Primary Diffuse Large B-Cell Lymphoma of the Bladder

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Abstract

Primary lymphoma of the bladder is quite rare; primarily, it is extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma). There is only one case report of primary diffuse large B-cell lymphoma (DLBCL) of the bladder, accompanied by diffuse wall thickening of the bladder. Here, we report a second case of primary DLBCL of the bladder in a 75-year-old woman patient, whose initial presentation was acute renal failure. Three courses of R-CHOP chemotherapy were effective to treat acute renal failure caused by post-renal obstruction and to attain clinical remission.

Key words: lymphoma, diffuse large B-cell lymphoma, bladder, rituximab, chemotherapy


Introduction

Involvement of the bladder in lymphoma is quite rare, and it represents 0.2% of primary lymphomas and 1.8% of secondary lesions of malignant lymphoma. Primary lymphoma of the bladder is mainly extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma) and less than 20% of cases are diffuse large B-cell lymphoma (DLBCL). In most cases of primary lymphoma of the bladder, a tumor is observed as a nodule in the bladder wall. There is only one case report of primary DLBCL of the bladder, accompanied by diffuse wall thickening of the bladder. Here, we report a second case of primary DLBCL of the bladder with diffuse wall thickening in a 75-year-old woman patient, whose initial presentation was acute renal failure.

Case Report

A 75-year-old woman patient with oliguria was admitted to the urology department. She did not have a history of fever, general fatigue, weight loss, or recurrent urinary infection. She was taking medicine for hypertension and dyslipidemia. One inguinal lymph node had swelled up to 2 cm. Microscopic blood and protein was observed from a urine specimen. Urine cytology did not show any malignant cells. Intravenous pyelography demonstrated a contrast defect in both the bladder and the left urinary tract, and dilatation of the right upper urinary tract (Fig. 1). An abdominal CT scan demonstrated left side hydronephrosis, hydroureter on both sides and severe thickening in the whole wall of the bladder with several swollen lymph nodes in the pelvic lesion (Fig. 2). Gallium scanning demonstrated a positive signal in the bladder and lymph nodes in the pelvis but not in other organs. Specimens from the bladder were transurethrally obtained for pathological evaluation. The bladder lesions were aggressively invaded by atypical large cells accompanied by follicles of small lymphoid cells (Fig. 3A, B). Immunohistochemical study demonstrated that the tumors were positive for CD20 (Fig. 3C) and CD79alpha, and negative for CD3 and pan-cytokeratin (data not shown). The atypical cells were not detected in bone marrow by pathological examination. From these results, we diagnosed primary diffuse large B-cell lymphoma (DLBCL) of the bladder in Stage IVA. In the initial presentation, we observed elevated white blood cell counts (WBC, 13,080/microL), and decreased red blood cell counts (RBC, 3.01 × 106/microL), hemoglobin levels...
Figure 1. Intravenous pyelogram of the 75-year-old female patient with oliguria. A contrast defect of the bladder and the left urinary tract were observed.

Figure 2. Abdominal CT images of the 75-year-old female patient with oliguria before treatment. Left hydronephrosis (left panel) and diffuse thickening of the bladder wall (right panel) were observed.

(Hb, 9.5 g/dL), hematocrit (Ht, 28.7%) and platelet counts (Plt, 6.7 × 10⁴/microL). The patient did not have a coagulation disorder. We observed markedly elevated levels of blood urea nitrogen (BUN, 72 mg/dL), creatinine (Cr, 4.4 mg/dL), uric acid (UA, 19.0 mg/dL) as well as markedly increased LDH (1,531 U/mL) and CRP levels (9.13 mg/dL) (Fig. 4). Serum soluble IL-2 receptor levels were increased to 13,400 U/mL. From these laboratory tests, the patient was diagnosed with acute postrenal failure caused by the obstruction of bilateral urinary tracts associated with bladder wall thickening (Fig. 2B). She was immediately hospitalized. For drainage, we made a left renal fistula one day after admission (day 2 in Fig. 4A) and observed drainage via the catheter in the fistula, followed by reduction of BUN, Cr and UA levels (Fig. 4A). A spinal tap could not be undertaken due to the low performance status in the patient. No abnormal findings were observed by neurological examination. Brain CT did not show any tumor formation. Because of the patient’s age and renal dysfunction, we halved the dose of R-CHOP chemotherapy (rituximab 375 mg/m² intravenously on day 1; cyclophosphamide 375 mg/m², doxorubicine 25 mg/m², vincristine 0.7 mg/m² intravenously on day 2; prednisolone 50 mg/body orally on day 2 to 6) on hospital day 8 (Fig. 4). After one cycle of the systemic chemotherapy, the urinary retention disappeared and a CT scan demonstrated an improvement of both bladder wall thickening and hydronephrosis. LDH levels decreased from 2,230 U/mL (hospital day 9) to 558 U/mL (day 29) (Fig. 4B). Soluble IL-2 receptor levels normalized to 463 U/mL (day 78). After three cycles of R-half CHOP, a pelvic CT scan showed remission (Fig. 5). Since the patient had incontinence after three cycles of chemotherapy, we did not add radiation or chemotherapy to maintain her quality of life after consultation with a radiologist and urologist. She was discharged on foot.

Discussion

Primary lymphoma of the bladder is a very rare disease, representing less than 0.2% of extranodal lymphomas (1). Approximately 60 cases of primary bladder lymphoma have been described in case reports (2-6). Primary lymphoma of the bladder affects women 6.5 times more than in men, with a mean age of 64 years ranging from 20 to 85 years. The major symptoms of primary bladder lymphoma are hematuria, urinary frequency and dysuria. A history of chronic cystitis has been shown to be a preceding feature in some cases (3, 7, 8). However, the present case did not have preceding cystitis. The most common images of a CT scan in the case of primary bladder lymphoma are nodule formation in the bladder wall. In our case, a CT scan demonstrated diffuse thickening of the bladder wall with left hydronephrosis and hydroureter. There are only three previous cases of primary lymphoma of the bladder, where the wall was diffusely thickened by tumor involvement (9-11).
Figure 3. Histology of the bladder in the 75-year-old female patient with oliguria. Atypical large cells showed a diffuse infiltration accompanied by follicles of small lymphoid cells in the bladder specimen (Hematoxylin and Eosin staining, A: ×50, B: ×100). A lympho-epithelial lesion was not observed in the same specimen. The atypical cells in the bladder were positive for the B-cell marker CD20 (×40 in C).

Figure 4. Clinical courses of the primary lymphoma of the bladder in the first R-CHOP chemotherapy. Abnormal BUN, Cr, UA and LDH levels improved during the first R-CHOP chemotherapy. The Y axis indicates the day after admission to the hospital. A renal fistula was made on day 2 and the first course of R-CHOP chemotherapy was started on day 8.
Figure 5. Body CT images of primary bladder lymphoma after three courses of R-CHOP chemotherapy. Both hydronephrosis and thickening of the bladder wall recovered after treatment.

Histopathological studies are necessary for the diagnosis of bladder lymphoma. Histological examination of primary bladder lymphoma generally indicates low grade non-Hodgkin’s lymphoma of the B-cell type. Approximately 20% of B-cell bladder lymphoma is high grade (5) and most such high grade bladder lymphomas are the diffuse large B-cell type (12). In the present case, atypical large cells in the bladder specimen were positive for CD20 and CD79alpha, indicating a diffuse large B-cell lymphoma. In previous reports, chemotherapy, radiotherapy and surgery were chosen as a single or combination therapy to treat patients with primary lymphoma of the bladder. There are 62 reported cases of primary bladder lymphoma, of which 18 cases received chemotherapy, 22 cases received radiotherapy and 9 cases were treated with both chemotherapy and radiation. Only one case underwent surgical treatment (1, 3, 6, 9). The most selected chemotherapy was R-CHOP for primary B-cell lymphoma of the bladder (9). Since our patient with high grade lymphoma of the bladder was in Stage IVA, we chose systemic chemotherapy but not radiation and surgery. Radiotherapy might have been chosen if the lymphoma was low grade and localized in the bladder. The role of surgery is controversial, as it is possible that the lymphoma will relapse in the other organs and surgical extraction of the bladder definitely reduces the quality of life. The prognosis of primary bladder lymphomas is usually favorable (4). The prognosis depends on the tumor grade, stage and complications (13). Primary diffuse large B-cell lymphoma of the bladder has been found in only six cases (5, 7). Of these six cases, only one had thickening of the whole wall of the bladder. The present case appears to be the second such reported case. Since there are small lymphocytes and plasma cells in mucosa-associated lymphoid tissue and follicles of small lymphoid cells in the bladder, it is possible that the preceding MALT-lymphoma might have transformed to high grade lymphoma. However, a lympho-epithelial lesion (LEL), which is one of the typical pathological findings of MALT-lymphoma, was not observed in the bladder specimen. It remains to be elucidated whether or not our patient had preceding chronic infection and low grade lymphoma.

References