

Oncology

Successful Preservation of the Bladder in a Case of Inflammatory Myofibroblastic Tumor with the Diagnostic Efficacy of ALK/p80 Immunohistochemistry and FISH Analysis: Case Report and Review of the Literature



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ABSTRACT

Inflammatory myofibroblastic tumor is a rare benign entity of unclear etiology. It can present with histological features that include a mixture of spindle cells, myofibroblasts and inflammatory cells. Positive immunohistochemical staining for ALK/p80 is often observed, and this marker has been considered diagnostically effective. Despite having these histological features, a previous case was incorrectly diagnosed as malignant disease and was treated with extensive surgical resection. Here we present a case of inflammatory myofibroblastic tumor in the bladder, diagnosed in part based on immunohistochemical and fluorescence in situ hybridization analysis of ALK/p80. The patient was successfully treated with bladder-preserving partial cystectomy.

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Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare entity with no established treatment. IMT can occur in any human organ. It is particularly common in the urogenital organs, including the bladder. IMT has also been called inflammatory pseudotumor, inflammatory pseudosarcomatous fibromyxoid tumor, plasma cell granuloma, nodular fasciitis, or pseudosarcomatous myofibroblastic tumor. Confusions regarding nomenclature might have contributed to the difficulty in establishing standard therapeutic procedures for this disease.

Thus far there has been limited clinical experience with IMTs originating in the bladder, although no metastases have been reported except for local recurrences that might have been due to incomplete tumor resection. Therefore, preoperative histological diagnosis is critical for preserving the bladder as a urinary tract. A number of immunohistochemical markers, including anaplastic

lymphoma kinase-1 (ALK-1) with expression analyzed by fluorescence in situ hybridization (FISH), have shown good efficacy for the diagnosis of IMTs. Nonetheless, misdiagnosis of cases still occurs.

Here we describe a case of IMT originating from bladder, diagnosed by trans-urethral resection of the tumor before eventual partial cystectomy. FISH analysis of ALK/p80 helped in formulating a treatment decision that ultimately preserved the bladder.

Case presentation

A healthy 17-year-old woman was hospitalized after presenting with gross hematuria and lower abdominal pain. Based on the magnetic resonance imaging (MRI) of the abdomen and pelvis revealed a huge pedunculated tumor that enhanced with contrast agent in the bladder (Fig. 1), with no lymph node enlargement or metastases of other organs. Trans-urethral coagulation was performed to stop tumor bleeding and the tumor was then resected to permit a pathological diagnosis. Pathological examination of the samples acquired via trans-urethral resection were indicative of IMT, due to the existence of spindle-shaped cells, myofibroblasts and inflammatory cells, and positive immunohistochemical

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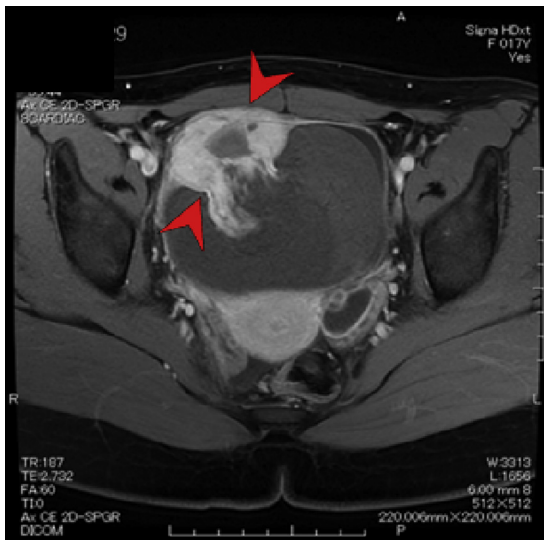


Figure 1. Enhanced magnetic resonance imaging (MRI) of the pelvis showed bladder tumor with high enhancement (red arrows).

staining for ALK/p80 (Fig. 2A and B), α SMA, CK-AE1/AE3 and CK-CAM5.2. In addition, there were numerous red blood cells and neutrophils among the tumor cells, as well as infiltration of inflammatory cells, composed mainly of neutrophils, in the stromal area beneath the epithelial cells.

It was decided that histological examination of the whole tumor was necessary to make a final pathological diagnosis, and thus partial cystectomy was performed. The tumor size was $10 \times 5 \times 4.5$ cm, with bladder mucosa ulceration that reached the serous membrane. The final pathological diagnosis of bladder IMT was confirmed by positive immunohistochemical staining for ALK/p80, α -SMA, CK-AE1/AE3 and CK-CAM5.2, the same results obtained via trans-urethral biopsy. To confirm the diagnosis of IMT, we also conducted FISH analysis of ALK-p80 (Fig. 3). The final diagnosis in this patient was IMT, and no extra treatment was deemed necessary. No adjuvant therapy was performed since IMT generally shows a benign clinical course even after limited resection. The patient has since been doing well and has demonstrated no evidence of local recurrence on surveillance imaging studies and cystoscopy at 12 months postoperatively.

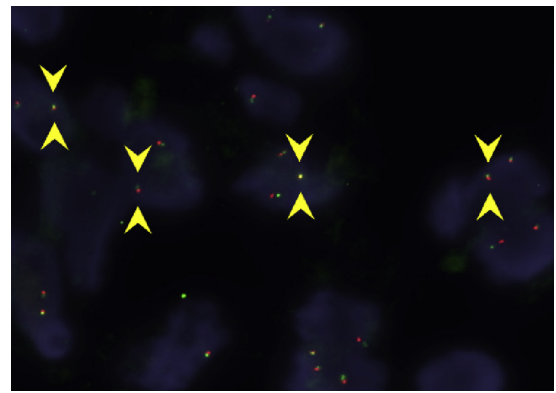


Figure 3. The partial cystectomy specimen of bladder tumor showed positive for ALK/p80 using FISH method. ALK/p80 positive findings were observed (arrow heads).

Discussion

The peculiar disease we have referred to as IMT has been assigned numerous other names, including inflammatory pseudo-sarcomatous fibromyxoid tumor.¹ This varied nomenclature might have contributed to the difficulty in accumulating clinical data for analysis of the disease histology and clinical course. The one of pathogenesis for IMT has been associated with diabetes.² Recent reports concerning this condition have highlighted the diagnostic utility of immunohistochemical and FISH analysis of ALK/80,³ and have shown that in cells that express it, t(2;5) translocation of this protein has an anti-apoptotic effect.⁴ This shows that anti-apoptotic processes may play a critical role in the histological development of IMT. With bladder IMT specifically, smoking and a history of transurethral surgery have been identified as pathogenic factors, but most frequently the condition is idiopathic.

IMT has been reported in patients with a wide range of ages, individuals are most likely to be affected while in their twenties, but the reason for this tendency is not yet understood. One study has reported that males have a higher likelihood of developing IMT than females.¹ The reason for this gender discrepancy is unknown, though it may involve differences in genetic vulnerabilities or a tendency for translocations in male chromosomes.

Among the urogenital organs, the bladder is the most likely to develop IMT. Any site in the bladder may be affected, but the trigon tends to be spared. These facts suggest that the pathogenesis of IMT may involve an unknown factor during bladder development.

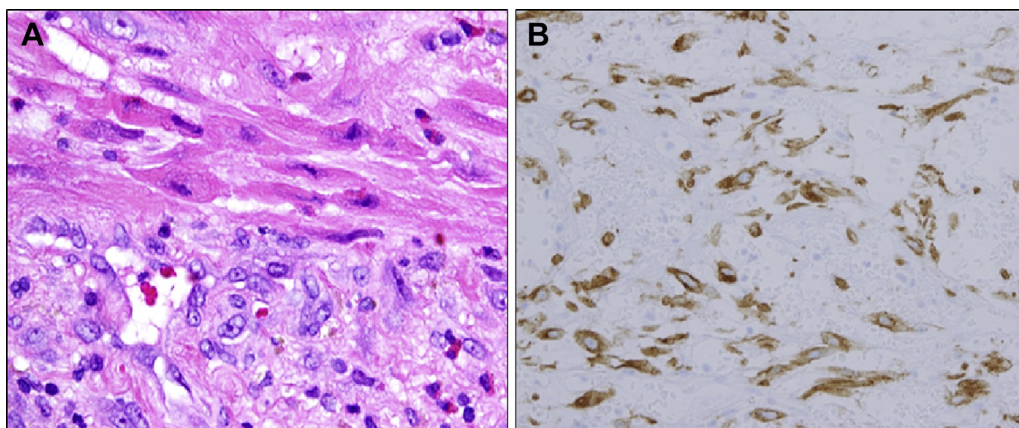


Figure 2. A: Histological examination showed the existence of spindle-shaped cells, myofibroblasts and inflammatory cells (HE $\times 200$). B: Immunohistochemical stain showed that the TUR biopsy specimen were positive for ALK/p80 (anti-ALK antibody staining $\times 200$).

Symptoms of bladder IMT include macrohematuria, dysuria, pelvic pain, and even fever and weight loss.³

Histologically, IMT is characterized by the presence of spindle cells, myofibroblastic cells and plasma cells, at various ratios.³ Immunohistochemistry shows cells positive for ALK/p80, CAM5.2, desmin, α SMA and vimentin.⁵

Differential diagnoses of IMT include rhabdomyosarcoma, leiomyosarcoma and sarcomatoid carcinoma.⁵ ALK/p80 is useful in identifying IMT, though these sarcomatoid variants may also express ALK/p80. Thus, histological data is needed to distinguish IMT, with its generally favorable clinical course, from more malignant diseases. Diagnostic uncertainty may result in excess treatment for IMT. Treatment should involve bladder function-preserving procedures such as trans-urethral resection or partial cystectomy. Almost all the cases were treated using a bladder-preserving procedure, either trans-urethral resection or partial cystectomy, though total cystectomy was performed. Some tumors were not immunohistochemically positive for ALK/p80. Increasing the accuracy of IMT diagnosis is desired in order to enable treatment choices that will preserve bladder function. In this case we evaluated ALK/p80 using both immunohistochemistry and FISH analysis. In conclusion, bladder IMT tends to occur in patients' twenties, though sometimes earlier, and demonstrates a good clinical course even with local incision. Precise histological diagnosis is necessary to preserve bladder function in these patients, and future research

should focus on developing additional effective diagnostic methods.

Conflict of interest

None.

Consent

Written consent with permission to submission was obtained from the patient.

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