Low-Grade Mucosa-Associated Lymphoid Tissue Lymphoma Involving the Kidney

Report of 3 Cases and Review of the Literature

Libo Qiu, MD; Pamela D. Unger, MD; Robert W. Dillon, MD; James A. Strauchen, MD

Mucosa-associated lymphoid tissue (MALT) lymphoma was first reported in 1983 by Isaacson and Wright, who described 2 cases of low-grade B-cell gastrointestinal lymphoma. The MALT lymphomas are in the group of marginal zone B-cell lymphomas that arise from extranodal mucosal-based proliferation of lymphoid cells. These cells have been called centrocyte-like cells or monocytoid B cells, often infiltrating normal epithelial structures with formation of so-called lymphoepithelial lesions. The MALT lymphomas usually occur in adults and are often associated with autoimmune disease such as Sjogren syndrome or Hashimoto thyroiditis or with chronic inflammation. These tumors tend to remain localized without rapid progression for prolonged periods and, if disseminated, have a tendency to involve other mucosal organs. The gastrointestinal tract is involved in two thirds of the cases, but a wide variety of sites such as the lung, thyroid, breast, salivary glands, orbit, conjunctiva, kidney, liver, and skin may be involved.

Kidney involvement with low-grade MALT lymphoma is extremely rare. Pelstring et al first reported a renal MALT lymphoma with focal high-grade transformation in 1991. A review of the literature revealed 12 cases of low-grade B-cell lymphoma of MALT with kidney involvement. Half of these cases have been described in association with MALT lymphoma at other sites. In this report we describe 3 cases of low-grade B-cell lymphomas arising in the kidney with histologic features of MALT lymphoma. In the first 2 patients, lymphomas were confined to the kidney; in the third patient, renal lymphoma was preceded by an orbital low-grade MALT lymphoma.

REPORT OF CASES

Case 1

An 83-year-old woman presented with a several-day history of back pain in September 2003. She denied a history of fever, night sweats, any urologic symptoms, or weight loss. She also denied a history of nephrolithiasis or autoimmune disease. The findings from her physical examination were unremarkable. A computed tomographic scan of her abdomen showed a markedly irregular left renal pelvis, and magnetic resonance imaging revealed an irregular left upper ureter and renal pelvis. The pain resolved within 2 days. The patient, however, developed persistent abdominal bloating. After a 3-month interval, the magnetic resonance imaging was repeated, showing the same abnormality. Cystoscopy and bilateral retrograde pyelograms were unremarkable. In March 2004, a computed tomographic scan of the abdomen with 3-dimensional imaging revealed evidence of an infiltrative process in the left renal hilum involving both the renal pelvis and sinus, and extending along and encasing the left proximal ureter as well as some subcapsular invasion (Figure 1, A). No lymphadenopathy was identified. The suspicion of a renal lymphoma was raised clinically. In June 2004, the patient underwent a retroperitoneal exploration on the left side; a biopsy was undertaken of a perirenal mass. The frozen section of the specimen was interpreted as low-grade lymphoma. The patient received chemotherapy (CVP-Rituxan) in August 2004. She was disease free at the follow-up at 8 months. A hematoxylin-eosin–stained slide with the block was sent in consultation to our institution.

Case 2

A 53-year-old man with a remote history of sarcoidosis presented for routine follow-up in October 2003. He was asymptom-
Figure 1. Patient 1. A, Computed tomography of the abdomen showed a left renal hilar mass encasing the proximal ureter (arrow). B, The neoplasm showed vaguely nodular proliferation of lymphoid cells infiltrating perirenal fat (hematoxylin-eosin, original magnification ×50). C, Neoplastic cells with slightly irregular nuclear contours and abundant eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×400) were positive for CD20 in immunohistochemical stain (inset).

Figure 2. Patient 2. A, The renal cortex showed extensive nodular infiltrate of lymphoid cells with effacement of kidney architecture (hematoxylin-eosin, original magnification ×50). B, The lymphoid cells infiltrated the kidney interstitium and surrounded renal glomeruli and tubules (hematoxylin-eosin, original magnification ×200). C, Neoplastic lymphoid cells with round to slightly irregular nuclear contours, clumped chromatin, and eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×400).

Figure 3. Patient 3. A, A pink-tan fleshy mass measuring 7.5 cm involved the renal pelvis and encased the proximal portion of the ureter. B, The renal pelvis showed lymphocytic infiltrate involving perirenal fat and focally extending into renal parenchyma (hematoxylin-eosin, original magnification ×50). C, Neoplastic centrocyte-like cells with irregular nuclear contours and pale cytoplasm were mixed with plasmacytoid cells and plasma cells (hematoxylin-eosin, original magnification ×400).

Mucosa-Associated Lymphoid Tissue Lymphoma

Case 3

A 72-year-old man presented in May 1999 with fever, chills, abdominal pain, and weight loss for 4 weeks. He had a past medical history of bilateral orbital low-grade B-cell MALT lymphoma and had undergone surgery and radiation therapy in February 1998, with no recurrences. Magnetic resonance imaging of the abdomen revealed a partially obstructing left-sided colon lesion with eccentric thickening of sigmoid colon, and an abnormal soft tissue density occupying the right renal collecting system and right renal pelvis. Subsequent workup for the colon lesion by colonoscopy and biopsy showed moderately differentiated colonic adenocarcinoma. The patient underwent subtotal colectomy in July 1999. Further imaging studies for the kidney lesion confirmed the right renal mass. A right nephrectomy was performed without complication in September 1999. Postoperatively, he developed pulmonary embolism and was treated with heparin and an inferior vena cava filter. After hospitalization for recurrent pulmonary embolism in December 1999, the patient was lost to follow-up.

MATERIALS AND METHODS

Hematoxylin-eosin–stained histology sections of formalin-fixed, paraffin-embedded tissue were prepared at either the sub-
malignant institution (cases 1 and 2) or in our laboratory at the Mount Sinai Medical Center (case 3). Immunohistochemical studies were performed on paraffin-embedded material using a standard avidin-biotin immunoperoxidase technique. The panel of primary antibodies included CD3, CD5, CD10, L26, CD23, CD43, LCA, CD79a, Bcl-1, Bcl-2, Bcl-6, and κ and λ immunoglobulin light chains.

**PATHOLOGIC FINDINGS**

Microscopic examination of a biopsy specimen of the perirenal mass in the first case showed infiltration of the perirenal fat by a vaguely nodular proliferation of relatively uniform medium-sized lymphocytes (Figure 1, B). At high power, these cells had round or slightly irregular nuclear contours with inconspicuous nucleoli and abundant eosinophilic cytoplasm. Immunohistochemical studies showed that the neoplastic lymphoid cells were positive for CD20, CD79a, and Bcl-2, and negative for CD5, CD10, and Bcl-1/cyclin D1, demonstrating B-cell phenotype consistent with marginal-zone B-cell lymphoma (Figure 1, C).

In the second case, a right partial nephrectomy specimen was received measuring 3.5 × 3.0 × 2.5 cm, with a 3.0 cm well-demarcated yellow-brown smooth mass. The cut surface was tan and solid. Histologically, the architecture of the involved kidney was effaced by extensive and nodular infiltrate of lymphoplasmacytic cells with residual tubules and glomeruli (Figure 2, A). These cells infiltrated the renal interstitium surrounding glomeruli and tubules (Figure 2, B). At high power, neoplastic cells had round to slightly irregular nuclear contours, clumped chromatin with inconspicuous nucleoli, and pink cytoplasm. Mitotic figures were rare (Figure 2, C). Immunohistochemical studies showed that the infiltrated cells were positive for CD20 and CD79a with immunoglobulin κ light-chain restriction, and negative for CD5, CD10, Bcl-2, and Bcl-6.

In the third case, a right nephrectomy specimen with an attached 1.5 cm length of ureter was received. The kidney measured 13.0 × 6.0 × 4.3 cm and contained a 7.5-cm pink-tan fleshy mass involving the renal pelvis and encasing the proximal portion of the ureter (Figure 3, A). Histologically, the renal pelvis showed a lymphoid mass abutting and focally extending into kidney parenchyma with involvement of perirenal soft tissue (Figure 3, B). The noninvolved kidney tissue was unremarkable. The neoplasm was composed predominantly of centrocyte-like cells with irregular nuclear contours, clumped chromatin with inconspicuous nucleoli, and abundant cytoplasm. Occasional plasma cells, plasmacytoid lymphocytes, and immunoblasts were admixed within the infiltrate (Figure 3, C). Immunohistochemical studies revealed that the centrocyte-like cells were positive for CD20 and CD79a, and negative for CD5, CD10, CD23, and CD43, demonstrating a B-cell phenotype consistent with a marginal-zone B-cell lymphoma. Immunostains for immunoglobulin κ and λ light chains showed monoclonal κ light-chain restriction.

**COMMENT**

Low-grade B-cell lymphoma of MALT arising from the kidney is extremely rare. In 1991, Pelstring et al. reported the first case of low-grade B-cell MALT lymphoma with focal transformation to high-grade lymphoma involving the kidney. After reviewing the literature, we identified 12 cases of renal MALT lymphomas. Because low-grade lymphomas of MALT type often have an indolent clinical course with a tendency to be localized at the time of diagnosis and to be curable with local therapy, it is important pathologically to distinguish MALT-type lymphoma from other types of renal lymphomas that pursue a more aggressive clinical course.

The MALT lymphoma represents a low-grade B-cell marginal zone lymphoma arising in extranodal tissue in which lymphoid tissues are usually absent, and it is usually acquired in response to chronic inflammation or in association with an autoimmune disorder. The biological behavior of the disease generally differs from the nodal low-grade B-cell lymphoma. Morphologically, MALT lymphomas are characterized by the presence of diffuse infiltrate of neoplastic centrocyte-like or monocyteid cells, frequently showing plasmacytic differentiation. The characteristic lymphoepithelial lesion is composed of a destructive infiltrate of neoplastic lymphoid cells within epithelium, and it is common to all MALT lymphomas. The immunophenotype is less specific. The lymphoma cells express monotypic surface immunoglobulins or, to a lesser extent, cytoplasmic immunoglobulins, usually immunoglobulin M. These cells are negative for CD5, CD10, CD23, and cyclin D1. Low-grade MALT lymphomas are positive for Bcl-2 protein, whereas the majority of the neoplastic cells of the high-grade tumor are negative.

Primary renal lymphoma (PRL) is a rare disease, accounting for only 0.7% of all extranodal lymphomas. Primary renal lymphoma is defined as a lymphoma that involves only the kidney at presentation, and manifests with renal involvement. Most PRLs that have been reported were classified as diffuse, large B-cell lymphoma, and almost all PRLs were of B-cell lineage. Low-grade MALT lymphomas may involve the kidney in a primary or secondary fashion. Six of 12 renal MALT lymphomas reported were confined to the kidney, and 2 of 3 cases in this report represented PRL (Table). Among these 15 cases, 5 (including 3 primary renal MALT lymphomas) showed predominant involvement of renal sinus and/or renal pelvis, which is a common site for other types of PRLs. The histogenesis of renal MALT lymphoma is unknown. Unlike MALT lymphoma from other sites, such as the stomach or thyroid, there was no associated chronic inflammation described in any of the reported cases or in our patients. There are not enough data to support an association of renal MALT lymphoma with autoimmune disorder.

The patients with low-grade renal MALT lymphoma have been reported to have a long survival with high response rate to local treatment. Kazuhiro et al. reported a 68-year-old man with MALT lymphoma involving the kidney, salivary glands, and prostate. The patient had remained alive without any treatment for 5 years from the first symptom of the disease. In another case of low-grade MALT lymphoma of kidney with perirenal nodal involvement, the patient was treated with irradiation to the renal bed after radial nephrectomy, and was free of disease at 17 months of follow-up. Adverse prognostic factors for low-grade MALT lymphomas may include high-grade transformation, bone marrow involvement, high tumor burden, or dissemination of disease. In the report by Pelstring et al., the patient with focal high-grade transformation of low-grade MALT lymphoma of kidney achieved only partial remission at 15 months after systemic chemotherapy. Tao and Kahn reported an unusual case of Epstein-Barr virus–associated MALT lymphoma involving the kidney, lung, and axillary lymph node in a 9-year-old...
Previously Published and Current Cases of Renal Mucosa–Associated Lymphoid Tissue Lymphoma*

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Age, y/sex</th>
<th>Location</th>
<th>Associated Disease</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelstring et al,7 1991</td>
<td>62/F</td>
<td>Kidney, parotid gland</td>
<td>Sjogren syndrome</td>
<td>Chemotherapy</td>
<td>Partial remission at 15 mo</td>
</tr>
<tr>
<td>Parveen et al,8 1993</td>
<td>69/M</td>
<td>Kidney, perirenal lymph node</td>
<td>None</td>
<td>Radical nephrectomy, irradiation</td>
<td>Disease free at 17 mo</td>
</tr>
<tr>
<td>Imahori,17 1994</td>
<td>56/M</td>
<td>Kidney, orbit</td>
<td>None</td>
<td>Nephrectomy</td>
<td>Died of disease 13 y after surgery</td>
</tr>
<tr>
<td>Mak et al,10 1998</td>
<td>62/M</td>
<td>Kidney, GI tract, tonsils, salivary glands, lung</td>
<td>IgA nephropathy</td>
<td>Chemotherapy</td>
<td>No recurrence of lymphoma at 20 mo</td>
</tr>
<tr>
<td>Kauzhiro et al,15 1998</td>
<td>68/M</td>
<td>Kidney, prostate, salivary glands</td>
<td>None</td>
<td>No treatment</td>
<td>Alive with disease at 5 y</td>
</tr>
<tr>
<td>Colovic et al,18 1999</td>
<td>50/M</td>
<td>Kidney</td>
<td>Helicobacter pylori gastritis</td>
<td>Nephrectomy</td>
<td>Not available</td>
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<tr>
<td>Tao and Khan,16 2000</td>
<td>9/M</td>
<td>Kidney, axillary lymph node</td>
<td>Epstein-Barr virus infection</td>
<td>Chemotherapy</td>
<td>Died of disease at age 13 y</td>
</tr>
<tr>
<td>Mhawech et al,19 2000</td>
<td>76/F</td>
<td>Kidney</td>
<td>None</td>
<td>Radical nephrectomy</td>
<td>Not available</td>
</tr>
<tr>
<td>Stokes et al,20 2002</td>
<td>68/F</td>
<td>Kidney</td>
<td>MPGN</td>
<td>Prednisone</td>
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<tr>
<td>Case 2</td>
<td>72/F</td>
<td>Kidney</td>
<td>MPGN</td>
<td>Prednisone</td>
<td>Partial remission of renal symptoms at 6 mo</td>
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<tr>
<td>Mita et al,21 2002</td>
<td>77/M</td>
<td>Kidney</td>
<td>None</td>
<td>Nephrectomy</td>
<td>Not available</td>
</tr>
<tr>
<td>Current case 1</td>
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<td>Kidney, perirenal fat</td>
<td>None</td>
<td>Radical nephrectomy</td>
<td>Disease free at 28 mo</td>
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<tr>
<td>Current case 2</td>
<td>83/F</td>
<td>Kidney, perirenal fat</td>
<td>None</td>
<td>Chemotherapy</td>
<td>Disease free at 8 mo</td>
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<td>Current case 3</td>
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<td>Sarcoïdosis</td>
<td>Partial nephrectomy</td>
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<tr>
<td>Current case 3</td>
<td>72/M</td>
<td>Kidney, orbit</td>
<td>None</td>
<td>Radical nephrectomy</td>
<td>Pulmonary embolism following surgery, further follow-up not available</td>
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</tbody>
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* GI indicates gastrointestinal; Ig, immunoglobulin; and MPGN, membranoproliferative glomerulonephritis.

boy with congenital hypoadrenalism and panhypopituitarism. The patient presented with an aggressive clinical course and histologic evolution following progression from a low-grade to a high-grade MALT lymphoma in all involved organs.

In summary, we have described a series of 3 cases of low-grade B-cell lymphoma of MALT type arising in the kidney. The first patient received chemotherapy without complications. She was disease free at the recent follow-up at 8 months. The second patient, who underwent a partial nephrectomy, was asymptomatic without evidence of recurrence at the subsequent follow-up at 10 months. The third patient developed a pulmonary embolism following nephrectomy, and further follow-up is not available.

References