Journal of BUON **13:** 277-279, 2008
© 2008 *Zerbinis Medical Publications. Printed in Greece*

Primary non-Hodgkin's lymphoma of the bladder: report of two cases and review of the literature

D. Pectasides, I. Iacovidou, A. Psyrri, E. Pectasides, G. Papaxoinis, T. Economopoulos

2nd Department of Internal Medicine, Oncology Section, University of Athens, "Attikon" University Hospital, Athens, Greece

Summary

Malignant lymphoma of the bladder is a rare entity which usually presents with nonspecific urologic symptoms such a dysuria, haematuria, nocturia and abdominal pain. Urologists should be familiar with the management of this disease as surgery alone often is not adequate treatment. We present herein 2 cases of non-Hodgkin's lymphoma (NHL) of the bladder and discuss their clinical-pathological features and management.

Key words: bladder, chemotherapy, lymphoma

Introduction

Primary NHL of the bladder is a rare condition, accounting for less than 1% of vesical tumors and for only 0.2% of all cases of extranodal lymphomas [1,2]. More than 100 cases have been previously reported in the literature, often as single case reports [3-6]. The disease is usually seen in patients aged 40-70 years with a marked female predominance. Haematuria, dysuria, nocturia, and abdominal pain are the commonest presenting symptoms of NHL of the bladder.

Herein, we describe 2 cases of NHL of the bladder presenting with urologic symptoms and review the relevant literature.

Case presentations

Case 1

A 60-year-old man presented to our department with urgency, painless haematuria, frequency, nocturia, and dysuria that were present the last month before the diagnosis. The patient had no fever, chills, night sweats, weight loss or pruritus at diagnosis. Physical examination revealed a blood pressure of 140/80 mm Hg and a pulse rate 84/min. Peripheral lymph nodes were not palpable. Cystoscopy showed an irregularly thickened, inflamed, haemorrhagic mucosa and an intravesical mass with no evidence of ureteral obstruction or distortion. Laboratory data showed a normal complete blood count, erythrocyte sedimentation rate (ESR) 60 mm, lactate dehydrogenase (LDH) 497 IU/L (normal range 80-220), and β_2 microglobulin 3230 ng/ml (normal range < 2500). Blood urea nitrogen (BUN), creatinine, carcinoembryonic antigen (CEA) and tumor polypeptide antigen (TPA) were within normal limits. Preoperative differential diagnosis included bladder carcinoma, unknown bladder neoplasm, or unknown pelvic mass. Abdominal and pelvic ultrasonography demonstrated a large intravesical mass, markedly thickened bladder wall and paraaortic lymphadenopathy. Abdominal computerized tomography (CT) scan showed an intravesical mass, thickening of bladder wall and enlarged paraaortic lymph nodes. The liver and spleen were normal. CT scan of the thorax revealed mediastinal lymphadenopathy.

Bladder biopsies showed extensive infiltration of the lamina propria and muscularis propria by a popula-

Correspondence to: Dimitrios Pectasides, MD. 2nd Department of Internal Medicine, Oncology Section, Attikon University Hospital. Rimini 1, Haidari, Athens, Greece. Tel: +30 210 5831691, 210 6008610, Fax: +30 210 5831690, 210 6008610, E-mail: pectasid@otenet.gr

Received 06-11-2007; Accepted 03-12-2007

tion of large cells (Figure 1). Tumor cells had abundant cytoplasm and eccentric, oval nucleus. There were frequent mitotic figures. An immunohistochemical panel showed that the tumor cells were negative for epithelial markers, positive for leukocyte common antigen (LCA-CD45) and for routine B-cell markers (CD20, CD79) and negative for T-cell markers (CD3, CD5). These findings were in favor of diffuse large-cell NHL of B-cell origin. Bone marrow biopsy showed no infiltration by lymphoma cells.

The patient was treated with 6 cycles of CEOP (cyclophosphamide, epirubicin, vincristine and prednisone) chemotherapy regimen with complete remission of the intravesical mass, and the enlarged paraaortic and mediastinal lymph nodes. The patient remains well with no evidence of relapse 5.5 years following completion of therapy.

Case 2

A 69-year-old female presented with complaints of urinary obstruction and haematuria of 3-week duration. She had a history of chronic and recurrent urinary tract infections. The patient had no B symptoms. Abdominal CT scan showed a diffuse thickening of the bladder wall involving mainly the floor and extending to the left posterior wall. The tumor was resected via transurethral resection and the histological diagnosis was diffuse large cell lymphoma extensively infiltrating the bladder wall. The immunostaining showed positivity to LCA-CD45 and CD20 characterizing a B-cell-derived NHL. A clonality study assessing the rearrangement of the immunoglobulin heavy chain by polymerase chain reaction showed a monoclonal pattern, diagnostic for lymphoma.

Her laboratory data were: haematocrit 36%, ESR 45 mm, LDH 620 IU/L (normal range 80-220), and β_2 microglobulin 2850 ng/ml (normal range < 2500). BUN, creatinine and CEA levels were normal. Postoperative workup for the lymphoma including repeat abdominal /thoracic CT scans, bone scan and bone marrow biopsies was negative for metastatic disease.

The patient was treated with 6 cycles of CNOP (cyclophosphamide, mitoxantrone, vincristine and prednisone) combination chemotherapy with complete response and relief of her symptoms. Two years after the completion of chemotherapy the disease recurred with a lymph node mass in the retroperitoneum and hepatic hilum causing obstruction of the biliary tract. Despite chemotherapy (CEOP-cyclophosphamide, epirubicin, vincristine, prednisone, and ESAP-etoposide, aracytin, cisplatin, methylprednisolone) and biotherapy with mabthera, she died 3 months later.

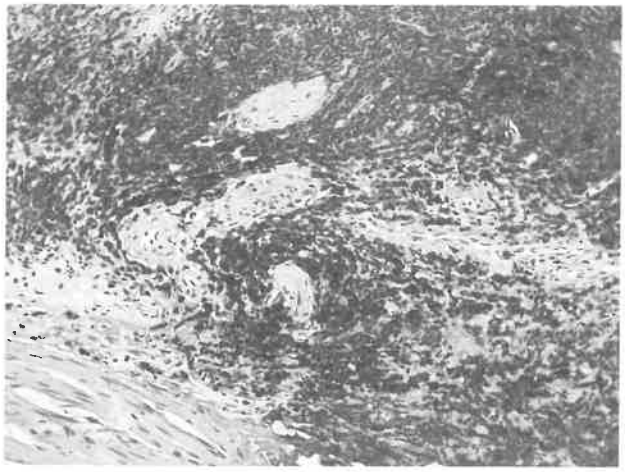


Figure 1. B-cell non-Hodgkin's lymphoma of the bladder (H&E ×200).

Discussion

Involvement of the bladder by NHL is a rare phenomenon that can occur in a primary or secondary form. The incidence of secondary involvement of the urinary bladder is 13-20% [7,8]. Primary NHL of the bladder is a rare condition, accounting for only 0.2% of all extranodal lymphomas and less than 1% of the primary bladder tumors [1,2,9]. In the last 40 years there have been approximately 100 case reports, with the largest study being the one reported by Kempton et al [9]. The median age of patients at diagnosis is 64 years (range 20-87) with a female predominance (gender ratio 1-1.8/ 3) which contrasts with male preponderance in nodal and extranodal NHL, except thyroid localized disease [2].

Periodic haematuria, usually macroscopic and massive, is the most common symptom found in 61-85% of patients [2,6,9]. The disease can also present with dysuria (27%), nocturia (13%), suprapubic pain (10%) and cystitis (7%) [2,6,10,11]. Approximately 20% of the patients have longstanding chronic cystitis. The lesions are single or multiple within the bladder and involve all sites, including the bladder wall, triangle, dome, and periurethral areas. Cystoscopically, they appear as rounded, intramural, submucosal masses, covered by normal intact epithelium, which can become ulcerated, or as very rapidly growing tumors [3,9].

Diagnosis must always be established by pathological examination of tumor material. Histological examination mostly indicates a low grade NHL of B-cell type. The majority of them are marginal zone lymphomas of mucosa-associated lymphoid tissue (MALT lymphomas) [2,8,9]. Primary diffuse large B-cell lymphoma of the bladder occurs less commonly, and isolated cases of follicular lymphoma, Burkitt's lymphoma,

Hodgkin's lymphoma, T-cell immunoblastic lymphoma and anaplastic large cell lymphoma occurring as primary bladder neoplasms have been reported [2,3,12-16]. Secondary bladder involvement usually occurs in patients with systemic lymphoma. Isolated cases of MALT lymphoma, diffuse large B-cell lymphoma and follicular lymphoma presenting with bladder involvement have been reported [9,17].

Intravenous urography shows a filling defect in the bladder [4,18,19]. On ultrasound examination, the tumor looks like a solid homogeneous mass [10,18,19]. The CT findings show a soft tissue density mass which enhances after intravenous administration of contrast medium [3,18,20,21]. The tumor appears most frequently as a sessile solitary mass, less frequently as multiple sessile masses and occasionally as a polypoid mass. The most frequent site is the lateral wall of the bladder. The other bladder walls can also be involved. The radiological findings can mimic a transitional carcinoma. However, infiltration seems to be more diffuse in lymphoma than in carcinoma. Hydronephrosis seems to be uncommon [5,10]. Magnetic resonance imaging findings show no signal difference between lymphoma and carcinoma.

As completely different therapies are indicated for bladder lymphoma and bladder carcinoma, it is of vital importance that these entities be distinguished and correctly diagnosed. Often a wide panel of immunohistochemical stains is required, including multiple epithelial and lymphoid markers.

Primary lymphoma of the bladder usually exhibits an indolent course with a favorable prognosis. However, prognosis is usually associated with the histology and the stage at presentation. A variety of therapies including chemotherapy, radiotherapy and surgery have been advocated for primary bladder lymphoma [13,21,22]. Patients with high-grade lymphoma should be considered to have systemic disease, and related to this, they require chemotherapy. Therefore, not only surgery, but also radiotherapy may not be sufficient as curative modalities. Systemic chemotherapy should be considered as first-line treatment. Surgical intervention may be used to prevent intractable irritative urinary symptoms that may arise. Generally, individual patient characteristics such as age, tumor grade and the coexistence of concurrent illnesses should be considered in selecting therapeutic modalities for patients with primary bladder lymphoma, even though all available therapeutic modalities have shown efficacy for this rare disease.

References

1. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer 1972; 29: 252-260.
2. Ohsawa M, Aozasa K, Horiuchi K, Kanamaru A. Malignant lymphoma of bladder. Report of three cases and review of the literature. Cancer 1993; 72: 1969-1974.
3. Mourad WA, Khalil S, Radwi A, Peracha A, Ezzat A. Primary T-cell lymphoma of the urinary bladder. Am J Surg Pathol 1998; 22: 373-377.
4. Arda K, Ozdemir G, Gunes Z, Ozdemir H. Primary malignant lymphoma of the bladder. A case report and review of the literature. Int Urol Nephrol 1997; 29: 319-322.
5. Tasu JP, Geffroy D, Rocher L et al. Primary malignant lymphoma of the urinary bladder: report of three cases and review of the literature. Eur Radiol 2000; 10: 1261-1264.
6. Hughes M, Morrison A, Jackson R. Primary bladder lymphoma: management and outcome of 12 patients with a review of the literature. Leuk Lymphoma 2005; 46: 873-877.
7. Sufrin G, Keogh B, Moore RH, Murphy GP. Secondary involvement of the bladder in malignant lymphoma. J Urol 1977; 118: 251-253.
8. Al-Maghrabi J, Kamel-Reid S, Jewett M, Gospodarowicz M, Wells W, Banerjee D. Primary low-grade B-cell lymphoma of mucosa-associated lymphoid tissue type arising in the urinary bladder: report of 4 cases with molecular genetic analysis. Arch Pathol Lab Med 2001; 125: 332-336.
9. Kempton CL, Kurtin PJ, Inwards DJ, Wollan P, Bostwick DG. Malignant lymphoma of the bladder: evidence from 36 cases that low-grade lymphoma of the MALT-type is the most common primary bladder lymphoma. Am J Surg Pathol 1997; 21: 1324-1333.
10. Davidson NG. Primary non-Hodgkin's lymphoma of the bladder. Case report and review of the literature. Scand J Urol Nephrol 1990; 24: 155-156.
11. Fernandez Acenero MJ, Martin Rodilla C, Lopez Garcia-Asenjo J, Coca Menchero S, Sanz Esponera J. Primary malignant lymphoma of the bladder. Report of three cases. Pathol Res Pract 1996; 192: 160-163.
12. Mantzarides M, Papathanassiou D, Bonardel G, Soret M, Gontier E, Foehrenbach H. High-grade lymphoma of the bladder visualized on PET. Clin Nucl Med 2005; 30: 478-480.
13. Bates AW, Norton AJ, Baithun SI. Malignant lymphoma of the urinary bladder: a clinicopathological study of 11 cases. J Clin Pathol 2000; 53: 458-461.
14. Jones MW. Primary Hodgkin's disease of the urinary bladder. Br J Urol 1989; 63: 438.
15. Mearini E, Zucchi A, Costantini E, Fornetti P, Tiacci E, Mearini L. Primary Burkitt's lymphoma of the bladder in a patient with AIDS. J Urol 2002; 167: 1397-1398.
16. Murphy AJ, O'Neill P, O'Brien F et al. Anaplastic large cell lymphoma: a unique presentation with urinary bladder involvement: a case report. Int J Surg Pathol 2005; 13: 369-373.
17. Givler RL. Involvement of the bladder in leukemia and lymphoma. J Urol 1971; 105: 667-670.
18. Amin R. Case report: primary non-Hodgkin's lymphoma of the bladder. Br J Radiol 1995; 68: 1257-1260.
19. Clarke NW, Maxwell AJ. Primary lymphoma of the urinary bladder. Br J Radiol 1991; 64: 761-762.
20. Yeoman LJ, Mason MD, Olliff JF. Non-Hodgkin's lymphoma of the bladder-CT and MRI appearances. Clin Radiol 1991; 44: 389-392.
21. Melekos MD, Matsouka P, Fokaefs E, Pantazakos A, Repanti M. Primary non-Hodgkin's lymphoma of the urinary bladder. Eur Urol 1992; 21: 85-88.
22. Coskun U, Gunel N, Eroglu A et al. Primary high grade malignant lymphoma of bladder. Urol Oncol 2002; 7: 181-183.