Diagnostic Pitfalls in the Diagnosis of Soft Tissue Bladder Tumors in Pediatric Patients

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ABSTRACT

This is a case report of a low-grade leiomyosarcoma of the bladder in a four-year-old girl. The pitfalls in diagnosing a soft tissue tumor of the bladder in pediatric patients are discussed. This case is particularly instructive because the differential diagnosis was broad, difficult, and of serious consequence. This report discusses the process by which histologic, immunohistologic and ultrastructural data were used to sidestep the pitfalls in diagnosing this unusual tumor. Clinical follow-up data bearing out our conclusion are also presented.

Introduction

Sarcomas of the bladder are a relatively rare set of tumors. Leiomyosarcomas are a small subset of these, even more so in the pediatric age group. Under light microscopy, sarcomas have a penchant for looking alike, even to investigators of experience and repute. Recent advances in immunochemistry and electron microscopy have helped considerably in classifying soft tissue neoplasms and differentiating them from reactive processes. In no case presented in the literature was the gross appearance considered of diagnostic importance for bladder neoplasms. Location has been suggested as a possible aid in differentiating bladder sarcomas, as will be discussed later. As noted, the light microscopic presentation can support several possible conclusions. The assessment of these rare bladder tumors is fraught with pitfalls and all modes of investigation must be utilized to provide the most accurate diagnosis.

Case Report

Our patient was a four-year-old Hispanic girl who had a several week history of gross hematuria and moderate dysuria. Mild anemia was also noted, with all other laboratory studies giving normal results. A
bladder mass was found and biopsied transurethrally. Initially a diagnosis of rhabdomyosarcoma was entertained, followed by that of a benign inflammatory pseudotumor. An intravenous pyelogram showed a large filling defect in the bladder and ultrasound confirmed the presence of a tumor mass with blood clot within the vesical. The mass was located in the right posterior wall of the bladder. A partial cystectomy was performed, allowing for ample margins. The patient's recovery was uneventful.

Pathologic Findings

The specimen was a segment of bladder containing a $5 \times 5 \times 3$ cm, 27 g encapsulated-looking irregular mass. One side was covered by an intact serosa. The mucosa had an ulcerated area measuring approximately one square centimeter and had several smaller hemorrhagic foci. Upon being sectioned, it appeared lobulated, whorled, fibrous, and had a tan-yellow color.

Under the light microscope, the tumor was highly varied in its presentation. In general, it was well circumscribed. The fibrous tissue around the perimeter of portions of the tumor was compressed into a pseudocapsule. This encapsulation was only partial, being interrupted by focal infiltration of the surrounding muscle by tumor cells. The cellularity varied greatly. Some foci were densely packed, with whorled and pallissading spindle cells having little or no intervening stroma (figure 1A). These cells possessed large nuclei with prominent nucleoli (figure 1B). Other areas were typified by isolated, often bizarre cells floating in a background of slightly basophilic mucoid substance (figure 2). These cells varied from spindle cells with moderately hyperchromatic nuclei and prominent nucleoli to tadpole or flag cells with hyperchromatic nuclei and occasional bizarre mitotic figures.

The mitotic rate varied from zero to four per high power field. Often the nuclei were irregular, cleaved and/or boxcar-shaped. Additionally, many of the cells had brightly eosinophilic, round, glassy inclusions in their cytoplasm. These structures corresponded to condensed myofilaments when viewed by electron microscopy. These were not membrane bound. Many foci of chronic inflammation were noted deep within the tumor.

Special stains were used to sort out the contradictive nature of the tumor. Phosphotungstic acid hematoxylin revealed no cross striations. Masson trichrome stain revealed bright red tumor cells resembling normal muscle and a blue-staining capsule. The periodic acid-Schiff (PAS) reaction was moderately positive for cytoplasmic glycogen. Immunohistochemistry was positive for vimentin and desmin, and was negative for myoglobin.

Lastly, there were areas demonstrating a moderate and diffuse inflammatory infiltrate. The infiltrate comprised lymphocytes, eosinophils, and scattered macrophages and neutrophils. No giant cells were seen (figure 3). These areas were unevenly distributed throughout the tumor and not limited to the areas adjacent to the mucosal ulceration.

Electron microscopy identified the following characteristics of the tumor: abundant rough endoplasmic reticulum and mitochondria, myofilaments affiliated with dense bodies, pinocytotic vesicles, basal laminae, deeply clefted nuclei and the absence of cross striations or Z bands (figure 4). The myofilaments were especially dense in areas corresponding to the eosinophilic "inclusions" seen on light microscopy. The dense bodies were scattered throughout the cytoplasm, and very often the myofilaments appeared to connect them to one another.

Discussion

The abundance of evidence gained by utilizing all modes of investigation makes the diagnostic process appear deceivingly simple. The ease with which one
may go astray in a case like this is exemplified by the response of our consultants. One source suggested that this was probably a rhabdomyosarcoma and recommended aggressive chemotherapy. The other source suggested a diagnosis of an inflammatory pseudotumor but said that it could also be a leiomyoblastoma. Both consultants had extensive experience in handling soft tissue tumors and underscored the care that must be taken by those who encounter these tumors ever so rarely.

Statistically, rhabdomyosarcomas must be considered first, being the most common bladder neoplasm in children. The
myxoid areas, tadpole cells, areas of high mitotic rate combined with the invasive quality of our tumor can raise this diagnosis. The location, on the other hand, does not. Rhabdomyosarcomas tend to arise from the trigone area,\textsuperscript{4} while leiomyosarcomas occur almost exclusively elsewhere in the bladder.\textsuperscript{3,6,7,9,10} Furthermore, both plasma thromboplastin (PTAH) staining and electron microscopy failed to reveal z bands. In addition, the immunochemical reaction with myoglobin was negative.

Fibrosarcoma is another candidate for misdiagnosis. The positivity for desmin identifies the tumor as one of muscle. Additionally, periodic acid-Schiff staining was highly suggestive of glycogen, a
feature common, in muscle tissue. The myxoid areas and presence of myofibers, too, argue against this diagnosis.

A lesion showing evidence of malignancy would not be expected to be confused with a non-neoplastic process. However, the overall bland appearance of the spindle cells, abundant cytoplasm, low mitotic rate, rarity of atypical mitoses, and presence of chronic inflammation deep in a soft tissue tumor of a child strongly suggest an inflammatory pseudotumor. This point of possible confusion has been eloquently discussed elsewhere. Distinction can be made on the grounds that pseudotumors sometimes contain many lymphocytes (more than seen by the authors), lack dense growth, are vascular, and are less destructive to adjacent tissue. Atypical mitoses also do not occur in inflammatory pseudotumors. A similar comparison could be made with nodular fasciitis (also referred to as pseudosarcomatous fasciitis), which may be related to inflammatory pseudotumors. The spindle cells of these lesions, however, are myofibroblasts, a fact that underscores

\textbf{Figure 4.} Tumoral ultrastructure. Note myofilaments and dense bodies, pinocytotic vesicles, and absence of desmosomes (17,000x).
Finally, given the evidence for this being a tumor of muscle origin, the distinction from a leiomyoma must be made. The areas of dense growth, encapsulation and low mitotic rate were highly suggestive of a leiomyoma. The rate of mitosis (4/10 high power field [HPF] in highest mitotic area averaging over many adjacent fields) and bizarre mitotic figures argue to the contrary. In addition, although the tumor displayed a pushing border in some areas, there was significant invasion and destruction of normal tissue, indicating malignant behavior. Although there were atypical mitoses and invasion, this tumor was considered to be a low-grade malignancy. It has been two years since the patient underwent surgery. She has been followed closely by cystoscopic and ultrasonic evaluation; there has been no recurrence of her tumor.

The prognostic implications of accurate diagnosis are great. All of the malignancies mentioned have a strong predilection for recurrence, especially if inadequately excised. Importantly, these malignancies tend to recur long before they metastasize. Leiomyomas and inflammatory pseudotumors have very low recurrence rates. In a leiomyosarcoma of the bladder, long term follow-up with cystoscopy and ultrasound is advisable for a period of 10 years, given the examples in the literature of recurrence at even this late date. Adjuvant radio- or chemotherapy has not proven helpful thus far. In fact, one group advocates against their use. Traditionally, the prognosis of leiomyosarcomas has been stated to be very poor. Some of the mortality experienced, especially that in children, appears to have had to do, in part, with the surgical procedure. Furthermore, improving clinical diagnosis by cystoscope and ultrasound should improve the chance of catching these malignancies early enough to prevent both extensive surgery and spread into surrounding tissues.

Summary

This paper has presented a case of a low-grade leiomyosarcoma of the bladder in a four-year-old child. Special emphasis has been placed on the diagnostic process and differential diagnoses. These sarcomas are rare and often confusing. Extreme care should be taken to avoid the potentially serious consequences of a misdiagnosis. Wide margin excision remains the treatment of choice.

References