Primary Paratesticular Lymphoma
A Report of 2 Cases and Review of the Literature

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- Non-Hodgkin lymphoma arising in the paratesticular organs without testicular involvement is rare. In most previously reported cases, the classification systems that were used are now outdated and/or immunologic studies were not done. We report the clinical and pathologic features of 2 cases of non-Hodgkin lymphoma arising in the epididymis and the spermatic cord. Patient 1 was a 35-year-old man who presented with a painless scrotal mass. Patient 2 was a 61-year-old man who presented with a right inguinal mass. Orchiectomy performed in both patients revealed a mass confined to the epididymis in patient 1 and to the spermatic cord in patient 2. Histologic examination in both cases revealed diffuse large cell lymphoma, and immunohistochemical studies supported B-cell lineage. Subsequent staging studies showed no other site of disease in patient 1 and an isolated mass anterior to the right psoas muscle in patient 2. Malignant lymphoma involving testicular adnexal structures without involvement of the testis is extremely uncommon. To our knowledge, only 6 cases confined to the epididymis and 12 cases confined to the spermatic cord have been reported previously.

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Testicular lymphoma is an aggressive extranodal non-Hodgkin lymphoma (NHL) that frequently invades the tunica albuginea, rete testis, epididymis, and spermatic cord by contiguous spread. In one large series, microscopic involvement of the epididymis and spermatic cord was observed in 60% and 39% of cases, respectively. However, NHLs that involve the epididymis or spermatic cord exclusively are extremely rare. To the best of our knowledge, only 6 cases confined to the epididymis and 12 cases confined to the spermatic cord have been reported previously.

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MATERIALS AND METHODS

Both patients underwent orchiectomy at another hospital. Hematoxylin-eosin-stained slides and representative tissue blocks for both patients were sent to the University of Texas M. D. Anderson Cancer Center (UTMDACC), Houston, Tex, for review. Patient 1 was referred to the UTMDACC for further evaluation and treatment. Clinical history for patient 1 was obtained from UTMDACC records. Clinical history and follow-up data for patient 2 were obtained from the referring pathologist and the patient's primary physicians. All hematoxylin-eosin-stained histologic slides were reviewed, and the NHLs were classified according to the Revised European-American classification of lymphoid neoplasms.

Immunohistochemical stains were performed on fixed, paraffin-embedded tissue sections using the avidin-biotin-peroxidase complex (ABC) method and an automated immunostainer (Ventana-Biotech, Tucson, Ariz). All tissue sections underwent heat-induced antigen retrieval. The antibodies used were specific for CD45RB (leukocyte common antigen; 1:300, Dako Corporation, Carpinteria, Calif), CD3 (1:150, Dako), CD20 (1:700, Dako), CD79a (1:50, Dako), Bcl-2 (1:200, BioGenex, San Ramon, Calif), Bcl-6 (1:10, Dako), epithelial membrane antigen (1:25, Dako), CD10 (1:70, Vector, Burlingame, Calif), CD30 (1:20, Signet, Dedham, Mass), Bcl-2 (1:200, BioGenex, San Ramon, Calif), Ki-67 (1:20, Beckmann Coulter, Miami, Fla), keratin (AE1/AE3; 1:500, Boehringer Mannheim, Indianapolis, Ind), α-fetoprotein (1:25, Zymed Lab, San Francisco, Calif), and placental alkaline phosphatase (1:20, Lab Vision Corp, Freemont, Calif).

RESULTS

Clinical Findings

Case 1.—A 35-year-old man presented in November 1999 with a left scrotal mass. The mass had waxed and waned in size during the previous 2 years, but had reached 8 cm at the time he sought medical attention. The patient was asymptomatic, and the physical examination was otherwise unremarkable. There was no lymphadenopathy, hepatosplenomegaly, or mass in the right testes. The patient underwent a left inguinal orchietomy that demonstrated a diffuse large B-cell lymphoma involving the epididymis. A subsequent complete staging evaluation that included chest radiograph, computed tomographic scans of the abdomen and pelvis, and ultrasound examination of the scrotum was negative for evidence of malignant lymphoma. Bilateral bone marrow aspirates and biopsies were negative for NHL. Laboratory studies that included a complete blood count with a differential count and serum lactate dehydrogenase and β2-microglobulin evaluations were unremarkable. The clinical stage was IEA. The patient received chemotherapy with CHOP (cy-

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Pathologic Findings

Case 1.—The left orchiectomy specimen consisted of testis, epididymis, and spermatic cord. On cut surface, the epididymis was replaced by a fleshy tan mass that measured $5 \times 6 \times 3$ cm and contained areas of necrosis and punctate hemorrhage.

Microscopically, the epididymis contained a dense infiltrate of atypical lymphoid cells with a diffuse growth pattern (Figure, A). The cells were large with oval to convoluted nuclear contours, vesicular chromatin, one to several nucleoli, and discernible cytoplasm (Figure, B). Mitotic figures and individually necrotic cells were easily identified. Throughout most of the neoplasm, fine bands of sclerosis surrounded aggregates of neoplastic cells. There were also areas of geographic necrosis and vascular

and the pattern of spread were unusual for primary nodal disease and were more consistent with a primary paratesticular neoplasm. Thus, the clinical stage was considered IIEA. The patient received CHOP chemotherapy. Two months after completing chemotherapy, the mass anterior to the right psoas muscle had resolved. The patient remains well and free of disease 13 months after presentation.

Case 2.—A 61-year-old man presented in November 1998 with a right inguinal mass that had been present for 3 months and was occasionally painful. He was otherwise asymptomatic. Physical examination revealed only a right inguinal mass. There was no lymphadenopathy, hepatosplenomegaly, or mass in the left testis. Laboratory studies that included a complete blood count with a differential count and serum lactate dehydrogenase and $\beta_2$-microglobulin evaluations were unremarkable. The patient underwent a right radical orchiectomy that demonstrated a diffuse large B-cell lymphoma of the spermatic cord. Subsequent computed tomographic scan of the abdomen and pelvis demonstrated a predominantly cystic, 8.5-cm mass on the anterior aspect of the right psoas muscle that extended along the right iliac vessels toward the femoral canal. There was no evidence of lymphadenopathy or involvement of the liver and spleen. Bilateral bone marrow aspirates and biopsies were negative for malignant lymphoma. At a multidisciplinary conference, the consensus opinion was that the 3-month history of an inguinal mass clophosphamide, Adriamycin, vincristine, prednisone), intrathecal chemotherapy (ara-C plus methotrexate), and scrotal irradiation. At the time of last clinical follow-up (6 months after diagnosis), the patient was in complete clinical remission.

Case 1. The neoplastic cells diffusely replace the parenchyma of the epididymis and infiltrate, but do not penetrate the tunica albuginea (hematoxylin-eosin, original magnification $\times 40$). B. Case 1. The malignant cells have large pleomorphic nuclei, and mitotic figures are easily identified. Fine bands of sclerosis surround aggregates of neoplastic cells (hematoxylin-eosin, original magnification $\times 400$). C. Case 2. The malignant cells are large with oval to irregular nuclear contours and frequently have conspicuous nucleoli. Mitotic figures are easily identified (hematoxylin-eosin, original magnification $\times 400$). D. Case 2. The malignant cells strongly express CD20 (immunohistochemistry, $\times 400$).
invasion. The testicular parenchyma and spermatic cord were free of lymphoma.

Immunohistochemical stains showed that the neoplastic cells strongly expressed CD45RB and CD20, and were weakly positive for CD10 and Bcl-6. Approximately 75% of the neoplastic cells reacted positively when stained with an antibody to Ki-67. The neoplastic cells failed to express CD3, immunoglobulin light chains, CD30, Bcl-2, keratin, epithelial membrane antigen, placental alkaline phosphatase, and α-fetoprotein.

**Case 2.**—The right orchiectomy specimen consisted of testis, epididymis, and spermatic cord. The spermatic cord contained a fusiform swelling that extended from 1 cm distal to the resection margin through the next 6 cm of the cord. On cut section, the swelling was due to a 3.5 × 3.2 × 3.2-cm firm, white-tan mass without areas of necrosis.

Microscopically, a population of large atypical lymphoid cells with a diffuse growth pattern infiltrated the spermatic cord. The nuclei were large and cytologically variable, with some showing prominent folding and others with an antibody to Ki-67. A few small foci of necrosis were present, but there was no sclerosis. A dense infiltrate of small, mature-appearing lymphocytes was present at the periphery of the lesion and was most conspicuous around vessels. The testis was atrophic and uninvolved by NHL. The spermatic cord resection margin was free of neoplasm.

Immunohistochemical stains showed that neoplastic cells expressed CD45RB, CD20 (Figure, D), and CD79a, and a subpopulation expressed Bcl-2. Approximately 50% of the neoplastic cells reacted positively when stained with an antibody to Ki-67. The neoplastic cells were negative for CD3, CD10, CD30, immunoglobulin light chains, Bcl-6, keratin, epithelial membrane antigen, placental alkaline phosphatase, and α-fetoprotein. The small, mature-appearing lymphocytes at the periphery of the mass and surrounding vessels were T cells (positive for CD3).

**COMMENT**

Tumors of the testicular adnexal structures comprise a heterogeneous group of uncommon lesions, most of mesenchymal origin. Adenomatoid tumors, pseudosarcomatous myofibroblastic proliferations, and rhabdomyosarcomas account for the large majority of these neoplasms. Non-Hodgkin lymphoma confined to testicular adnexal structures is rare.

In our review of the literature, we identified 6 previously reported cases of NHL confined to the epididymis (Table 1), of which only a subset have had immunophenotypic analysis. Gowing, in a review of material submitted to the British Testicular Tumour Panel, reported that the epididymis was the only site involved in 2 (1.5%) of 128 cases of lymphoma, but no descriptions or illustrations were provided. Of the 6 previously reported cases of lymphoma of epididymis, 3 have had diffuse growth patterns and were classified as intermediate or high-grade NHL. The remaining cases were mucosa-associated lymphoid tissue–type lymphoma, follicular large cell lymphoma, and intravascular large T-cell lymphoma. The patients’ mean age was 44.5 years (range 20–73 years). In 5 cases the neoplasm involved the right epididymis. One case, the follicular large cell lymphoma, was bilateral. Patients with NHL of the epididymis most often present with a hard, nontender, unilateral mass clearly separable from the testis, or with asymptomatic hemiscrotal swelling. In 2 of the 6 cases, the patients reported pain. Clinical diagnoses were epididymitis in 3 cases, testicular neoplasm in 1 case, adenomatoid tumor in 1 case, and unknown in 1 case. It is difficult to determine the behavior of these neoplasms and survival of these patients owing to the small number of reported cases and lack of clinical data, especially follow-up data.

Non-Hodgkin lymphoma involving the spermatic cord is also rare. Banowski and Schultz found only 2 cases (1.9%) of possible lymphoma in their review of 101 primary malignant spermatic cord tumors, but clinical data were unavailable for these cases. We identified 12 previously reported cases (Table 2), only 3 of which were analyzed immunophenotypically. Patients with primary spermatic cord lymphoma usually present with a tumor in the groin or in the upper part of the scrotum, separable from the testis. Thus, the clinical presentation resembles an inguinoscrotal hernia. Most patients are middle-aged (mean, 52 years; range, 21–89 years). The neoplasms usually have a diffuse growth pattern and are classified as intermediate or high grade. The prognosis is poor for patients treated with surgery or radiation therapy alone. Thus, the clinical behavior of primary NHL of the spermatic cord appears to be similar to that of primary NHL of the testis. Both have a propensity to progress rapidly and to relapse in nodal and extranodal sites, such as the central nervous system. Although the staging procedures and treatment were not uniform in the previously reported cases of spermatic cord NHL, the risk of recurrence appears to be high. It has been proposed, therefore, that patients with NHL originating in the spermatic cord

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**Table 1. Clinicopathologic Features of Patients With Lymphoma of Epididymis**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Stage</th>
<th>Histology</th>
<th>Immunophenotype</th>
<th>Size, cm</th>
<th>Therapy</th>
<th>Response</th>
<th>Relapse Site</th>
<th>Follow-up, mo</th>
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<tbody>
<tr>
<td>Case 1</td>
<td>35</td>
<td>IE</td>
<td>DLC</td>
<td>B</td>
<td>6</td>
<td>O, CT, RT</td>
<td>CR</td>
<td>None</td>
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<tr>
<td>Ref 2</td>
<td>26</td>
<td>IE</td>
<td>“Histiocytic”</td>
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<td>3.4</td>
<td>O, RT</td>
<td>CR</td>
<td>None</td>
</tr>
<tr>
<td>Ref 4</td>
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<td>IE</td>
<td>“Histiocytic”</td>
<td>NA</td>
<td>3</td>
<td>RT</td>
<td>CR</td>
<td>None</td>
</tr>
<tr>
<td>Ref 5</td>
<td>68</td>
<td>IE</td>
<td>DLC</td>
<td>CD45RB1</td>
<td>7</td>
<td>O, CT</td>
<td>NR</td>
<td>Skin</td>
</tr>
<tr>
<td>Ref 6</td>
<td>34</td>
<td>IE</td>
<td>FL</td>
<td>B</td>
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<td>O, CT</td>
<td>CR</td>
<td>None</td>
</tr>
<tr>
<td>Ref 7</td>
<td>20</td>
<td>IE</td>
<td>MALT</td>
<td>B</td>
<td>3</td>
<td>SR</td>
<td>CR</td>
<td>None</td>
</tr>
<tr>
<td>Ref 8</td>
<td>56</td>
<td>IE</td>
<td>IVL</td>
<td>NA</td>
<td>CT</td>
<td>NR</td>
<td>Lung, pleura, spleen epididymis</td>
<td>NED, 12</td>
</tr>
</tbody>
</table>

* DLC indicates diffuse large cell; FL, follicular large cell lymphoma; MALT, low-grade B-cell lymphoma of mucosa associated lymphoid tissue; IVL, intravascular large cell lymphoma; O, orchiectomy; CT, chemotherapy; RT, radiotherapy; SR, surgical resection; CR, complete remission; NR, no remission; NED, no evidence of disease; DOD, died of disease; and NA, not available.

1. Markers of B-cell and T-cell differentiation were not studied.

2. Histiocytic lymphoma

3. DOD indicates diffuse large cell; FL, follicular large cell lymphoma; MALT, low-grade B-cell lymphoma of mucosa associated lymphoid tissue; IVL, intravascular large cell lymphoma; O, orchiectomy; CT, chemotherapy; RT, radiotherapy; SR, surgical resection; CR, complete remission; NR, no remission; NED, no evidence of disease; DOD, died of disease; and NA, not available.

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should receive systemic chemotherapy, radiation therapy, and central nervous system prophylaxis, regardless of clinical stage.20

Primary testicular NHLs that secondarily involve the epididymis or spermatic cord may simulate primary paratesticular tumors.27 Similarly, generalized NHL may present with involvement of the testicular adenial structures.20 For these reasons, a complete clinical and pathologic staging, including careful examination of the orchiectomy specimen, is indicated before the diagnosis of primary epididymal or spermatic cord lymphoma can be established.

In the 2 cases presented in this report, immunohistochemical studies demonstrated that the neoplasms were of B-cell lineage. In case 1, the neoplastic cells were positive for CD10 and Bcl-6, but failed to express Bcl-2. These findings suggest that this neoplasm was of follicle center cell origin. In case 2, the neoplastic cells were weakly positive for Bcl-2, but were negative for CD10 and Bcl-6. The immunohistochemical heterogeneity of these 2 cases has been shown by others for diffuse large B-cell lymphoma as a whole. For example, in one study approximately 25% of de novo diffuse large B-cell lymphomas coexpress CD10 and Bcl-6, 47% express only Bcl-6, and 25% express neither CD10 nor Bcl-6.28 Similarly, Bcl-2 is expressed by a subset of diffuse large B-cell lymphomas, and Bcl-2 expression is associated with a poor prognosis.30,31

In summary, primary paratesticular NHLs are extremely rare. Patients with these lymphomas should be thoroughly staged to exclude generalized lymphoma and primary testicular lymphoma. Primary NHL of spermatic cord and primary NHL of the testis appear to behave similarly. Both have a propensity to progress rapidly and to relapse in nodal and extranodal sites. Additional cases of primary NHL of the epididymis must be studied to discern the behavior of these neoplasms.

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Table 2. Clinicopathologic Features of Patients With Lymphoma of Spermatic Cord*

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Stage</th>
<th>Histology</th>
<th>Immunophenotype</th>
<th>Therapy</th>
<th>Response</th>
<th>RFS, mo</th>
<th>Relapse Site</th>
<th>Survival, mo</th>
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</thead>
<tbody>
<tr>
<td>Case 2</td>
<td>61</td>
<td>IE</td>
<td>DLC</td>
<td>B</td>
<td>O, CT</td>
<td>CR</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ref 9</td>
<td>48</td>
<td>IV</td>
<td>CBD</td>
<td>B</td>
<td>O, CT</td>
<td>PR</td>
<td>1</td>
<td>CNS</td>
</tr>
<tr>
<td>Ref 10</td>
<td>89</td>
<td>IE</td>
<td>CBD</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>DOD, ½</td>
</tr>
<tr>
<td>Ref 11</td>
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<td>IE</td>
<td>CBD</td>
<td>NA</td>
<td>O</td>
<td>CR</td>
<td>5</td>
<td>Supravaccular fossa, liver</td>
</tr>
<tr>
<td>Ref 12</td>
<td>46</td>
<td>IE</td>
<td>CB/CC</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ref 13</td>
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<td>IE</td>
<td>LRS</td>
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<td>CR</td>
<td>6</td>
<td>Mediastinum</td>
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<tr>
<td>Ref 14</td>
<td>57</td>
<td>IE</td>
<td>CB/CC</td>
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<td>O, RT</td>
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<td>NA</td>
<td>DOD, 6</td>
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<td>Ref 15</td>
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<td>IE</td>
<td>LS</td>
<td>NA</td>
<td>O</td>
<td>CR</td>
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</tr>
<tr>
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<td>IE</td>
<td>LB</td>
<td>NA</td>
<td>O</td>
<td>PR</td>
<td>½</td>
<td>DOD, 1</td>
</tr>
<tr>
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<td>IE</td>
<td>LS</td>
<td>NA</td>
<td>O</td>
<td>CR</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>Ref 18</td>
<td>21</td>
<td>IE</td>
<td>RS</td>
<td>NA</td>
<td>O, RT</td>
<td>CR</td>
<td>7</td>
<td>Widespread</td>
</tr>
<tr>
<td>Ref 19</td>
<td>64</td>
<td>IE</td>
<td>RES</td>
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<td>O</td>
<td>CR</td>
<td>62</td>
<td>NA</td>
</tr>
<tr>
<td>Ref 20</td>
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<td>IE</td>
<td>DLC</td>
<td>B</td>
<td>O, RT CT</td>
<td>PR</td>
<td>1</td>
<td>Pelvic lymph nodes, CNS</td>
</tr>
</tbody>
</table>

* RFS, relapse-free survival; O, orchectomy; CT, chemotherapy; RT, radiotherapy; CR, complete remission; CNS, central nervous system; CBD, centroblastic diffuse; CB/CC, centroblastic/centrocytic; LB, lymphoblastic; LS, lymphosarcoma; RS, reticulosarcoma; LRS, lymphoreticulosarcoma; RES, reticuloendotheliosarcoma; DLC, diffuse large cell; NA, not available; and DOD, died of disease.

References