Primary Extranodal Marginal Zone Lymphoma of the Renal Pelvis: A Case Report and Review of the Literature

Maria I. Volkova\textsuperscript{a} Yana V. Gridneva\textsuperscript{a} Natalia A. Probatova\textsuperscript{b} Valeria V. Mochalnikova\textsuperscript{b} Kirill A. Turupaev\textsuperscript{a} Vsevolod B. Matveev\textsuperscript{a}

\textsuperscript{a}Urological Department of FSBI N.N. Blokhin National Medical Research Center for Oncology, Moscow, Russia; \textsuperscript{b}Department of Morphological and Molecular Genetic Diagnostics of Tumors of FSBI N.N. Blokhin National Medical Research Center for Oncology, Moscow, Russia

Keywords
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue · Mucosa-associated lymphoid tissue lymphoma · Renal pelvis · Ureter

Abstract
Lymphomas account for approximately 5% of nonurothelial tumors of the urinary tract and develop in the bladder in 90% of cases. The most common lymphomas histologic type of this location is extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). MALT lymphoma of the upper urinary tract is casuistically rare. The current study describes a case of a 74-year-old female patient with MALT lymphoma of the renal pelvis with metastases to the retroperitoneal lymph nodes who underwent radical surgical treatment with subsequent follow-up.

Introduction
Marginal zone lymphomas are low-grade non-Hodgkin B-cell lymphomas that are subdivided into extranodal marginal zone lymphomas of mucosa-associated lymphoid tissue (MALT lymphoma), nodal marginal zone lymphomas, and spleen marginal zone lymphomas. MALT lymphomas account for 8% of all non-Hodgkin's lymphomas [1]. Most often, MALT
lymphoma develops in the stomach. In addition, in descending order, the involvement of spleen, eye, uterine adnexa, lungs, skin, salivary glands, thyroid gland, small intestine, breast, synovial membrane, dura mater, and soft tissue was described. Primary upper urinary tract MALT lymphomas are casuistically rare. Gastric, skin, thyroid, and salivary glands MALT lymphomas are associated with chronic inflammation caused by pathogenic microorganisms or autoimmune disease [2]. However, the pathogenesis of upper urinary tract MALT lymphomas is unknown. We offer a description of a rare case of primary MALT lymphoma of the renal pelvis with retroperitoneal lymph node involvement.

Case Report

A 74-year female patient complaining with low urinary tract symptoms and progressive fatigue was admitted to the Oncourology department. Computed tomography (CT) revealed a contrast enhanced tumor, of the right kidney, 5.8 × 3.0 cm, which involved renal pelvis and renal sinus with the infiltration of upper and middle thirds of the right ureter and right m. iliopsoas (Fig. 1). Aorto-caval and para-aortic lymph nodes were enlarged up 1.4–1.6 cm. Two small calculi, 5 mm and 8 mm in diameter, were revealed in the middle and upper calyces of the right kidney. No other abnormalities were seen on chest, abdominal, and pelvic CT scans. Cystoscopy showed no tumors of the bladder mucosa. An attempt of ureteropyeloscopy failed due to a narrowing of the right ureter. Cytological examination of urine from the bladder and
the right ureter did not reveal any tumor cells. No other significant laboratory abnormalities were detected. The patient was clinically diagnosed with cT4N2M0 urothelial carcinoma of the right renal pelvis. The patient underwent right nephroureterectomy with resection of the right ureteric orifice, and the right psoas muscle, bilateral retroperitoneal, and right-sided pelvic lymphadenectomy.

The surgical specimen contained an infiltrative tumor 13 × 7 × 5 cm. The tumor was located at the hilum of the kidney and invaded adipose tissue of the sinus, the wall of the renal pelvis, and the ureter down to its lower third. The tumor was gray, dense, and homogeneous. Microscopically, the kidney tumor had the structure of a small round cell malignant tumor (Fig. 2a). A diffuse lymphoid tumor infiltration was revealed in three lymph nodes with a diameter of 4.0 cm, 3.5 cm, and 3.0 cm, respectively. An immunohistochemical study was performed using antibodies to CD3, CD5, CD10, CD20, CD23, CD43, BCL2, BCL6, cyclinD1, Ki67. The tumor cells expressed CD20 (Fig. 2b), BCL2 (Fig. 2c), and the marker of proliferative activity Ki67 was expressed in 7% of the cells. The tumor cells were negative with regard to other markers. The tumor had a moderate number of reactive CD3+ T lymphocytes, some of which expressed CD5, CD43, with numerous foci of CD23 + network of follicular dendritic cells (Fig. 2d). Thus, lymphoma of the marginal zone (MALT lymphoma) was verified morpho-immunohistochemically.

There were no postoperative complications. Gastric and bone marrow involvement was excluded. The patient was consulted by a hematologist and close follow-up was recommended. Positron emission tomography with 11C choline combined with CT was performed 15 months later and did not reveal any recurrent tumor.
Discussion

Lymphomas account for approximately 5% of nonurothelial tumors of the urinary tract and develop in the bladder in 90% of cases. The most common variant of lymphomas of this location is MALT lymphoma [3]. MALT lymphoma of the bladder develops more often in women and is usually associated with chronic cystitis [3, 4]. In the available literature, we found a description of 10 clinical cases of morphoimmunohistochemically confirmed MALT lymphomas localized in the renal pelvis (n = 7) or the ureter (n = 3) (Table 1) [5–14]. Most of the patients were men aged 30–77 years without a pre-existing urinary infection [5–14]. In our case, the patient suffered from urolithiasis. A possible prerequisite for the development of MALT lymphoma could be chronic inflammation, which provided long-term antigenic stimulation, attracting lymphoid cells, which subsequently transformed into B-cell lymphoma in the intraorgan lymphatic vessels.

Unlike urothelial tumors of the upper urinary tract, MALT lymphomas are often asymptomatic, although some patients complain of pain [5, 7, 8] or, as in our case, progressive fatigue. CT and/or magnetic resonance tomography usually reveals a thickening of the renal pelvis and ureter walls. There are no specific signs to differentiate lymphoma from other tumors of this location. Although Hara et al. [8] (2002) noted that MALT lymphomas of the renal pelvis and ureter may demonstrate low signal on T2-weighted magnetic resonance tomography images, locally advanced growth of MALT lymphoma is able to mimic the radiological signs of invasive urothelial cancer of the upper urinary tract.

MALT lymphoma is an indolent tumor that remains localized for a long time. In all described cases, the primary upper urinary tract MALT lymphomas were unilateral [5–14]. As well as in our patient, in 3 previously described observations, MALT lymphomas had a locally advanced growth with involvement of the renal pelvis, sinus, and paraureteral tissue [9, 12, 14]. In our case, a patient with the advanced primary tumor developed metastases in three retroperitoneal lymph nodes. Regional metastasizing was also revealed in 3 out of 10 patients described in the literature, including 1 case with metastatic lymphoma [11, 12, 14]. Bone marrow involvement, which is registered in approximately 20% of cases with MALT lymphomas of other sites, has been diagnosed in no patient with primary tumor of the upper urinary tract [5–14]. Other authors described cases of MALT lymphoma dissemination, including 2 patients with a primary tumor of the kidney pelvis. Interestingly, in 1 case, the peripheral lymph nodes were affected [14], and in the other, the renal pelvis MALT lymphoma was combined with a lesion of more typical for this type of extranodal marginal zone lymphomas localization in salivary gland and prostate involvement [5]. In 10% of cases, MALT lymphoma can transform into aggressive B-cell lymphoma, but such cases have not been described in primary lesions of the upper urinary tract [15].

Management approaches in extragastric MALT lymphomas depend on the primary tumor site and extent. In contrast to the gastric form of the disease in which the efficacy of Helicobacter pylori eradication has been proven, the data on the possible role of antibacterial therapy in MALT lymphomas originating from other organs are contradictory. The method of choice in localized extragastric MALT lymphoma is radiotherapy. Monotherapy with monoclonal antibodies to CD20 (rituximab) can be administered in cases when the tumor site is unsuitable for optimal irradiation. Common indolent nature of the disease also allows using of watchful waiting tactics. Surgical excision usually has only a diagnostic value. However, surgical removal is permitted in selected MALT lymphoma patients, which are not candidates for radiotherapy. Disseminated MALT lymphoma is an indication for systemic antitumor treatment with rituximab as a single-agent therapy, or as a component of different combinations. For rituximab-resistant and recurrent MALT lymphoma, chemotherapy or chemoinmunotherapy containing alkylating agents or purine nucleoside analogs is used [16].
| Author [reference] | Gender | Age | The primary tumor site | Other tumor sites | Management | Status |
|-------------------|--------|-----|------------------------|------------------|------------|--------|
| Araki et al. [5]  | M      | 68  | Renal pelvis           | Prostate, salivary gland | Watchful waiting | Alive with disease for 60 months |
| Colovic et al. [6] | M      | 50  | Ureter                 | –                | Watchful waiting | Alive with disease |
| Mita et al. [7]   | M      | 77  | Renal pelvis           | –                | Watchful waiting | Alive with disease for 10 months |
| Hara et al. [8]   | M      | 72  | Ureter                 | –                | Watchful waiting | Alive with disease for 9 months |
| Qiu et al. [9]    | F      | 83  | Renal pelvis, ureter   | –                | R-CVP       | Alive without disease for 8 months |
| Kato et al. [10]  | M      | 30  | Renal pelvis           | –                | Nephrectomy  | Alive without disease |
| Numakura et al. [11] | M   | 54  | Ureter                 | Retroperitoneal lymph nodes | R-CHOP     | Alive with disease for 5 months |
| Otsuki et al. [12] | M    | 69  | Renal pelvis, ureter   | Retroperitoneal lymph nodes | Rituximab   | Alive without disease for 78 months |
| Makino et al. [13] | M    | 70  | Renal pelvis           | –                | Nephrectomy  | Alive without disease for 8 months |
| Lee et al. [14]   | M      | 73  | Renal pelvis, ureter   | Retroperitoneal, intra-abdominal, intrathoracic, neck lymph nodes | Nephroureterectomy + R-CHOP | Alive without disease for 14 months |
Patients with MALT lymphoma usually have a good prognosis with a median survival of >10 years [15]. This fact is confirmed by the results of management in patients with the primary upper urinary tract tumors [5–14]. Four out of 10 previously described patients with MALT lymphomas of the renal pelvis and ureter are under close follow-up with no treatment without signs of the disease progression within 9–60 months. Four patients with locally advanced or metastatic MALT lymphomas who received rituximab with or without chemotherapy are alive (one with tumor within 5 months of treatment, two with continuing complete response for 8, 14, and 78 months, respectively). The rare primary site of MALT lymphoma in our patient, as well as in several cases described by other authors [10, 13, 14], did not allow differentiating lymphoma of the renal pelvis from urothelial cancer, and the patient underwent radical surgery. No adjuvant treatment was administered as in two previously described patients with no additional tumor foci identified after surgery [10, 13].

Conclusion

Lymphomas account for approximately 5% of nonurothelial tumors of the urinary tract and develop in the bladder in 90% of cases. The most common lymphoma type of this location is MALT lymphoma. MALT lymphoma of the upper urinary tract is casuistically rare, as a rule, is diagnosed as a localized tumor; however, over time it can metastasize to regional and nonregional lymph nodes. The combination of MALT lymphoma of the upper urinary tract with other extranodal foci is possible. Preoperative differentiation of urothelial cancer and MALT lymphoma of the upper urinary tract is not always possible. No cases of radiation therapy administration have been reported for upper urinary tract MALT lymphomas. Watchful waiting and CD20 inhibitor-based systemic therapy were described to be successfully used in the primary upper urinary tract MALT lymphomas. The prognosis in patients with MALT lymphoma of the renal pelvis and ureter is good. We offer a literature review and a description of the clinical case of a 74-year-old female patient with MALT lymphoma of the renal pelvis and retroperitoneal lymph node metastases, who underwent surgical treatment with no adjuvant treatment.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This study protocol was reviewed and approved by the Ethics Committee of the Federal State Budgetary Institution « N. N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation on November 25, 2021.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors received no funding for this case report.
Author Contributions

Volkova M.I.: literature review and manuscript writing. Gridneva Y.V., Probatova N.A., and Mochalnikova V.V.: assisting in manuscript writing. Turupaev K.A.: preparation of the manuscript for publication. Matveev V.B.: writing of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1. Vannata B, Stathis A, Zucca E. Management of the marginal zone lymphomas. Cancer Treat Res. 2015; 165: 227–49.
2. Thieblemont C, Bertoni F, Copie-Bergman C, Ferreri AJ, Ponzoni M. Chronic inflammation and extra-nodal marginal-zone lymphomas of MALT-type. Semin Cancer Biol. 2014; 24: 33–42.
3. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. World Health Organization classification of tumours. Pathology and genetics of tumours of the urinary system and male genital organs. Lyon: IARC Press; 2004.
4. Matsuda I, Zozumi M, Tsuchida YA, Kimura L, Liu NN, Fujimori Y, et al. Primary extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue type with malakoplakia in the urinary bladder: a case report. Int J Clin Exp Pathol. 2014; 7(8): 5280–4.
5. Araki K, Kubota Y, Iijima Y, Suzuki H, Sasagawa I, Nakada T, et al. Indolent behaviour of low-grade B-cell lymphoma of mucosa-associated lymphoid tissue involved in salivary glands, renal sinus and prostate. Scand J Urol Nephrol. 1998; 32(3): 234–6.
6. Colović M, Hadzi-Djokić J, Cemerikić V, Colović R, Janković G, Dacić M. Primary MALT lymphoma of the kidney. Hematol Cell Ther. 1999; 41(5): 229–32.
7. Mita K, Ohnishi Y, Edahiro T, Fuji T, Yamasaki A, Shimamoto F. Primary mucosa-associated lymphoid tissue lymphoma in the renal pelvis. Urol Int. 2002; 69(3): 241–3.
8. Hara M, Satake M, Ogino H, Itoh M, Miyagawa H, Hashimoto Y, et al. Primary ureteral mucosa-associated lymphoid tissue (MALT) lymphoma: pathological and radiological findings. Radiat Med. 2002; 20(1): 41–4.
9. Qiu L, Unger PD, Dillon RW, Strauchen JA. Low-grade mucosa-associated lymphoid tissue lymphoma involving the kidney: report of 3 cases and review of the literature. Arch Pathol Lab Med. 2006; 130(1): 86–9.
10. Kato Y, Hasegawa M, Numasato S, Monma N, Fujioka T. Primary mucosa-associated lymphoid tissue-type lymphoma arising in the kidney. Int J Urol. 2008; 15(1): 90–2.
11. Numakura K, Tsuchiya N, Obara T, Tsuruta H, Saito M, Narita S, et al. A case of ureteral malignant lymphoma diagnosed by laparoscopic needle biopsy. Jpn J Clin Oncol. 2011; 41(3): 440–2.
12. Otsuki H, Ito K, Sato K, Kosaka T, Shimazaki H, Kaji T, et al. Malignant lymphoma of mucosa-associated lymphoid tissue involving the renal pelvis and the entire ureter: a case report. Oncol Lett. 2013; 5(5): 1625–8.
13. Makino T, Miwa S, Koshiba K, Kawashima A. Mucosa-associated lymphoid tissue lymphoma involving the kidney: a case report and review of the literature. Int Cancer Conf J. 2015; 5(2): 82–9.
14. Lee H, Joo JE, Hong YO, Lee WM, Kim EK, Woo JW, et al. Ureteral marginal zone lymphoma of mucosa-associated lymphoid tissue, chronic inflammation, and renal artery atherosclerosis. J Pathol Transl Med. 2015; 49(4): 339–42.
15. Zinzani PL. The many faces of marginal zone lymphoma. Am Soc Hematol Educ Program. 2012: 426–32.
16. Zucca E, Arcaini L, Buske C, Johnson PW, Ponzoni M, Raderer M, et al. Marginal zone lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020; 31(1): 17–29.