views of the bladder, where they manifest as a focal filling defect. Performing fluoroscopy is not recommended when the specific clinical application is the identification and characterization of a bladder mass, because it has low sensitivity in the identification of these masses and radiation exposure is required. In one study (1), the sensitivity of fluoroscopy in the identification of bladder masses in patients younger than 40 years was found to be as low as 44%.

When cross-sectional imaging is required, MR imaging facilitates excellent soft-tissue definition and enables assessment of the extent of disease and delineation of the anatomy. These functions are particularly helpful when there is uncertainty as to whether a pelvic mass is arising from the bladder or the adjacent structures. At The Hospital for Sick Children, we use a routine pelvic-urogenital tumor MR imaging protocol, which includes a coronal wide-field-of-view short tau inversion-recovery (STIR) sequence, diffusion-weighted imaging ( $b = 0, 100, \text{ or } 600 \text{ sec/mm}^2$ ), nonenhanced and contrast material-enhanced imaging of the pelvis, a three-dimensional volumetric T1-weighted sequence, and axial and sagittal T2-weighted fat-saturated sequences (2). Nonenhanced T1-weighted MR images are most useful for the delineation of lesions, as many hyperintense lesions can be masked by urine on T2-weighted MR images. It is important to “catch” the enhancement of the lesion by using fast-acquisition contrast-enhanced MR imaging sequences before the accumulation of excreted gadolinium-based contrast material in the bladder,

as the accumulated medium may mask the pathologic entity (3). The utility of diffusion-weighted MR imaging for assessment of bladder tumors in children is yet to be established. However, as with other tumors with high cellularity and restricted diffusion, this sequence might be helpful when a small bladder lesion is difficult to differentiate from the highly intense signal of urine on STIR or T2-weighted MR images. The urine would be suppressed on diffusion-weighted images.

CT facilitates less soft-tissue definition than does MR imaging and has the disadvantage of involving radiation exposure. However, it may be useful for the characterization of widespread metastatic disease—especially in the lungs or bone—rather than the primary identification and characterization of a bladder mass. Nevertheless, it is still beneficial to perform imaging with the patient's bladder full to better delineate the pelvic anatomy. A longer examination time and (potentially) general anesthesia are required with MR imaging, and CT may be a useful alternative examination when anesthesia might be harmful to the patient.

There are no standardized protocols for long-term imaging follow-up after a bladder lesion in a child has been identified and treated. Owing to reports of recurrent tumor, especially neoplasms such as papilloma and urothelial carcinoma, many advocate performing annual US examinations combined with clinical outpatient visits. Concomitant clinic visits for urologic assessment also may be required for these lesions. For other pathologic entities such as hemangioma, only US follow-up, without clinical assessment, may be required—unless the imaging findings and/or clinical symptoms dictate substantial changes in the follow-up (4).

### Clinical Investigations

Aside from their utility in confirming the presence of hematuria and excluding urinary tract infection, urinalysis and cytologic analysis generally are not useful for the detection or follow-up of bladder masses in children. The low rates for the identification of tumor presence and recurrence at cytologic urine analysis are postulated to be secondary to the benign nature of many pediatric bladder lesions, which leads to a low cell turnover rate in the urine (5).

Blood sampling may be useful for hemoglobin quantification (eg, in cases of massive hemorrhage from a vascular bladder mass), assessment of increased inflammatory marker levels (eg, in the setting of indwelling infection), and determining renal function (eg, when a mass is causing hydronephrosis). However, it is not performed for the identification or differential diagnosis of bladder lesions, or for assessment of treatment

response. There are no serum-based tumor markers for rhabdomyosarcoma, which is the most common bladder malignancy in childhood, or urothelial carcinoma (6).

The reference-standard procedure for the diagnosis (and sometimes treatment) of bladder lesions is tissue biopsy by means of cystoscopy, at which the mass can be directly visualized and even excised (if its size and anatomy are suitable). Owing to the invasive nature of cystoscopic biopsy, it is usually performed when the presence of a bladder lesion has been confirmed with imaging or when imaging does not depict an abnormality but recurrent urinary symptoms persist without any other feasible clinical explanation. Drawbacks to performing this procedure include difficulty in assessing the depth of lesion invasion or the distant spread of disease. Complications are related to the use of general anesthesia and the potential risk of urethral damage from manipulation, the latter of which can occur in both sexes, although it is more common in boys because they have a longer urethra.

### Embryologic and Pathologic Analyses

In utero, the bladder and urethra arise from the endodermal urogenital sinus after the cloaca has partitioned into the ventral urogenital sinus and dorsal rectum. At around 5 weeks gestation, the urogenital sinus further divides into the anterior vesicourethral canal and posterior urogenital sinus. The anterior vesicourethral canal becomes the bladder, with a patent outflow tract at its apex connected to the allantois. By 15 weeks gestation, the bladder separates from the umbilicus with regression of the allantois, which becomes a remnant called the urachus. The lumen of the urachus subsequently obliterates to become the median umbilical ligament (7).

Histologically, the bladder wall comprises four distinct tissue layers (listed here from superficial to deep aspects): the urothelium, lamina propria, muscularis propria, and adventitia (Fig 1). However, the different layers are not well visualized with any imaging modality. Neoplasms arising from the bladder can originate from any of these layers and are very broadly divided into tumors that have an epithelial origin (ie, arising from the urothelium) and those that have a nonepithelial origin, which are sometimes referred to as mesenchymal neoplasms (8). In contrast to most bladder masses in adults, the majority of childhood bladder lesions are mesenchymal in origin, with rhabdomyosarcoma being the most common bladder malignancy in children (9). Other subtypes of mesenchymal neoplasms include rarer and mainly benign lesions such as inflammatory myofibroblastic tumors (IMTs), neurofibromas, and leiomyomas.

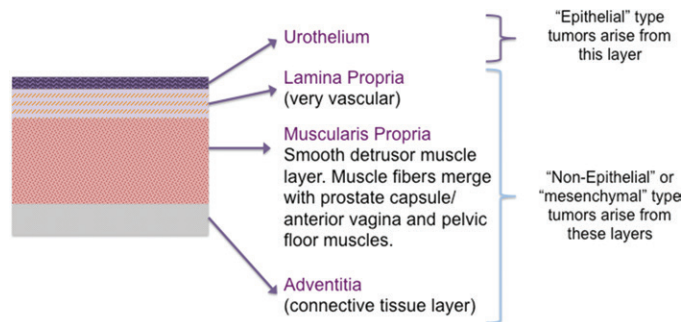


Figure 1. Diagram illustrates the various layers of a normal bladder wall.

**Most Common Bladder Tumors in Children**

| Tumor*                                         | Age- and Sex-related Features                                                                                                                                                                                                                 |
|------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Urothelial tumors</b>                       |                                                                                                                                                                                                                                               |
| Infiltrative urothelial carcinoma (high grade) | Infiltrative urothelial carcinoma and noninvasive urothelial carcinoma are more common in adolescents; they occur in individuals younger than 10 years in only one-third of cases                                                             |
| Noninvasive urothelial carcinoma (low grade)   |                                                                                                                                                                                                                                               |
| PUNLMP                                         | Age range of affected individuals is variable in childhood                                                                                                                                                                                    |
| Urothelial papilloma                           | Age range of affected individuals is variable in childhood                                                                                                                                                                                    |
| Fibroepithelial polyp                          | Manifests in individuals with a mean age of 9 years; more common in males                                                                                                                                                                     |
| <b>Mesenchymal tumors</b>                      |                                                                                                                                                                                                                                               |
| Rhabdomyosarcoma                               | Manifests in individuals in a bimodal age distribution (within first 2 years of life and during adolescence); certain genetic syndromes, such as Li-Fraumeni cancer syndrome and neurofibromatosis type 1, are associated with increased risk |
| Leiomyoma                                      | Rare in children, with only two case reports to date; more common in women aged 30–60 years                                                                                                                                                   |
| Neurofibroma                                   | Majority of tumors are first detected in individuals younger than 18 years; manifests in individuals at variable ages, depending on symptoms                                                                                                  |
| IMT                                            | Manifests in individuals with a mean age of 7 years                                                                                                                                                                                           |
| Leiomyosarcoma                                 | Exceedingly rare in children; the youngest affected person reported in the literature was aged 10 years                                                                                                                                       |
| Angiosarcoma                                   | Extremely rare; more common in males; manifests in individuals with an average age of 2 years                                                                                                                                                 |
| Hemangioma                                     | Rare; usually occurs in individuals younger than 5 years                                                                                                                                                                                      |
| <b>Neuroendocrine tumors</b>                   |                                                                                                                                                                                                                                               |
| Paraganglioma                                  | Exceedingly rare in children; more common in individuals aged 30–60 years; the youngest affected patient reported was aged 10 years                                                                                                           |

\*PUNLMP = papillary urothelial neoplasm of low malignant potential.

Epithelial neoplasms, or more specifically, urothelial neoplasms, are rare in children. In a 21-year retrospective pathologic analysis–based review (10), these neoplasms accounted for only 9% of all bladder tumors. In the 2016 World Health Organization classification of urothelial tract tumors (11), this subgroup of tumors is divided into invasive urothelial carcinomas and noninvasive urothelial neoplasms, the latter of which are much more common in children. Although this system was not designed specifically for the classification of childhood bladder

cancers, it forms a basis on which to organize our understanding of different pathologic bladder neoplasm types. In addition to the aforementioned urothelial and mesenchymal tumors, neuroendocrine tumors—specifically, paragangliomas—another rare yet relevant subgroup of neoplasms seen in the pediatric population, are briefly described in this review. The common pediatric bladder neoplasms classified in the three tumor subtypes (urothelial, mesenchymal, and neuroendocrine) are listed and described in the Table.



## Mesenchymal Neoplasms

### Rhabdomyosarcoma

Rhabdomyosarcomas are the most common malignant tumors of the urinary bladder in children younger than 10 years and account for 5% of all childhood solid cancers (9). Although rhabdomyosarcomas can arise from any location in the body where there are primitive muscle cells, they manifest in the bladder and prostate in approximately 20% of cases (12). Bladder and prostate rhabdomyosarcomas have a bimodal age distribution, with the peak incidence occurring within the first 2 years of life and another peak occurring during adolescence (13). The majority of rhabdomyosarcomas occur sporadically; however, certain genetic syndromes, such as Li-Fraumeni cancer syndrome, neurofibromatosis type 1, and multiple endocrine neoplasia type 2A, may predispose a person to developing this tumor (14,15). Approximately 10%–20% of patients with rhabdomyosarcoma (regardless of the origin site) are found to have metastatic disease at the time of diagnosis (16). The spreading is typically to the lungs, cortical bone, and/or regional lymph nodes, with the incidence and pattern of disease differing according to the site and histologic features of the tumor.

The histopathologic subtypes of rhabdomyosarcoma include embryonal rhabdomyosarcoma, which accounts for more than 90% of cases and includes botryoid and variant spindle cell forms, and the rarer, more aggressive alveolar and undifferentiated sarcoma types (17). Macroscopically, these lesions are typically polypoid, gelatinous, and multilobulated. Microscopically, the embryonal subtype is composed of small, dark, spindle-shaped or round cells with minimal cytoplasm, mixed with a variable number of cells resembling rhabdomyoplasts (18). The alveolar subtype exhibits thin fibrovascular septae that resemble alveolar airspaces and are lined by a single layer of cuboidal tumor cells with hyperchromatic nuclei (19).

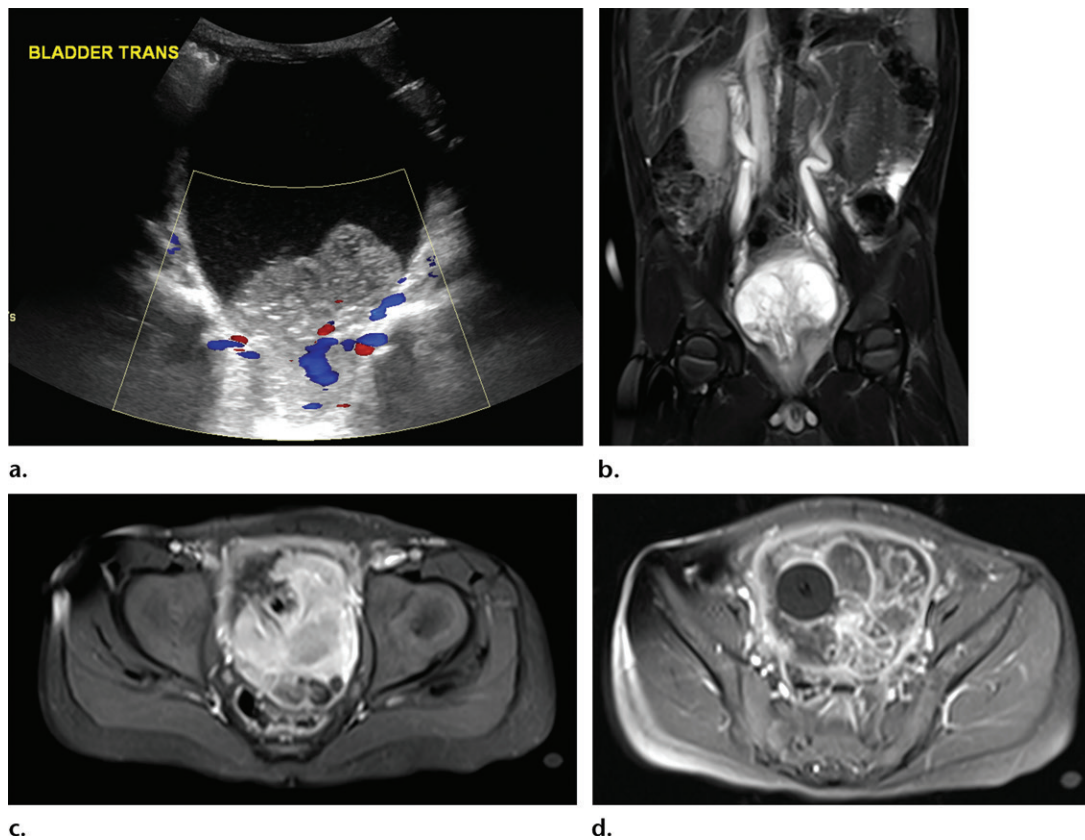
Stratification of the risk of rhabdomyosarcoma is complex and based on a pretreatment TNM staging system and a post-biopsy and resection clinical grouping system established by the Intergroup Rhabdomyosarcoma Study Group (IRSG), which has been incorporated into the Children's Oncology Group Soft-Tissue Sarcoma Committee (20). Information from both of these systems is taken into account to assign the patient a risk level (low, intermediate, or high). The IRSG staging system is based on the size ( $\leq 5$  cm or  $> 5$  cm), invasiveness (ie, whether the tumor is localized to the anatomic site of origin), and nodal status (ie, whether regional nodes are involved, as deter-

mined at histologic analysis) of the tumor, and the site of the primary cancer (classified as an unfavorable anatomic site for lesions originating from the bladder and prostate). The affected person's age and the tumor subtype affect the outcome. Individuals younger than 1 year and those aged 10 years or older fare worse; 51%–53% of persons in these age groups, as compared with 71% of persons aged 1–9 years, have a 5-year event-free survival (21). The embryonal histopathologic subtype of rhabdomyosarcoma is associated with an 82% 5-year event-free survival rate, as compared with the alveolar subtype, which is associated with a 65% 5-year event-free survival rate (20).

With consideration of the risk stratification, CT of the chest, CT or MR imaging of the pelvis and regional lymph nodes, bone scintigraphy, and potentially bone marrow aspiration are required for the formal imaging workup and staging of rhabdomyosarcoma. In addition, there is increasing evidence supporting the use of functional imaging with fluorine 18 fluorodeoxyglucose positron emission tomography (PET) for workup and staging—especially for the identification of distant metastases and monitoring the response to treatment (22).

On US images, bladder rhabdomyosarcomas are typically large and nodular and frequently associated with urinary tract obstruction (23). The mass is usually well defined and mildly hypoechogenic and homogeneous (Fig 2). The botryoid subtype of rhabdomyosarcoma may have the appearance of a bunch of grapes (Fig 3). These lesions are commonly located at the vesical trigone and bladder neck. On CT images, the mass normally has heterogeneous attenuation but overall lower attenuation compared with the normal muscle tissue. At MR imaging, the mass typically has uniform low signal intensity on T1-weighted images and heterogeneous high signal intensity on T2-weighted and contrast-enhanced T1-weighted fat-saturated images (24). The more uniform low signal intensity on T1-weighted MR images is mainly due to areas with low-signal-intensity necrotic tissue, which are easier to differentiate on T2-weighted and contrast-enhanced MR images (25). Although the nonembryonal rhabdomyosarcoma subtypes are more aggressive, a study (26) involving 14 pediatric patients with rhabdomyosarcoma revealed no convincing evidence of cross-sectional imaging features that could help predict the tumor subtype.

Chemotherapy is normally the first line of treatment for rhabdomyosarcoma, before surgery or radiation therapy (16). In a large international series involving patients treated for bladder rhabdomyosarcoma, 78 (48%) of 164 patients were cured with chemotherapy, 49 (30%) patients



**Figure 2.** Urinary bladder embryonal rhabdomyosarcoma in a 3-year-old boy with localized disease. (a) Transverse color Doppler US image of the bladder shows a well-defined mass with minimal internal vascularity at the base. (b) Coronal STIR MR image shows bilateral ureteric dilatation due to obstruction. (c, d) Axial contrast-enhanced T1-weighted fat-saturated MR images of the inferior (c) and superior (d) aspects of the bladder mass show a solid enhancing component at the inferior aspect and a more cystic component at the superior aspect.

required a partial cystectomy, and 34 (21%) of them underwent a complete cystectomy (27). Patients with no progressive or residual disease after completing therapy are usually followed up with surveillance imaging for at least 5 years for monitoring of possible recurrence. The tumor recurs in approximately 30% of patients, with 95% of relapses occurring within 3 years of the commencement of therapy (28). Patients with metastatic disease have much poorer outcomes—especially if there is cortical bone or bone marrow involvement. Fourteen percent to 16% of these patients have a 3-year event-free survival, compared with an overall 3-year event-free survival rate of approximately 30% (29).

### Inflammatory Myelofibroblastic Tumors

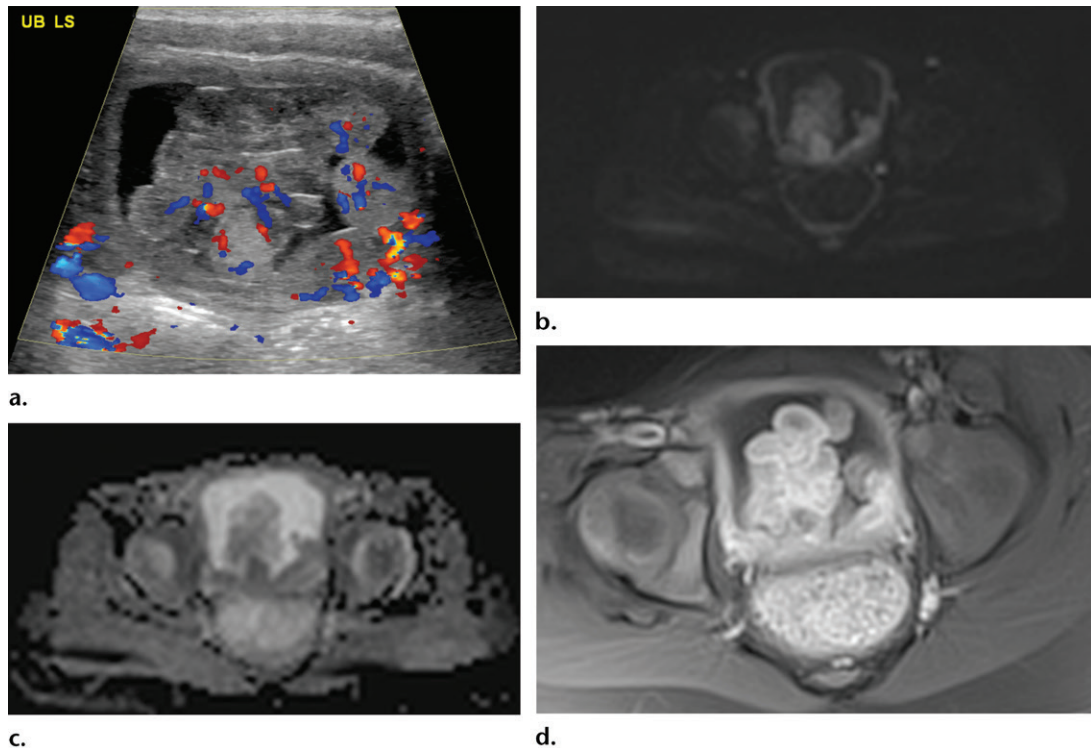
IMTs have previously been described in the literature under a variety of names, including pseudosarcomatous tumor, spindle cell tumor, and atypical fibromyxoid tumor (30). Although these tumors can occur in a variety of locations, their presence in the bladder is rare, and these lesions are considered to be benign. Approximately 25% of all bladder IMTs manifest in children with a mean age of approximately 7 years. The most

common symptoms at manifestation include hematuria and abdominal pain (31).

Macroscopically, IMTs appear as polypoid, pale, firm masses with surface ulceration. Microscopically, they comprise spindle cells in a myxoid stroma with scattered chronic inflammatory cells. Although their cause is uncertain, some experts postulate an infective or traumatic precursor owing to the presence of inflammatory cells (30).

At imaging, IMTs are normally seen at the bladder dome (Fig 4). They can be large at manifestation, probably owing to their location and slow growth, with a mean size of 5.5 cm; however, they can range in size from 1.8 to 13.0 cm (32). Because these tumors can have an appearance similar to that of rhabdomyosarcomas, a definitive diagnosis cannot be made with radiologic examinations alone; tissue biopsy is required (33). Even with a biopsy-based diagnosis, the cellular features of an IMT can mimic those of a malignant spindle cell tumor, and testing for anaplastic lymphoma kinase protein positivity can be helpful, as it is seen in approximately 33%–89% of cases of IMT (34).

Although local tumor recurrence is known to occur after IMT resection in adults, the biologic



**Figure 3.** Urinary bladder embryonal rhabdomyosarcoma in a 5-year-old boy with stage 4 (distant metastatic) disease. (a) Longitudinal-section color Doppler US image of the urinary bladder shows a multilobulated mass with internal vascularity. (b, c) Axial diffusion-weighted ( $b = 1000 \text{ sec/mm}^2$ ) MR image (b) and apparent diffusion coefficient map (c) show restricted diffusion within the mass. (d) Axial contrast-enhanced T1-weighted fat-suppressed MR image shows the lesion with avid and heterogeneous enhancement. (e) Findings on the sagittal T2-weighted fat-saturated MR image helped to determine that the origin of the mass is the base of the bladder. This lobulated lesion has internal high signal intensity.

behavior of pediatric bladder IMTs is unknown. The investigators in one study (30) reviewed 42 case reports of childhood bladder IMT and found no published articles describing local recurrence or metastatic involvement in the pediatric population.

### Leiomyoma

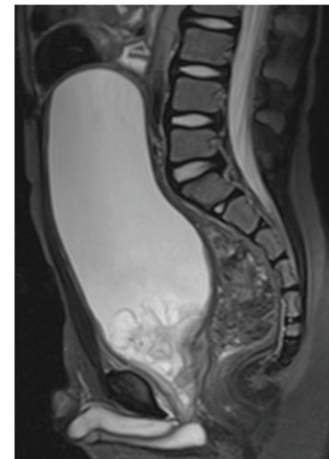
Bladder leiomyomas are rare, accounting for 0.43% of all mesenchymal bladder tumor subtypes (35); to our knowledge, there are only two published case reports involving children to date. General manifestations of bladder leiomyomas include urinary obstruction, frequent urination, dysuria, and hematuria. These tumors are more typically found in women aged 30–60 years (36).

In terms of location, bladder leiomyomas may be endovesical (in 86% of cases), intramural (in 11% of cases), or extravesical (in 11% of cases), with the endovesical subtype being the most likely to cause obstructive urinary symptoms (37). The imaging features of these tumors are very similar to those of uterine fibroids: a typically solitary, homogeneously attenuating solid mass with variable enhancement characteristics at cross-sectional imaging, with intermediate to low signal intensity

on T1- and T2-weighted MR images (38) (Fig 5b). However, histopathologic analysis is required to confirm the diagnosis and exclude an underlying leiomyosarcoma (39). Excision is curative, with no risk of recurrence or spreading.

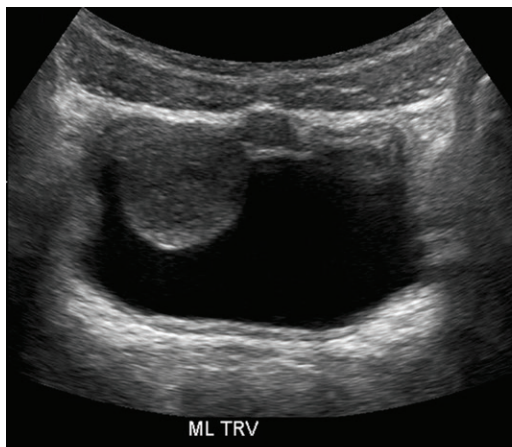
### Neurofibroma

Benign nerve sheath tumors rarely occur in the bladder, but when they do, they are generally plexiform. Approximately 63%–75% of bladder neurofibromas are detected in patients younger than 18 years (40), and the bladder is the most common site for neurofibromas that affect the genitourinary system (41). They affect both the spinal and the autonomic nerves of the bladder wall (42), although the ability to void may not necessarily be affected, and in some cases, the



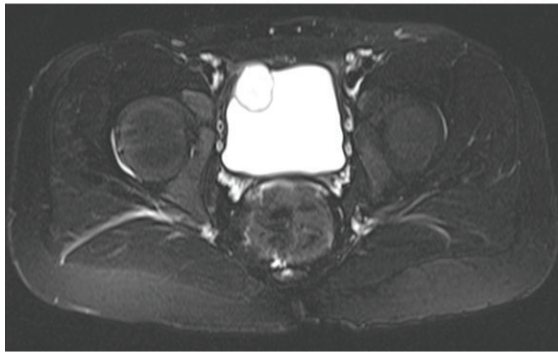
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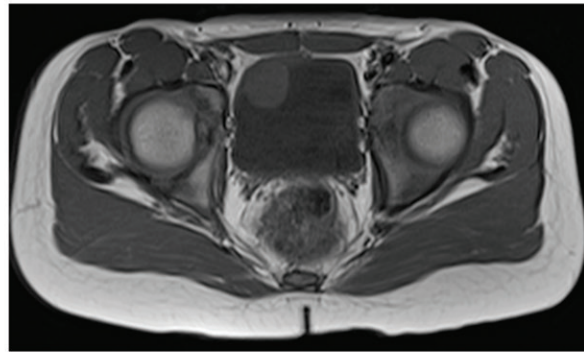


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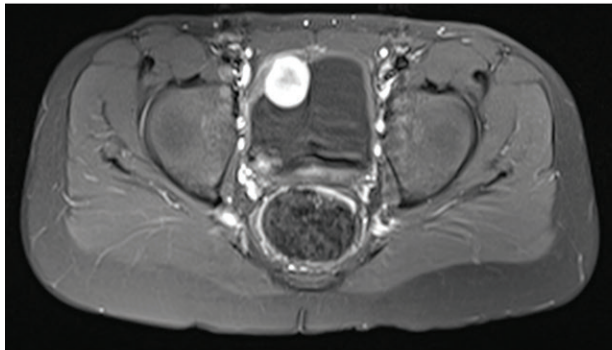
**Figure 4.** IMT in an 8-year-old boy. (a) Midline transverse US image shows a well-defined round soft-tissue lesion adherent to the anterior urinary bladder wall. (b) Axial T2-weighted fat-saturated MR image shows the lesion with high internal signal intensity, which, paradoxically, can make the tumor harder to identify when the bladder is full of urine. This factor highlights the importance of correlating these findings with those seen with other MR imaging sequences. (c, d) Axial nonenhanced non-fat-saturated (c) and contrast-enhanced fat-saturated (d) T1-weighted MR images show avid enhancement of the lesion. (e) The surgically resected lesion is well defined and polypoid, and it appears to be vascular.



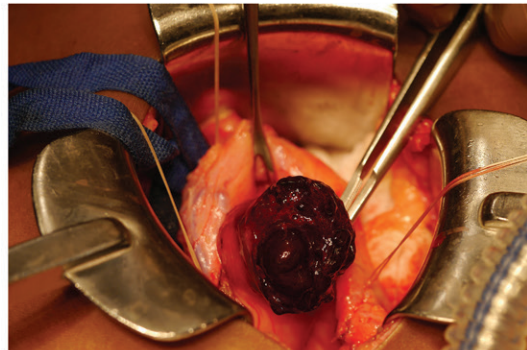
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patient may be asymptomatic (43). Bladder imaging findings may be the first manifestation of neurofibromatosis type 1, and, therefore, knowledge of the underlying syndrome is not always a prerequisite to the diagnosis, although one may identify the cutaneous stigmata of the syndrome at the time US is performed or by the referring clinician's description of the lesions from the clinical examination.

At imaging, neurofibroma appears as a solid mass and can manifest as a focal lesion or diffuse bladder wall thickening (Fig 6). At MR imaging, these lesions generally have homogeneous low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. On T2-weighted MR images, plexiform neurofibromas often exhibit a target sign, with high signal inten-

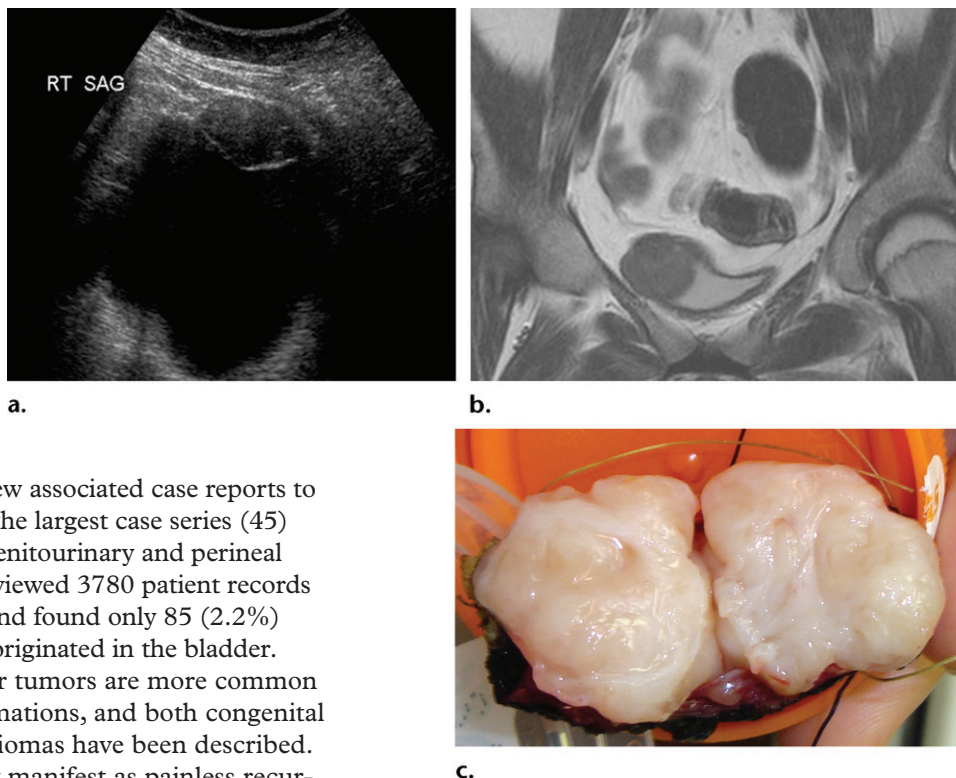
sity peripherally and lower signal intensity centrally. The differential diagnosis includes rhabdomyosarcoma and ganglioneuroma (44). Although debulking resection may alleviate the symptoms of the mass effect exerted by the neurofibroma, total resection is difficult because the majority of these tumors are plexiform. There is a risk of malignant transformation of neurofibroma; however, in a case series (40) involving four pediatric patients with bladder neurofibroma, these patients were not found to have developed a malignancy during a mean follow-up period of 9.6 years.

### Vascular Anomalies

In children, vascular anomalies are common outside of the bladder but exceedingly rare within the



**Figure 5.** Bladder leiomyoma in an 18-year-old woman. (a) Right sagittal US image shows a hypoechoic anterior bladder wall lesion. (b) Coronal T2-weighted MR image shows a round bladder mass that is isointense to muscle. (c) Photograph of the tumor divided into halves after resection shows the pale interior of the lesion; this is a typical macroscopic appearance of leiomyomas.



bladder, with only a few associated case reports to date. Investigators in the largest case series (45) involving childhood genitourinary and perineal vascular anomalies reviewed 3780 patient records over a 5-year period and found only 85 (2.2%) cases, none of which originated in the bladder.

In general, vascular tumors are more common than vascular malformations, and both congenital and infantile hemangiomas have been described. These tumors usually manifest as painless recurrent macroscopic hematuria; rarely, hypovolemic shock caused by massive hemorrhage occurs (46). Histopathologically, the appearances of bladder hemangiomas are no different from those of hemangiomas identified elsewhere in the body.

At US, a vascular tumor may appear as a polypoid intraluminal solid mass with increased vascularity or less commonly as hyperemic diffuse bladder wall thickening, which sometimes contains punctate calcifications (Fig 7a). The lesions are more commonly located at the bladder dome or in the posterolateral walls and are usually solitary. Multiple bladder hemangiomas may be seen with Klippel-Trenaunay-Weber or Sturge-Weber syndrome (47). However, even in the absence of a vascular malformation syndrome, cutaneous vascular malformations can be seen elsewhere in the body in approximately 30% of cases (48).

Vascular tumors are usually treated with lesion ablation; however, partial or total cystectomy may be required if the mass is large, with deep extension, and causing substantial hemorrhage (46). Differential diagnoses may include urachal remnant abscess (if a mass is seen at the bladder dome), cystitis, rhabdomyosarcoma, and even hyperemic granulation tissue from a site of prior bladder biopsy.

Other bladder vascular anomalies seen in children include lymphatic and arteriovenous malformations (49,50) and bladder wall telangiectasia (in

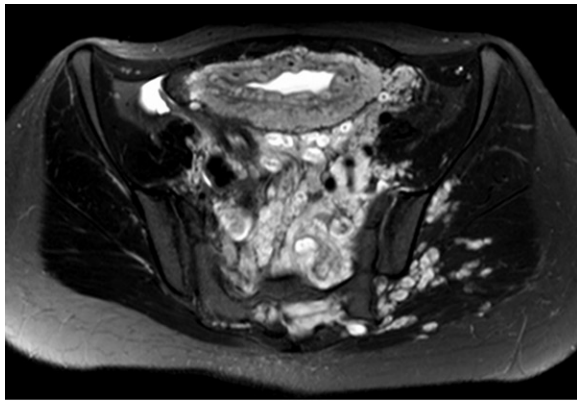
the setting of ataxia-telangiectasia) (51). Aggressive and potentially malignant vascular tumors include epithelioid hemangioendothelioma (52) and angiosarcoma (53). However, these are exceedingly rare tumors; those seen are limited to tumors described in case reports and small case series.

### Urothelial Neoplasms

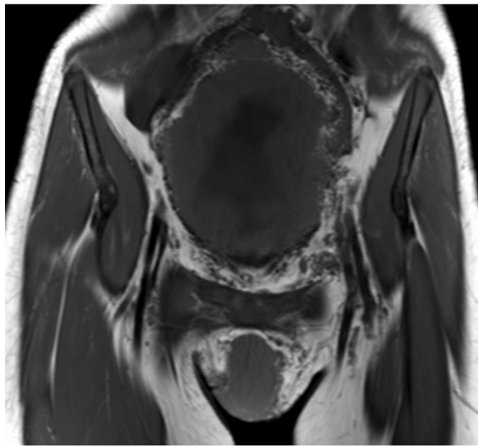
Urothelial neoplasms in children are rare and predominantly noninvasive. In a case series (54) involving the review of urothelial bladder lesions in 23 patients younger than 20 years, 10 (43.5%) of the cases involved PUNLMPs; eight (34.8%), low-grade urothelial carcinomas; and two (8.7%), urothelial papillomas. Three (13%) of the cases involved high-grade urothelial carcinomas. The various subtypes of urothelial bladder neoplasms cannot be distinguished from each other at imaging. However, knowledge of the patient's medical history—for example, history of a prior surgical intervention or a syndrome that predisposes individuals to cancer—may make certain urothelial lesion subtypes more likely.

### Urothelial Carcinoma

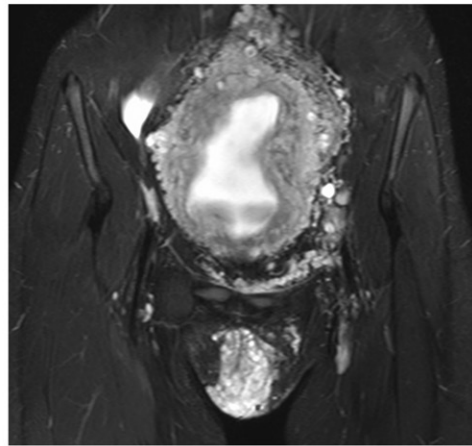
Although urothelial carcinomas are the most common urinary tract malignancy in adults, they



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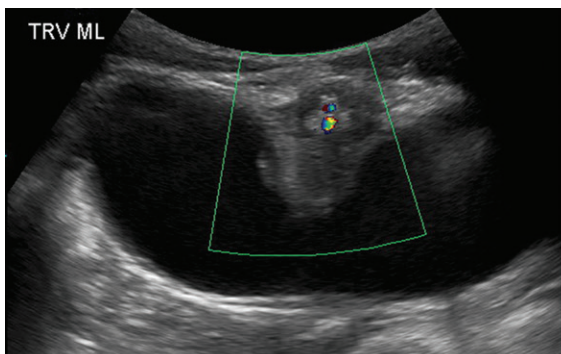


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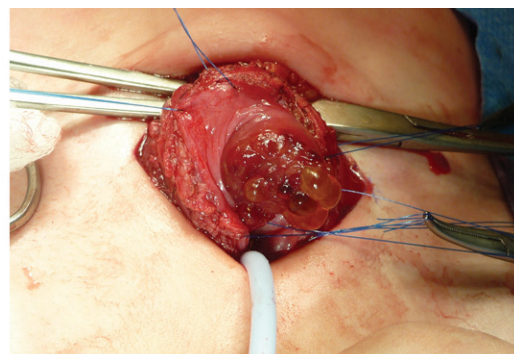


c.

**Figure 6.** Extensive pelvic plexiform neurofibroma in a 12-year-old girl with neurofibromatosis type 1. (a) Axial T2-weighted fat-saturated MR image shows an extensive lobulated soft-tissue mass surrounding and interspersed between multiple pelvic structures, and affecting the entire urinary bladder wall. (b, c) Coronal non-fat-saturated (b) and contrast-enhanced fat-saturated (c) T1-weighted MR images show marked enhancement of the plexiform neurofibroma. The additional high signal intensity of the soft tissues inferior to the bladder represents further extension of the neurofibroma within the vulva, which was enlarged at clinical examination.



a.

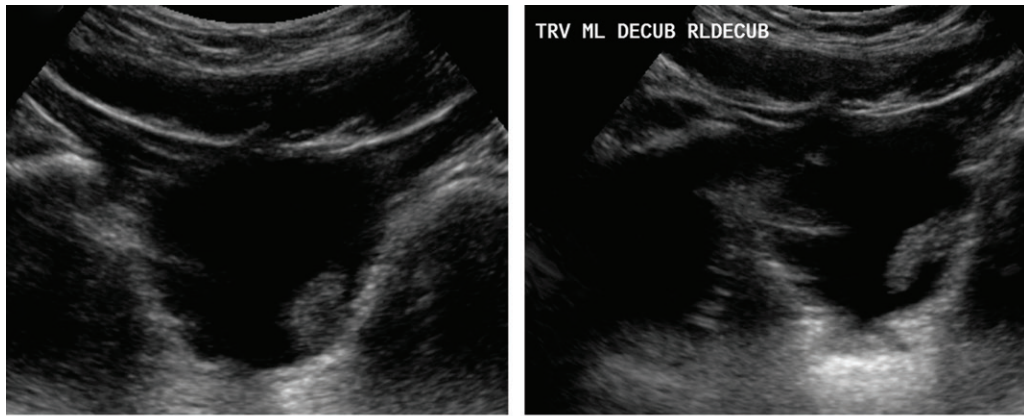


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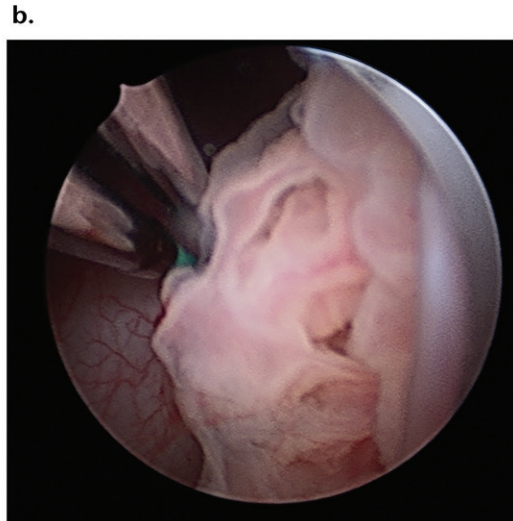
**Figure 7.** Hemangioma in an 8-year-old boy with Klippel-Trenaunay-Weber syndrome. (a) Transverse midline color Doppler US image of the urinary bladder shows a lesion that is adherent to the anterior bladder wall with internal flow. (b) Intraoperative photograph shows the bladder lesion before resection.

are rare and have a distinctly different clinical course in children. When present, the majority of these tumors are of low-grade morphology and solitary (in 94% of cases [55]). They are associated with a low risk of recurrence and rarely in-

volve the upper urinary tracts. Urothelial carcinomas typically manifest in adolescents; they occur in persons aged 10 years or younger in only 30% of cases (54). At imaging, there are no specific features that distinguish urothelial carcinomas



**a.**  
**Figure 8.** Urothelial cell carcinoma in an 8-year-old boy. (a, b) Transverse midline US images of the bladder obtained with the patient supine (a) and rolling to the right (b) show a lesion adherent to the left lateral bladder wall. (c) Image obtained during cystoscopic biopsy shows the lobulated appearance of the lesion.



**b.**  
**c.**

from other urothelial bladder lesions; however, they have a tendency to occur at the vesical trigone and ureteric orifices (56) (Fig 8).

Urothelial carcinoma may occur as a secondary primary tumor in young adult survivors of retinoblastoma or in the setting of other childhood cancer–predisposing syndromes, such as Costello syndrome and hereditary nonpolyposis colorectal cancer syndrome (10). Patients with a history of augmentation cystoplasty have an increased risk of developing urothelial carcinoma, which in this setting occurs more frequently at bladder–intestine anastomosis sites and is more likely to be of high grade and have an aggressive clinical course (57). For this reason, some clinicians recommend endoscopic surveillance of patients who have this history. This surveillance should begin 10 years after the initial surgery owing to the considerable time required for the lesion to develop (58).

The treatment of choice for low-grade urothelial carcinomas is transurethral resection; however, partial cystectomy may be required in some (rare) cases (54). There is no standard surveillance protocol for the imaging follow-up of treated patients, and recurrences have been reported—especially when multiple tumors were originally present (59). Although some recommend performing regular US examinations, the frequency of these examinations and length of the follow-up are debatable.

### Papillary Urothelial Neoplasm of Low Malignant Potential

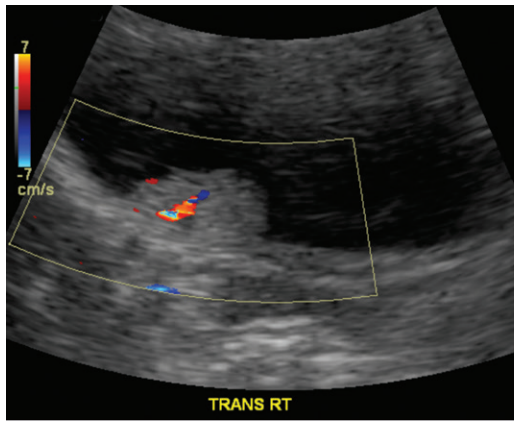
PUNLMPs are common bladder lesions in children. Of 140 bladder tumors in the Surveillance,

Epidemiology and End Results database (60) that were analyzed from 1973 to 2003, 71 (50.7%) were PUNLMPs. The term *papillary urothelial neoplasm of low malignant potential* was added to the 2004 World Health Organization–International Society of Urological Pathology classification system to describe a urothelial tumor that resembles exophytic urothelial papilloma but has increased cellular proliferation, the thickness of which exceeds that of the normal urothelium (61). Before the reclassification, these lesions were known as grade 1 urothelial carcinomas (62).

At imaging, PUNLMPs are difficult to differentiate from noninvasive urothelial carcinomas. They are normally solitary, measure 1–2 cm, and have been described as having a “seaweed in the ocean” appearance (61) (Fig 9). They commonly occur at the posterior lateral walls and ureteric orifices of the bladder, are noninvasive, and do not metastasize.

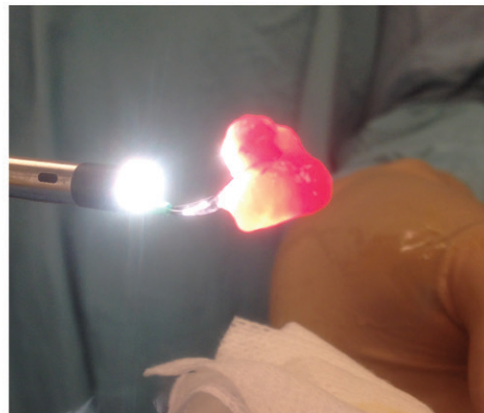
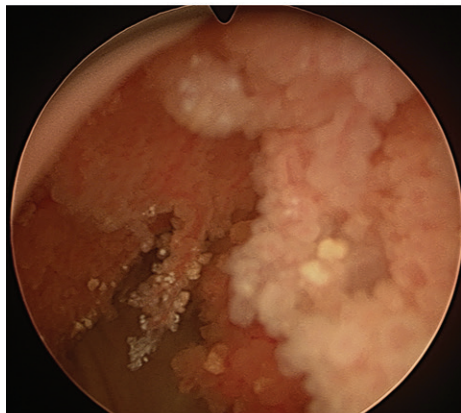
Approximately 35% of PUNLMPs reportedly recur after resection, and 11% of them increase in size if they are not treated; therefore, imaging surveillance is advocated. The starting time and length of the surveillance are not standardized (63).





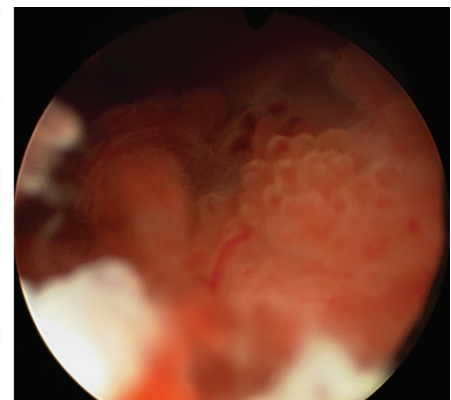
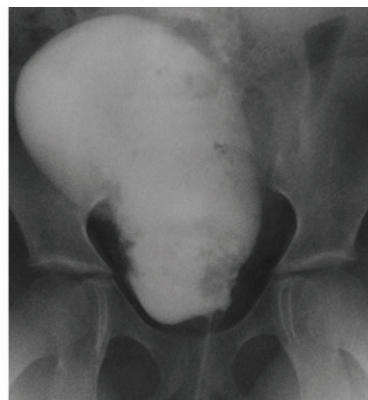
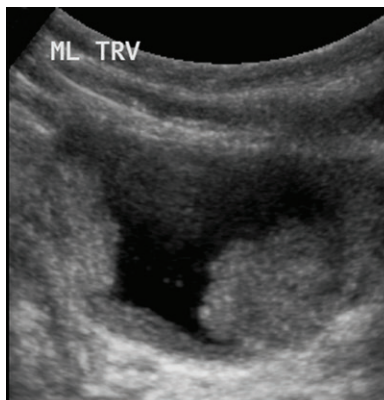
**Figure 9.** PUNLMP in an 8-year-old boy. (a) Right transverse color Doppler US image shows a lobulated vascular soft-tissue lesion adherent to the right inferolateral bladder wall, with minimal internal flow. (b) Image obtained during cystoscopic biopsy shows a flesh-colored cauliflower-like mass. (c) Photograph shows the excised lesion attached to the cystoscopy snare.

a.



b.

c.



a.

b.

c.

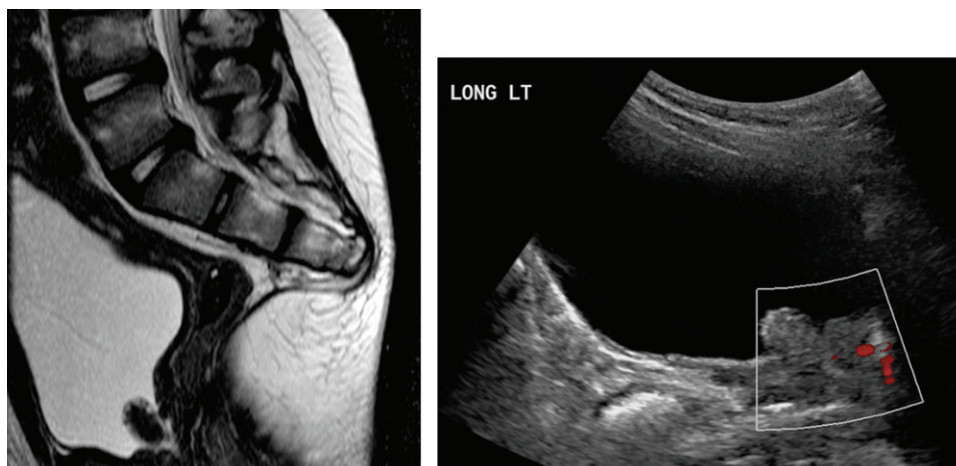
**Figure 10.** Bilateral urinary bladder papillomas in a 6-year-old girl. (a) Midline transverse US image shows bilateral lobulated soft-tissue masses at the vesicoureteric junctions. (b) Voiding cystourethrogram shows multiple filling defects in the urinary bladder, along the lateral walls. (c) Cystoscopic image obtained during biopsy shows flesh-colored lobulated lesions. The biopsy findings confirmed the diagnosis of urothelial papillomas.

### Urothelial Papilloma

Urothelial papillomas are benign polypoid urothelial neoplasms that are typically seen in male persons younger than 50 years; they have been infrequently reported in children. Microscopically, these lesions demonstrate a fibrovascular core covered by a normal urothelium and no cytologic atypia. Occasionally, large papillary structures may bud, giving rise to smaller fronds

or anastomoses of papillae, which help to distinguish these tumors from fibroepithelial polyps at pathologic analysis.

Urothelial papillomas have been described as having a frondlike appearance at imaging, although this feature is not pathognomonic, and to occur near the ureteric orifices or along the posterior bladder wall (64) (Fig 10). Transurethral excision is the treatment of choice. Owing



**Figure 11.** Urinary bladder fibroinflammatory polyp in an 8-year-old boy. The polyp was initially identified incidentally at MR imaging of the lumbar spine. **(a)** Sagittal T2-weighted lumbar spine MR image shows an incidentally discovered bladder lesion at the urethral orifice. **(b)** Sagittal color Doppler US image of the urinary bladder shows the lobulated lesion with mild internal vascularity. The lesion was subsequently removed at cystoscopy.

to limited experience with this rare tumor in children, management options remain controversial. Because the urothelial papillomas seen in adults are known to recur, US follow-up has been advocated. Again, there is no standardized time interval for this follow-up in any treatment protocols (65).

### Fibroepithelial Polyp

Fibroepithelial polyps are benign urothelial lesions and are more commonly seen in the upper urinary tract in adults. In children, they typically occur at or near the bladder neck (66). They manifest in children with a mean age of 9 years, can manifest during infancy, and have a strong male predilection (67).

The manifestations of fibroepithelial polyps include gross hematuria and flank pain, which may be due to torsion of the polyp (68) if it reaches a substantial size. However, the majority of these lesions are solitary and smaller than 5 cm (69) (Fig 11). Microscopically, fibroepithelial polyps are composed of papillary fronds lined by a normal-appearing urothelium without cellular atypia. Some of them may exhibit focal areas of ulceration (70).

There are no specific radiologic features (66) that distinguish fibroepithelial polyps from other pathologic bladder lesions, and the differential diagnoses include urothelial papillomas and botryoid-type rhabdomyosarcomas (70).

### Neuroendocrine Tumors: Paraganglioma

Pheochromocytomas of extra-adrenal origin are known as paragangliomas, and the urinary bladder is the most common site for genitourinary

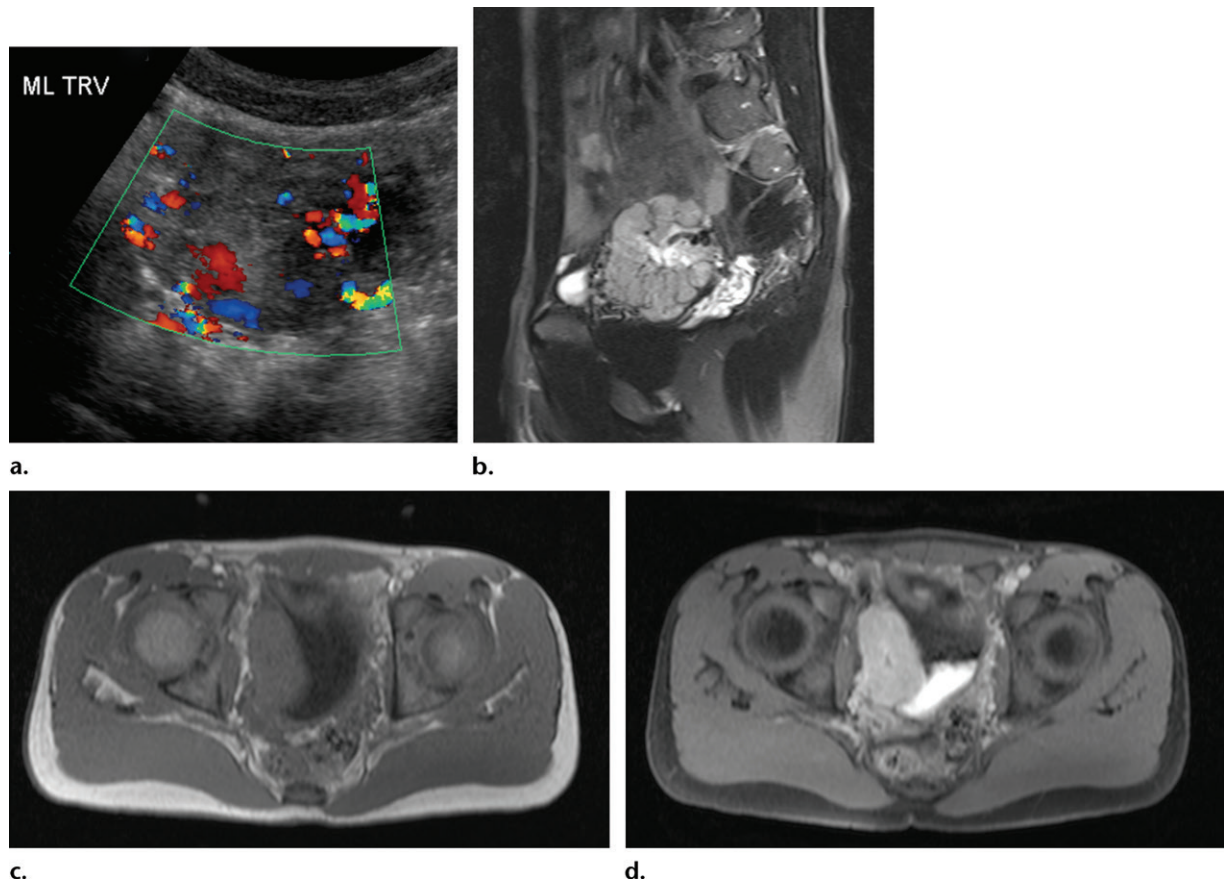
paragangliomas (71). These tumors arise from embryonic rests of chromaffin cells in the sympathetic plexus of detrusor muscle. They are more common in adults between the ages of 30 and 60 years but can occur in persons aged 10–88 years. Genitourinary paragangliomas are exceedingly rare, accounting for less than 0.5% of all bladder tumors in adults and children combined (72).

Genitourinary paragangliomas are usually benign, but 10% of them may be malignant, and they are often hormonally active. The symptoms at manifestation are related to catecholamine excess and usually include hypertension and headache, which can be related to micturition (73).

These tumors usually are intramural and located in the lateral or posterior bladder wall (74). At MR imaging, they are typically mildly hyperintense relative to muscle on T1-weighted images and hyperintense on T2-weighted images (75) (Fig 12b–12d). Paragangliomas tend to be vascular tumors that demonstrate avid enhancement characteristics. The presence of increased tracer activity on nuclear medicine images, such as iodine 131 metaiodobenzylguanidine and fluorine 18 fluorodeoxyglucose PET scans, can be useful for confirming the diagnosis and identifying metastatic lymph nodes. Surgical excision, if localized, is usually curative, although care must be taken, given the potential for an intraoperative hypertensive crisis (76).

### Glandular Bladder Lesions: Nephrogenic Adenoma

*Nephrogenic adenoma of the urinary bladder* is defined as a metaplastic change in the urinary bladder, with papillary or cryptic structures similar



**Figure 12.** Imaging findings in a 15-year-old boy with hypertension secondary to bladder paraganglioma. (a) Midline transverse color Doppler US image of an underfilled urinary bladder shows a round soft-tissue mass in the right lateral bladder wall, with marked vascularity. (b) Sagittal T2-weighted fat-saturated MR image shows a tortuous vessel leading into the lesion. (c, d) Axial nonenhanced (c) and contrast-enhanced fat-saturated (d) T1-weighted MR images obtained at the level of the urinary bladder show avid enhancement of the bladder wall lesion.

to those seen in renal tubules. These tumors are rare, with only about 400 cases reported to date (77) and approximately 10% of cases identified in children. There is typically a history of a surgical procedure of the genitourinary tract—with approximately 10% of patients having undergone renal transplantation (78)—or an underlying inflammatory or traumatic process such as calculi, trauma, immunosuppression, or cystitis. In contrast to other bladder masses, nephrogenic adenomas commonly manifest with frequent urination rather than hematuria.

At macroscopic analysis, approximately half of these neoplasms appear as papillary lesions, 35% of them appear as sessile lesions, and 10% of them appear as polypoid lesions. The size of these lesions varies considerably, from microscopic to larger than 4 cm (in 10% of cases). The largest reported lesion in a child measured up to 7 cm (79). The imaging features of nephrogenic adenomas are similar to those of urothelial neoplasms. For treatment, removal of the causative factors, if known (eg, calculi), and excision of the lesion are required. However,

in a case report (80) of disseminated polypoid nephrogenic adenomas in a 12-year-old boy, successful resolution of the symptoms and lesions was achieved by means of regular intravesical administration of sodium hyaluronate every 2 weeks for 5 months.

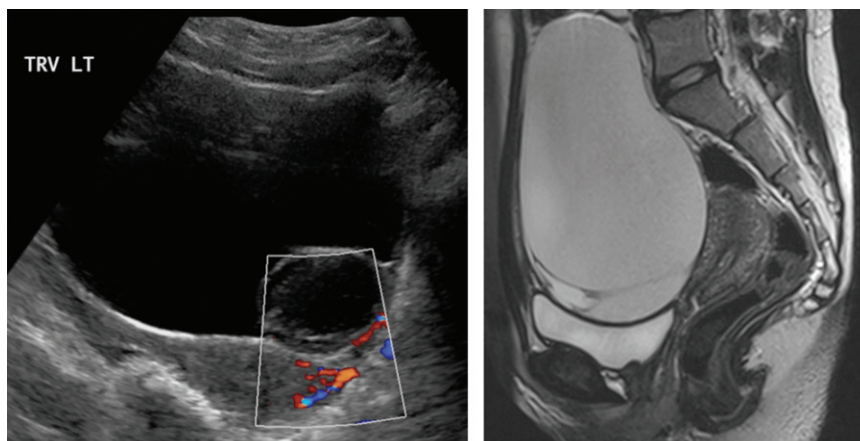
### Imaging Pitfalls

Several potential pitfalls are related to imaging the urinary bladder in children. These pitfalls are categorized and described briefly in the following sections to emphasize the importance of exercising caution when imaging the pelvis—especially when considering pathologic conditions of the bladder.

#### Pelvic Mass Misinterpreted as Arising from the Bladder

Owing to the anatomy of the pelvis, inflammatory or malignant lesions arising from adjacent structures are a source of potential pitfalls related to misinterpreted imaging findings. These misinterpretations may involve lesions arising from the ovary (Fig 13), bowel, osseous structures, or





**Figure 13.** Ovarian mucinous cyst, initially misinterpreted as a bladder mass, in a 12-year-old girl. **(a)** Left transverse color Doppler US image shows an avascular cystic structure that appears to be lying at the left vesicoureteric junction. **(b)** Sagittal T2-weighted MR image shows a large septated cystic structure that is separate from and superior to the urinary bladder.

lymph nodes. The lesions may abut the urinary bladder and appear to be arising from it, or they may actually arise from the bladder but be misinterpreted as arising from an adjacent structure. Paradoxically, the larger the mass, the harder it is to determine the site of its origin.

If a pelvic structure is seen and found to be filled with fluid, it is important to remember a few crucial facts and take some practical measures before rendering the diagnosis. First, it is important to determine whether a normal urinary bladder can be seen separate from the structure. A normal bladder wall generally exhibits a more echogenic inner luminal layer and hypoechoic detrusor muscle layer at US. When the bladder is filled (to 90%–100% capacity), the bladder wall can measure up to 0.3 mm in thickness (81,82), whereas a cyst may have a pencil-thin echogenic wall. When an inflammatory mass is present, the wall may be thicker.

If it is difficult to identify the bladder, then reexamining the patient with an emptied or filled bladder may be helpful, as this enables one to see whether the pelvic structure now disappears (with an emptied bladder) or the filled bladder now readily appears as a separate structure. If a catheter is inserted, the US examination can be repeated by instilling the bladder with warmed sterile water just before the reexamination or clamping the catheter for at least 1 hour before repeating the examination.

#### Normal Variant or Bladder Wall Impression Misinterpreted as a Mass

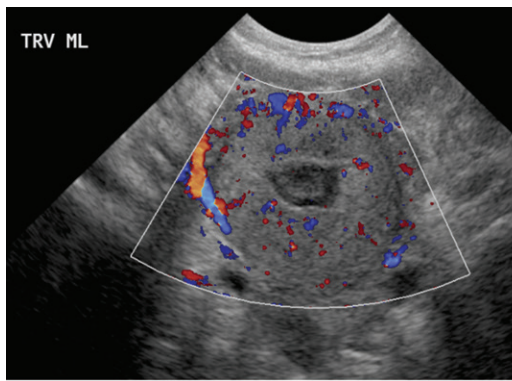
Owing to the mass effect on the posterior bladder wall or the presence of a filling defect at fluoroscopy, a normal anatomic variant such as a bulky uterus (due to uterine didelphys related to a mass

effect) or a ureterocele (related to a filling defect) may give the impression of a bladder lesion. Careful assessment with use of US techniques similar to those described earlier usually can help to clarify the pelvic anatomy.

#### Inflammatory or Nonneoplastic Lesion Misinterpreted as a Tumor

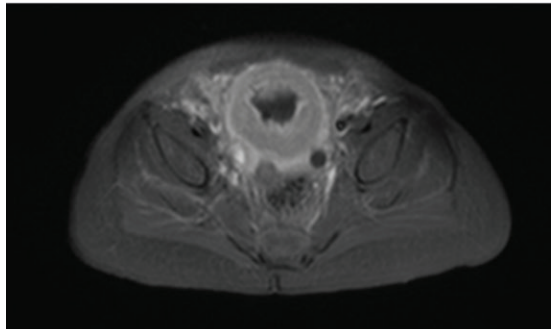
Rarely, cystitis mimics a bladder neoplasm such as rhabdomyosarcoma. The terms *pseudotumoral cystitis*, *cystitis follicularis*, *cystitis glandularis*, and *bullous cystitis* have been used in the literature to describe benign inflammatory masslike lesions of the bladder wall (83). BK virus–associated hemorrhagic cystitis, which was seen as vascular mural nodules on a background of diffuse bladder wall thickening in a child who underwent hematopoietic stem cell transplantation, also has been described (84) and may simulate bladder masses. Such masslike appearances may be due to focal edematous changes within the lamina propria or the proliferation of mucosal and submucosal glands in the epithelial layer, with either phenomenon causing cystlike elevations and simulating a polypoidal appearance on images.

Eosinophilic cystitis is a rare differential diagnosis, and it also can have a masslike appearance on images. The bladder wall may have a markedly hyperemic appearance at color Doppler US (Fig 14a), and there may be clinical signs of macroscopic hematuria. The urine is usually sterile, and there may be a history of atopy (85). The masslike appearance with this condition is thought to be due to an antigenic stimulus that promotes the immunoglobulin E–mediated attraction of eosinophils throughout the bladder wall, with subsequent mass cell degranulation and releasing of inflammatory mediators (86).

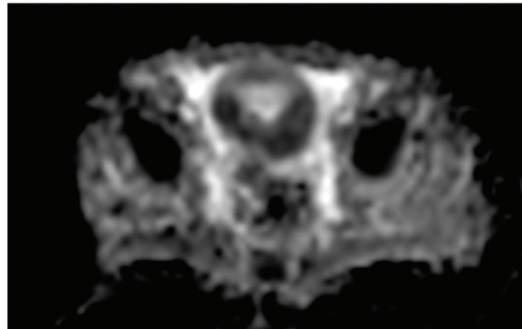


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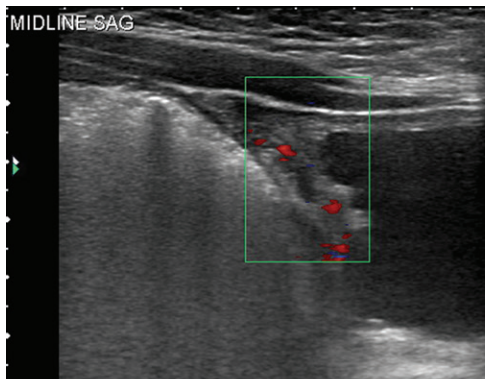
**Figure 14.** Eosinophilic cystitis in a 5-month-old boy. (a) Transverse midline color Doppler US image shows marked bladder wall thickening with mild hyperemia. (b) Axial contrast-enhanced T1-weighted fat-saturated MR image shows homogeneous and avid contrast enhancement of the thickened bladder wall. (c) On the axial apparent diffusion coefficient (ADC) image, the bladder wall has low ADC values internally, indicating restricted diffusion.



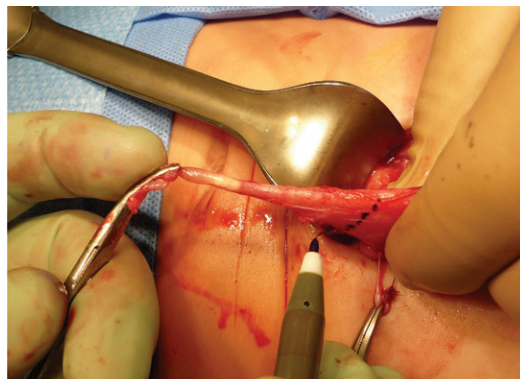
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a.



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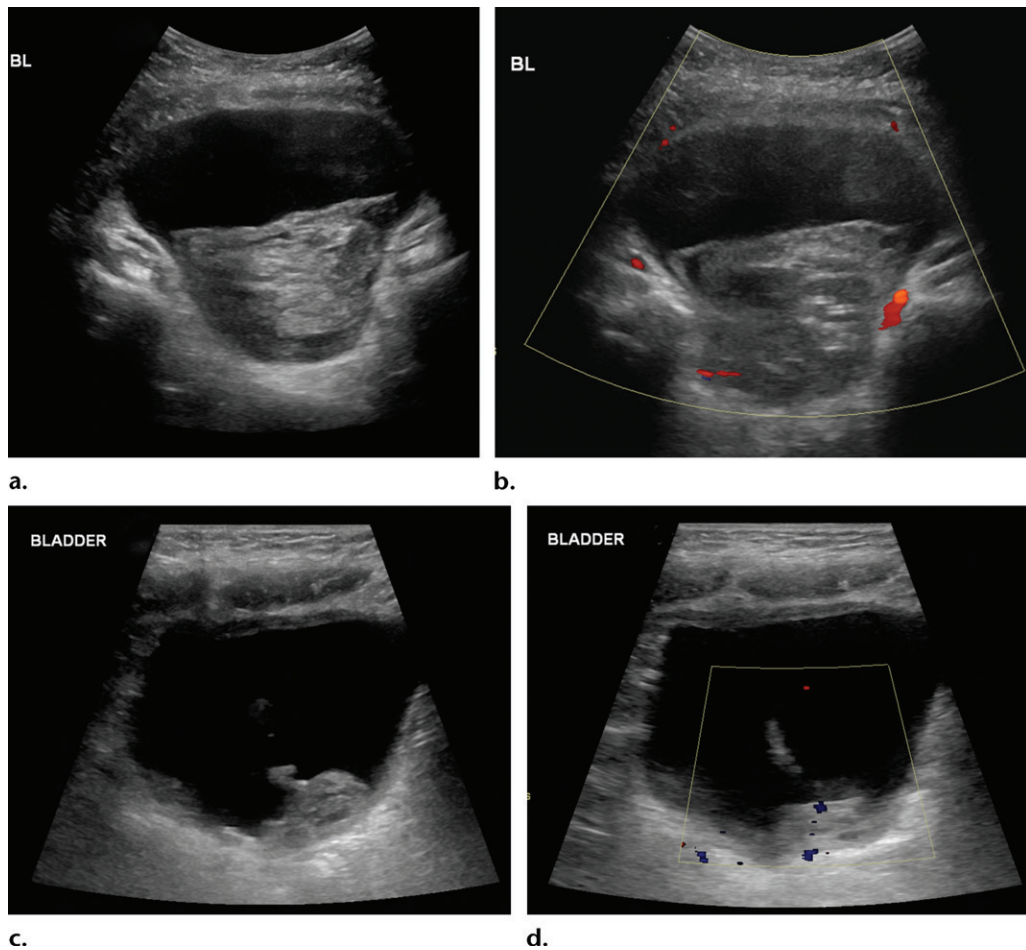
**Figure 15.** Inflamed urachal remnant in a 9-year-old girl. (a) Midline sagittal color Doppler US image shows a focal area of soft-tissue thickening at the bladder dome, with internal vascularity. (b) Intraoperative photograph shows the area of soft-tissue thickening being excised (dotted black line). The thickened tissue was sent for histopathologic analysis, which did not reveal malignant cells.

Therapy is usually conservative, and the disease is mainly self-limiting (87).

Congenital urachal remnants, urachal cysts in particular, are typically described as being external to the bladder. Nevertheless, there are reported instances in which these cysts, located at the antero-superior aspect of the bladder, have appeared as intravesical lesions, ballooning into the bladder lumen or discharging intravesically (88). When infected, urachal cysts can appear with a hypervascular and heterogeneous echotexture at US and have variable enhancement at cross-sectional imaging (Fig 15). Therefore, these cysts can be easily misinterpreted

as other bladder masses such as hemangiomas, rhabdomyosarcomas, or IMTs. Tumors arising from urachal remnants rarely occur during childhood; however, given the increased risk of adenocarcinoma arising from these remnants during adulthood, they are typically treated surgically when they are discovered incidentally (89).

To the untrained eye, the US appearance of a thickened bladder in a neonate with posterior urethral valves also may be masslike. However, this pathologic entity is far more common than neonatal bladder masses. The typical findings of a dilated posterior urethra and trabeculated



**Figure 16.** Bladder hematoma in a 10-year-old boy after suprapubic catheter insertion. (a) Transverse US image obtained after the procedure shows a large heterogeneous bladder lesion. (b) Transverse color Doppler US image shows no internal vascularity. (c) Transverse US image obtained 5 days later shows an interval reduction in lesion size. (d) Most recently obtained transverse color Doppler US image still shows no internal vascularity.

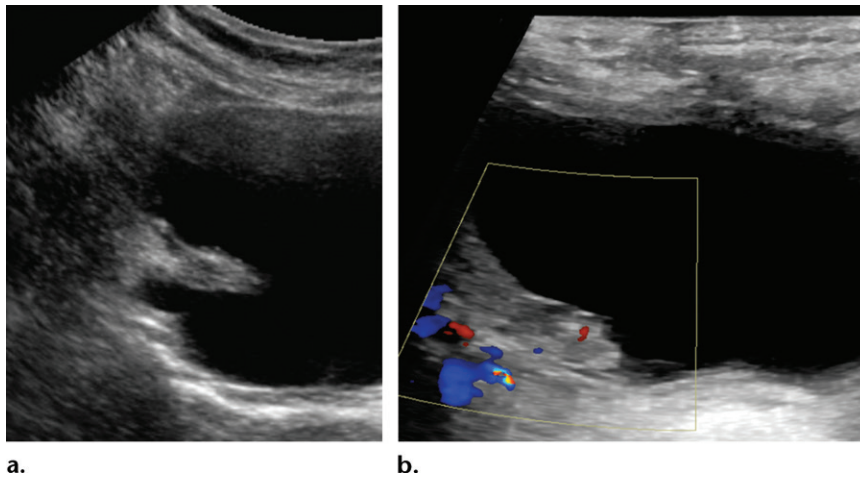
small-volume bladder at subsequent micturating cystourethrography help to confirm the diagnosis.

### Mobile or Iatrogenic Material within the Bladder Misinterpreted as a Mass

Mobile bladder material may include bladder calculi, layered debris, and/or hematoma. These pathologic entities should demonstrate some mobility when the patient is turned on his or her side and at repeated imaging; thus, it is important to determine whether a bladder mass is truly adherent to the bladder wall. Hematomas may be associated with known underlying pathologic conditions and therapies such as hemorrhagic cystitis and anticoagulation medication, respectively. They do not have internal flow at color Doppler US and may demonstrate interval reductions in size at follow-up imaging, as shown in Figure 16. The worldwide popularity of a dextranomer–hyaluronic acid copolymer (Deflux; Salix Pharmaceuticals, Bridgewater, NJ) that is endoscopically injected into the subureteric space as a minimally invasive treatment of vesicoure-

teric reflux has increased in recent years. The calcification of this iatrogenic material is common and can be misinterpreted as a distal ureteric or bladder calculus or a mass at imaging (Fig 17). This lesion does not become mobile when the patient's positioning changes and is echogenic on US images. At CT, findings that distinguish this lesion as injected dextranomer–hyaluronic acid copolymer include a lack of associated ureteric dilatation and attenuation values lower than 400 HU (90). In one study (91) of dextranomer–hyaluronic acid copolymer involving 16 children who underwent imaging 1–40 months after the injection procedure, this material had increased signal intensity on T2-weighted MR images but was not identified with any other MR imaging sequences, including gadolinium-enhanced imaging (91). In general, if an echogenic lesion is seen near the ureteric orifice or distal ureter, the absence of clinical symptoms of renal colic combined with knowledge of a recent urologic procedure for reflux should alert the radiologist to the potential presence of this imaging phenomenon.





**Figure 17.** Dextranomer–hyaluronic acid copolymer material in a 10-year-old boy who underwent imaging 2 years after subureteric injection of this material for treatment of vesicoureteric reflux. **(a)** Transverse US image of the bladder shows a nipple-shaped lesion, which has internal hyperechogenic foci, adjacent to the right ureteric orifice. **(b)** Sagittal color Doppler US image shows a subtle “twinkle” artifact in the hyperechogenic region. Although there is no posterior acoustic shadowing of this lesion, it can be present with the larger foci of calcification that can be seen after the copolymer injection procedure.

## Conclusion

Compared with the bladder neoplasms seen in adults, bladder neoplasms in children are rare and have a different histologic spectrum. The majority of these lesions are benign. The most common malignancy of the genitourinary tract in children is rhabdomyosarcoma, followed by urothelial lesions. PUNLMPs are reportedly the most prevalent urothelial tumors in the pediatric population. The initial imaging examination should include US—preferably with the patient’s bladder full.

Owing to the anatomy of the pelvis, inflammatory or malignant lesions arising from adjacent structures are a source of potential misinterpretation pitfalls at imaging. These misinterpretations may involve lesions arising from the ovary, rectum, osseous structures, or lymph nodes. In addition, some nonneoplastic bladder lesions, such as cystitis-related bladder wall thickening and bladder calculi, may be masslike and misinterpreted as tumors. An awareness of these pitfalls is essential to avoiding diagnostic dilemmas.

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