Inflammatory Myofibroblastic Tumor of the Urinary Bladder: Differential Diagnosis

İnflamatuar Miyofibroblastik Mesane Tümörü

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ABSTRACT Inflammatory myofibroblastic tumor (IMT) is a rare proliferative lesion that needs to be differentiated particularly from sarcoma and sarcomatoid carcinoma. We describe a 57-year-old male with IMT of the bladder who presented with the complaints of pelvic pain, hematuria, malaise, weight loss and dysuria. Ultrasonography revealed a mass 4 cm in diameter in the bladder. On computed tomography, a hyperdense, nodular mass with the maximum size of 4 cm was detected on the right lateral wall of the bladder. The bladder mass was excised by transurethral resection. Pathologic findings revealed that the tumor had spindle-shaped cells with eosinophilic cytoplasm in myxoid stroma with abundant inflammatory infiltrate. There has been no evidence of recurrent tumor in 45 months postoperatively. It is concluded that IMT needs to be differentiated particularly from sarcoma and sarcomatoid carcinoma.

Key Words: Urinary bladder; sarcoma; granuloma, plasma cell; diagnosis

ÖZET İnflamatuar myofibroblastik tümör (İMT), özellikle sarkom ve sarkomatoid karsinomdan ayırt edilmesi gereken nadir bir proliferatif lezyondur. Pelvik ağrı, hematüri, halsizlik, kilo kaybı ve sık idrara çıkma ile idrar yaparken yanma yakınmaları olan mesanede lokalize İMT'lü 57 yaşında erkek hasta sunulmuştur. Ultrasonografisinde mesanede 4 cm çaplı kitle, bilgisayarlı tomografisinde de mesane sağ yan duvarında maksimum büyüklüğü 4cm' yi bulan hiperdens, nodüler kitle tespit edilmiştir. Mesanedeki kitleye transüretral rezeksiyon uygulanmış, patolojik değerlendirmesinde ise yaygın inflamatuar infiltrasyon içeren miksoid stromada eozinofilik sitoplazmalı, iğsi şekilli hücreler görülmüştür. Postoperatif 45. ayda tümörde nüks görülmemiştir. İMT' nin özellikle sarkoma ve sarkomatoid karsinomdan ayırt edilmesi gereken bir lezyon olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Mesane; sarkoma; granülom, plazma hücresi; tanı

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Inflammatory myofibroblastic tumor (IMT) is a rare proliferative lesion that can occur both in children and adults. IMT was originally described in the lung.[1] However recently it has been identified at multiple extrapulmonary locations, particularly in the soft tissues and solid organs of children and young adults.[2] Urinary bladder is the most common site of localization in the genitourinary tract. Although the histological features often mimic those of a malignant neoplasm, the clinical course is benign; the tumor grows slowly and does not metastasize or undergo malignant transformation. It is important, however, to differentiate it from either a sarcoma or a sarcomatoid carcinoma.[3] The recom-

mended management of most cases is the local excision and a close follow-up. The etiology of these lesions remains unclear.We present a, 57- year-old male with IMT of the bladder with clinicopathologic and immunohistochemical features, and review the literature.

CASE REPORT

A 57-year-old male presented to the hospital with pelvic pain, hematuria, malaise, weight loss and irritative symptoms such as urgency, nocturia and frequency. In the rectal examination, mild prostatic hyperplasia was found. PSA value was in normal limits. Ultrasonography revealed a mass 4 cm in diameter in the bladder. On computed tomography, a hyperdense, nodular mass with the largest dimension of 4 cm was found in the right lateral wall of bladder. There was a simple cyst in the left kidney. Other visceral organs were normal. The mass was excised by transurethral resection. On gross pathological examination, the lesion composed of 18 cc, soft, polypoid, nodular, curettage material.

Microscopical examination of the specimen showed a variable cellular proliferation of mesenchymal cells in an edematous myxoid background with many inflammatory cells, particularly granulocytes. The pathologic cells had long, tapering, eosinophilic cytoplasm which is characteristic of myofibroblasts (Figures1a-b-c). Although there was nuclear pleomorphism, significant cytologic atypia was not observed (Figures 1d-2a). Mitotic figures were rare and no atypical mitoses were observed. Most of the epitelium was denuded ex-

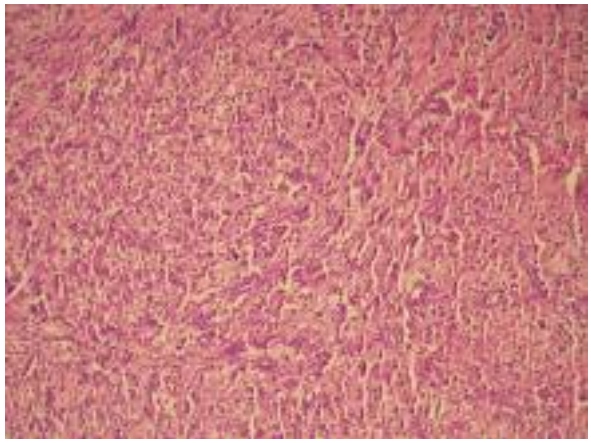

FIGURE 1a: Spindle cell proliferation on a background of loose myxoid stroma and mononuclear inflammatory cells are seen (H&E, X100).

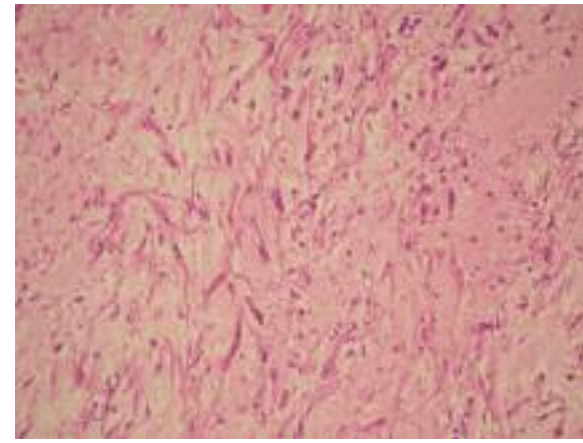

FIGURE 1b: More dense proliferation of spindle cells, blood vessels, and inflammation resembles granulation tissue (H&E, X200).

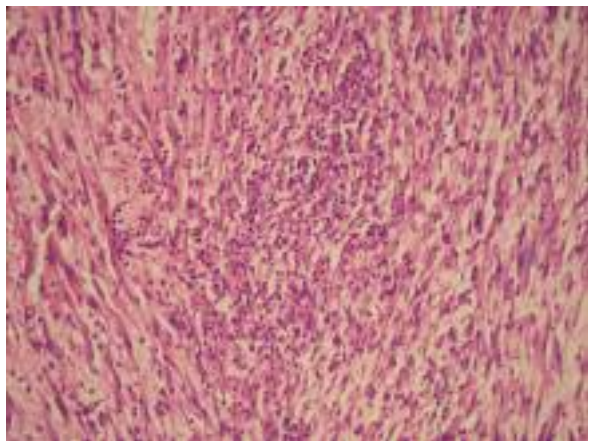

FIGURE 1c: Exuberant proliferation of spindle cells on a background of loose myxoid stroma and mononuclear a inflammatory cells (H&E, X200).

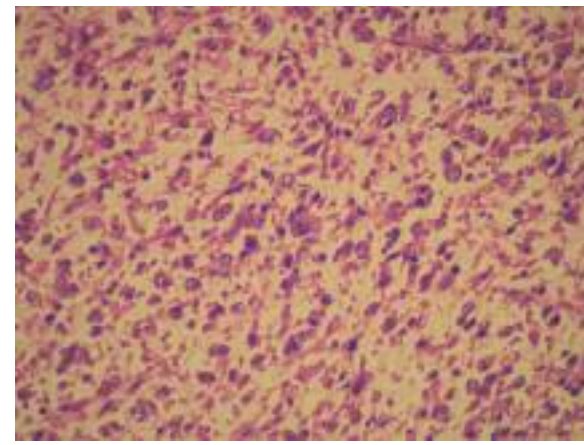

FIGURE 1d: Moderately pleomorphic cells with oval nuclei, small prominent nucleoli (H&E, X400).

cept for a partial transitional cell covered layer. There was focal involvement of the muscularis propria. Histochemically, the stroma was stained intensely by alcian blue (Figure 2b). Immunohistochemically, strong diffuse positivity was observed for vimentin and smooth muscle actin in the spindle cell cytoplasm was focally stained (Figure 2c). The desmin immunostaining was weakly and focally positive. Immunostaining for pancytokeratin, EMA, S100 protein, myoglobin, ALK and p53 were all negative. Ki67 was weakly positive in less than 1% of the spindle cells. Cytokeratin 7 was partially positive in transitional cell covered layer (Figure 2d).

We diagnosed IMT with clinicopathologic and immunohistochemical features in this case.

DISCUSSION

The first description of a sarcomatous lesion which turned out to be a benign proliferative myofibroblastic tumor was in a female with recurrent cystitis displaying an ulcerated spindle cell tumor. Then, two cases of benign mesenchymal tumors arising from the bladder, initially clinically diagnosed as sarcomas and histologically resembled nodular fasciitis without malignant features were reported by Nochomovitz and Orenstein.[4] They named this entity as "inflammatory pseudotumor of the bladder".[4] Ro et al. performed a detailed immunohistochemical and clinicopathologic study of the disease in 1986 and used the term "pseudosarcomatous fibromyxoid tumor" to emphasize the histopathologic feature of

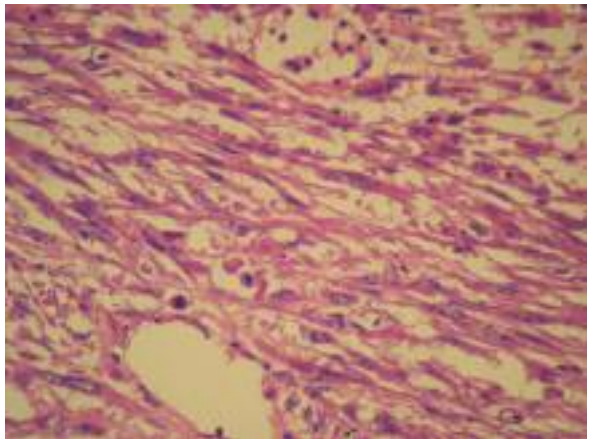

FIGURE 2a: Loosely organised spindle cells admixed with inflammatory cells (H&E, X400).

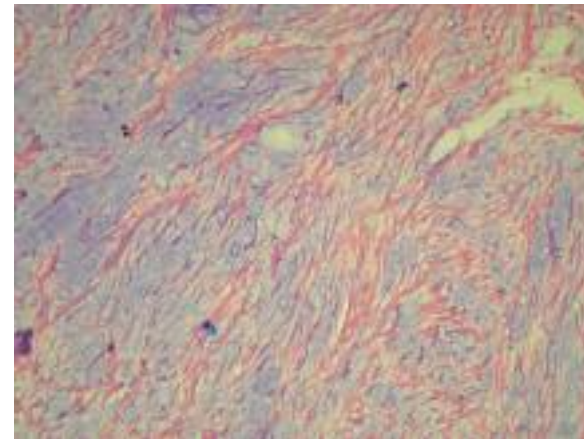

FIGURE 2b: Myxoid stroma was stained by alcien blue (Alcian Blue staining, X200).

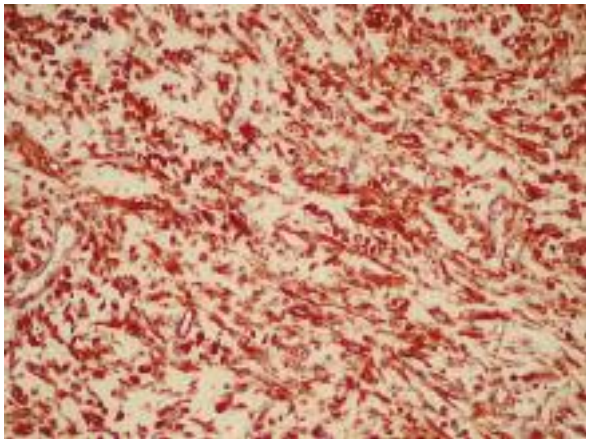

FIGURE 2c: Strong diffuse positivity for vimentin in the spindle cell cytoplasm (H&E, X400).

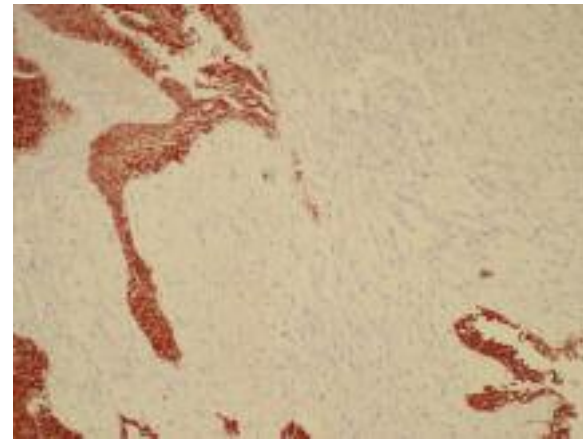

FIGURE 2d: CK 7 positivity for transitional cells but negativity the spindle cells (CK7, X200).

these lesions.[5] Many of the lesions diagnosed as inflammatory pseudotumor, pseudosarcomatous fibromyxoid tumor, inflammatory myofibroblastic tumor, plasma cell granuloma, fibroxanthoma, and histiocytoma are closely related processes. In recent years, the term "inflammatory myofibroblastic tumor" has been proposed. In this condition, the predominant element is a spindle cell with immunohistochemical and ultrastructural features (actin reactivity, cytoplasmic filaments) consistent with that of myofibroblastic, or possibly the cells of the accessory immune system known as fibroblastic (myoid) reticulum (dendritic) cells. Immunohistochemical cytoplasmic positivity for ALK using a variety of monoclonal antibodies is detectable in approximately 50% of IMTs and is uncommon in IMT-diagnosed adults beyond 40 years of age. The consistent finding of chromosomal rearrangements involving 2p23 and ALK- expression supports the neoplastic nature of this subset. On the other hand IMT probably includes several different entities from reparative lesions to aggressive myofibroblastic tumors. Thus, the nature of IMT remains controversial: a real neoplasm or a reactive process.[1] The growth of the tumor is relatively slow and it is initially found as a solitary lesion 1-4 cm in size. The lesions are usually composed of spindle cells with elongated cytoplasms sparsely embedded in myxoid stroma with prominent vascularity. The stroma is rich in acid-mucopolysaccharides stained intensely by alcian blue. Diffuse infiltration of acute or chronic inflammatory cells can usually be seen. Mitoses are only occasionally found and atypical or bizzare mitotic figures are notably absent. Strong diffuse cytoplasmic reactivity for vimentin is typical for virtually all IMT. Smooth muscle actin and muscle specific actin varies from a focal to a diffuse pattern in the spindle cell cytoplasm. Desmin is identified in many cases. However, staining for myoglobin, S-100 protein and keratin are usually negative.[5]

Immunohistochemical studies support the myofibroblastic nature of this lesion with consistent expression of vimentin and smooth muscle actin together with negative staining for keratin. The result of immunohistochemical staining in our case showed immunoreactivity to vimentin and smooth muscle actin and, together with negative staining for both myoglobin and S-100, suggested myofibroblastic and nonskeletal muscle origin.

The differential diagnosis includes sarcomas because of the mesenchymal proliferation. These are inflammatory fibrosarcoma, malignant fibrous histiocytoma and myxoid leiomyosarcoma. However, IMT usually lacks severe cytologic atypia and contains fewer mitoses than sarcomas. The diagnosis, especially on biopsy, may be difficult. Although the myxoid pattern may also cause confusion with myxoid liposarcoma, no lipoblasts are present in IMTs.

In rare cases, carcinomas of the bladder may have spindle-cell morphology (so-called sarcomatoid carcinomas) and indeed may occasionally be confused with sarcoma. Although myofibroblastic cells may express focally cytokeratins, the positive stains for cytokeratin and EMA favor the diagnosis of sarcomatoid carcinoma. The lesion most closely related to the IMT is the postoperative spindle-cell nodule. The spindle-cell nodule, however, in contrast to all other spindle-cell proliferations of the bladder, has a unique relation to recent performance of a bladder procedure, usually transurethral resection of the bladder. It has very similar morphologically to IMT. The main differences with postoperative spindle cell nodule are the tendency to reach a larger size, greater prominence of the myxoid stroma, lesser degree of cellularity, greater plemorphism, and lesser tendency for keratin immunoreactivity (which may still be present).

In IMTs, local recurrences and rare metastases are described. The principal treatment is surgery. Follow-up consists of urinary cytology and cystoscopy every three months, and computed tomography if necessary. In a follow-up period of 45 months, our patient had no recurrence or metastasis.

In conclusion, IMT is an unusual, benign locally aggressive urinary bladder lesion that may easily be mistaken for an postoperative spindle cell nodule, or even several sarcomas and sarcomatoid carcinomas. Accurate identification of IMT is clinically important to avoid unnecessary radical treatments. Optimal management may be transurethral resection or segmental cystectomy and a close follow-up with cystoscopy and biopsy.

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