CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 48 (2018) 1–4

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Neoadjuvant crizotinib in ALK-rearranged inflammatory myofibroblastic tumor of the urinary bladder: A case report

Yoshiyuki Nagumo[a,*], Aiko Maejima[a], Yuta Toyoshima[a], Motokiyo Komiyama[a], Kan Yonemori[b], Akihiko Yoshida[c], Hiroyuki Fujimoto[a]

[a] Department of Urology, National Cancer Center Hospital, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0054, Japan
[b] Department of Breast and Medical Oncology, National Cancer Center Hospital, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0054, Japan
[c] Department of Pathology and Clinical Laboratories, National Cancer Center Hospital, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0054, Japan

ARTICLE INFO

Article history:
Received 15 February 2018
Accepted 19 April 2018
Available online 1 May 2018

Keywords:
Inflammatory myofibroblastic tumor
Urinary bladder
ALK
Crizotinib

ABSTRACT

INTRODUCTION: Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor that involves various organs, but has a predilection for the urinary bladder in the genitourinary tract. Given that approximately half of all IMT cases have anaplastic lymphoma kinase (ALK) rearrangements, the ALK inhibitor crizotinib is suggested as a promising treatment for unresectable cases. No reports on neoadjuvant crizotinib therapy for locally advanced IMT of the bladder are available.

PRESENTATION OF CASE: We report a case of a 17-year-old Japanese boy referred to our institution for painful urination and increased urinary frequency. He was diagnosed with ALK-positive IMT via transurethral resection of the bladder tumor. Computed tomography (CT) revealed a 5-cm mass and extramural invasion at the bladder dome. The diagnosis was locally advanced IMT of the bladder. We decided that partial cystectomy can be performed if neoadjuvant crizotinib therapy reduced the tumor size. After 2 months of administration, CT showed that the longest tumor diameter was reduced by 48%. Thus, we performed partial cystectomy, and the surgical margin was negative. No recurrence developed for over 1 year.

DISCUSSION: IMT has intermediate malignant potential because its clinical course is relatively indolent with low risk of distant metastasis. As this patient is young and IMT of the bladder has good prognosis after surgical resection, bladder-preserving surgery is the most preferred approach.

CONCLUSION: Neoadjuvant crizotinib therapy may be effective for large, locally advanced, and difficult to resect tumors.

1. Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor that has intermediate malignant potential. It arises from various organs, such as the lung, retroperitoneum, and pelvis [1]. Surgical resection is the primary treatment for IMT, but unresectable cases have limited response to steroids, non-steroidal anti-inflammatory drugs (NSAIDs), radiotherapy, and chemotherapy [2–4]. A total of 50% of IMTs have anaplastic lymphoma kinase (ALK) rearrangement and overexpress ALK protein [5]. The ALK inhibitor crizotinib is effective for unresectable cases [6]. IMTs of the genitourinary tract frequently develop in the urinary bladder [7]. Transurethral resection of bladder tumor (TURBT) is often performed for pathological examination, and additional TURBT or partial cystectomy for radical resection is selected according to histologic outcomes [8]. Currently, no reports on neoadjuvant crizotinib therapy for locally advanced IMT of the bladder are available. Herein, we report a case of IMT that was successfully treated with partial cystectomy following neoadjuvant crizotinib therapy.

This work has been reported in line with the SCARE criteria [9].

2. Case presentation

A 17-year-old boy, presenting with a 2-week history of painful urination and increased urinary frequency, was referred to the first clinic. Computed tomography (CT) scan revealed an enhanced mass measuring 5 cm in diameter at the dome of the urinary bladder. Magnetic resonance imaging showed extramural invasion of the bladder, and the left ischial bone and right humerus presented high intensity on T2-weighted images and diffusion-weighted images (see Fig. 1). Thus, bone metastases was suspected. Cystoscopy demonstrated locally thickened and edematous mucosa from the posterior wall to the bladder dome. TURBT was performed for pathologic evaluation. The histological findings and

* Corresponding author.
E-mail address: yonagumo@ncc.go.jp (Y. Nagumo).

https://doi.org/10.1016/j.ijscr.2018.04.027

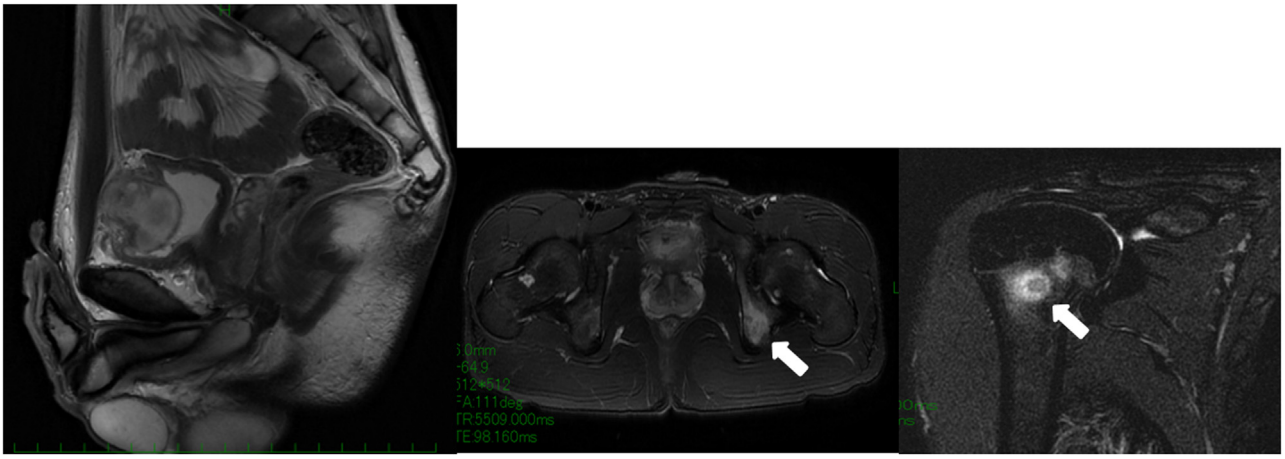

Fig. 1. *Left*, Sagittal T2-weighted MRI showed a mass measuring 5 cm in diameter at the urinary bladder dome with extramural invasion. *Middle*, The left ischial bone presented high intensity on axial T2-weighted image. *Right*, Coronal T2-weighted imaging showed local high-intensity area in the right humerus.

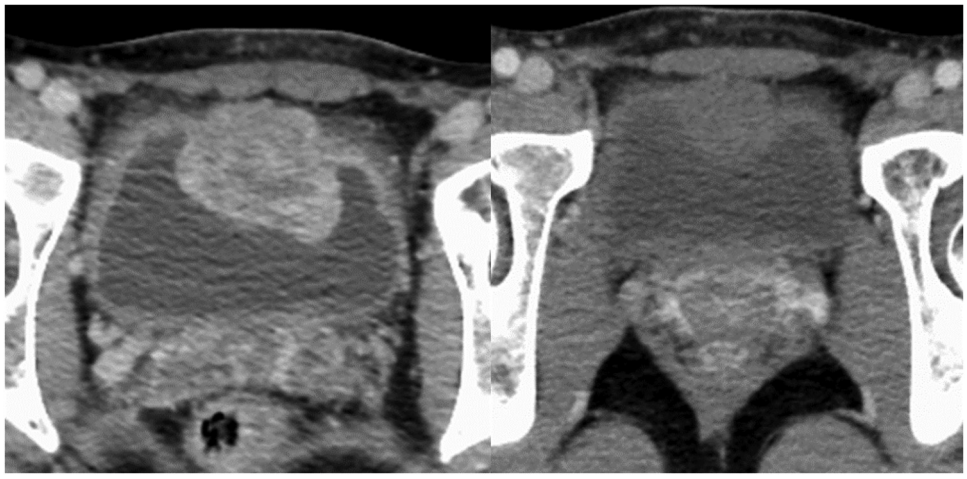

Fig. 2. *Left*, Before treatment, CT showed a mass measuring 49 mm in diameter. *Right*, After treatment, the tumor size reduced to 25 mm.

immunohistochemical staining indicated ALK-rearranged IMT. Combined ^{18}F-fluorodeoxyglucose positive-emission tomography and CT revealed hypermetabolic masses in the left ischial bone and right humerus. Therefore, he was referred to our hospital because rapid progression with distant metastases was suspected. Ischial bone biopsy was performed, and the results showed chronic inflammation but no malignant tumor. Accordingly, the patient was diagnosed with locally advanced IMT of the urinary bladder. Although we initially considered radical cystectomy for curative treatment, we decided that partial cystectomy can be performed instead if the tumor size was reduced with neoadjuvant crizotinib therapy. Thus, crizotinib was started at a dose of 250 mg twice daily. After 2 months, CT images showed a 48% reduction in the sum of the longest diameter (see Fig. 2). Adverse events were mild nausea and overlapping shadows, and no hematologic events occurred. The overlapping shadows were treated. Cystoscopy showed a nodular tumor at the bladder dome (see Fig. 3); thus, we decided that we could resect the tumor with enough surgical margin and preserve adequate capacity of the bladder after surgery. Partial cystectomy was performed. Histological examination demonstrated intersecting fascicles of spindle cell proliferation admixed with a few inflammatory cells within a myxoid stroma (see Fig. 4). Although no necrotic cells were seen, a hyalinizing area was recognized. We suspected the change as a form of therapeutic response. Immunohistochemical staining showed that the spindle cells were positive for ALK (5A4, Abcam, Cambridge, UK), and fluorescence in situ hybridization using a break-apart probe (Vysis ALK Break Apart FISH Probe Kit, Abbott Molecular, Abbott Park, IL) showed ALK rearrangement (see Fig. 5). These findings were characteristic of ALK-rearranged IMT. The patient's urination remained unchanged after surgery, and no local recurrence and distant metastases were observed 1 year after treatment.

3. Discussion

Although IMT occurs over a wide age range, it has been mostly reported in adolescent patients [10]. IMT has a relatively good prognosis and is considered to be a tumor with intermediate biologic potential because of its low risk of distant metastases [11]. On one hand, IMTs of the bladder have a local tumor recurrence rate after surgery of only 4%, and no patients with distant metastases have been reported [8]. On the other hand, IMT arising from other organs sometimes has poor prognosis because of the high rate of recurrent local relapse or distant metastases.

Surgical resection is the main therapeutic strategy for localized IMT. Most patients with IMT of the bladder undergo TURBT for pathologic evaluation and treatment. After diagnosis of IMT, cases with no residual tumor may not require further treatment, while a second TURBT or partial cystectomy may be performed for complete resection in other cases. A study that reviewed 120 cases of