CASE STUDY

A Case of an Abdominal Mass: Follicular Lymphoma

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Abstract

Follicular lymphoma (FL) is the second most common subtype of non-Hodgkin lymphoma. The disease usually affects older individuals, with the average age at diagnosis being 63.5 years. Only in 4% of cases is the disease diagnosed in individuals younger than age 40 years. The case presented in this report describes the diagnosis of FL in a 38-year-old woman and highlights the variability of this disease. Tumor grading, disease staging, and the Follicular Lymphoma International Prognostic Index score can be valuable aids in prognosis. Treatment consists of close observation or radiation therapy for early-stage disease, and rituximab with combination chemotherapy regimens for more advanced disease. Cure is rare. Treatment is predominately handled by oncologists, but these patients will likely first present to their primary care physicians. Symptoms can be subtle at times, so it is essential to be able to recognize them to provide the patient with timely treatment.

Introduction

Lymphomas are divided into two general categories, Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). NHL is far more common than Hodgkin lymphoma.[1] Differences between these two major types of lymphoma can be detected by microscopy. Within these two large groups, there are a myriad of subtypes. Of instances of NHL, 22% are follicular lymphoma (FL). Diffuse large B-cell lymphoma is the most common lymphoma in the US, and FL is the second most common.[1] The mean age of persons in Sweden when their FL is diagnosed is 63.5 years, and only 4% are younger than age 40 years at time of diagnosis.[2]

Presentation varies widely among patients with FL. It can include palpable adenopathy detected by the patient or clinician during examination. Adenopathy can be present peripherally throughout the body, including in the cervical, axillary, and inguinal areas. Often adenopathy is intermittent, with waxing and waning symptoms, for unclear reasons. It can also take the form of palpable abdominal masses, which can be asymptomatic or can cause obstructive symptoms in the gastrointestinal or genitourinary tract.[3]

Systemic complaints, or B symptoms, are reported in approximately 20% of patients with FL[4] and consist of fever, unexplained weight loss, and profuse night sweats. Considering the vagueness of symptoms or the lack of symptoms altogether, the variation in patients' presentation is considerable. This can make detecting FL in the primary care setting a challenge. Because the presenting symptoms of fatigue and lymphadenopathy are so nonspecific, the diagnosis of FL is frequently delayed, and disease is usually found in multiple sites once discovered. The following case illustrates a presentation of FL in the primary care setting and the diagnostic testing that revealed its presence.

Case Report

A 38-year-old Hispanic woman presented to our clinic with pain in the center of her lower abdomen. The pain was sharp, constant, and severe and radiated to her back. Symptoms had begun three days earlier and were getting worse. She reported feeling feverish and chills intermittently during the preceding three days. She also described, on questioning, increased urinary frequency during that time. Her medical history included a previous diagnosis of Hashimoto thyroiditis and bilateral conductive hearing loss. She had three pregnancies and has two children. She had a diastasis recti separation in the abdominal wall noted after the birth of her last child. She was taking no medications regularly. She reported never smoking, never taking street drugs, and drinking alcohol sparingly. Her family history provided no additional information.

On examination, the patient was in no distress. Her temperature was 37.3°C (99.1°F); blood pressure, 101/69 mm Hg; pulse, 105 beats per minute, and respirations, 20 breaths per minute. Her height was 1.626 m (5'4"), and

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her weight was 59.603 kg (131 lb 6.4 oz). Her weight was essentially unchanged during the preceding year. There was no palpable adenopathy. Her heart rhythm was regular, and her lungs were clear. A large diastasis recti separation was felt in the center of the abdomen, which was also noted on examination two months before this visit. A large, firm, tender, mobile mass was palpated in the left lower quadrant of her abdomen.

The abdominal mass was initially thought to be an enlarged spleen, and an ultrasound was ordered. The patient's condition was diagnosed as cystitis, and she was given trimethoprim-sulfamethoxazole, 160-800 mg, as oral tablets, which she took twice daily for 10 days.

Laboratory tests were ordered. Urinalysis showed a specific gravity of 1.004. All other components of urinalysis were within normal limits. A urine culture yielded no growth. The patient's hemoglobin level was 12.3 g/dL, and her white blood cell count was 10,600 per mm^3 (10.6×10^9 per liter), with 82.2% neutrophils. Serum electrolyte, blood urea nitrogen, and creatinine levels were within normal limits. Her alanine aminotransferase and aspartate aminotransferase levels were within normal limits, as was the total bilirubin level. Findings on the mononucleosis test for heterophile antibody were negative. An abdominal ultrasound revealed a $8.4 \times 6.8 \times 7.5$ cm heterogeneous solid mass in the anterior lower left. Of note, an ultrasound of the abdomen produced unremarkable findings 7 months earlier when the patient presented with right-sided flank pain. A computed tomography (CT) scan of the abdomen and pelvis was suggested and performed with administration of oral and intravenous contrast.

CT scans showed a large, lobulated mass within the left small-bowel mesentery (Figure 1). Mesenteric vessels in the area were encased. There were several adjacent prominent lymph nodes within the mesentery of the small bowel. The state of other abdominal and pelvic organs were unremarkable, as was that of bony structures. There was no bowel obstruction. The Surgery Department recommended a CT-guided needle biopsy of the mass. This was performed, and the pathology findings were FL, grade 3. Immunohistochemistry showed a B-cell type with positive findings for cluster of differentiation (CD) 10, CD20, B-cell lymphoma 2 (BCL-2), and BCL-6.

The patient was referred to the Oncology Department. Her serum lactate dehydrogenase level was within normal limits at 132 IU/L. Positron-emission tomography (PET) scanning revealed lymphoma, and no disease was seen above the diaphragm, in the spleen, or in the bone marrow (Figure 2). Bone marrow biopsy showed no evidence of involvement by lymphoma. A multigated acquisition scan was performed, and the patient's cardiac ejection fraction was measured at 67%. She underwent six cycles of R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). A subsequent PET scan obtained 2.5 months after the first scan showed complete response of the lymphoma to therapy, with no evidence of active residual lymphoma (Figure 3). The Oncology Department continues to monitor her closely.

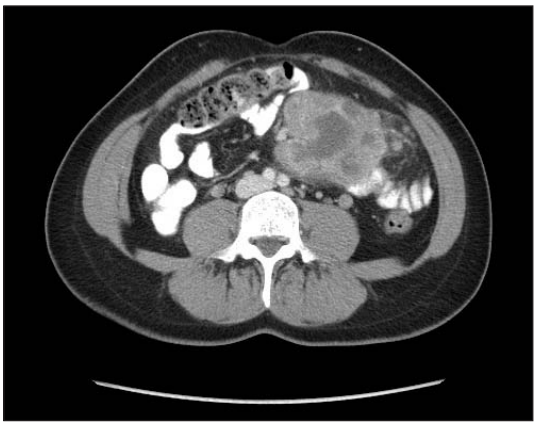

Figure 1. Cross-sectional computed tomography image of the abdomen and pelvis with oral and intravenous contrast showing a mass in the left small-bowel mesentery and several prominent lymph nodes in the adjacent small bowel.

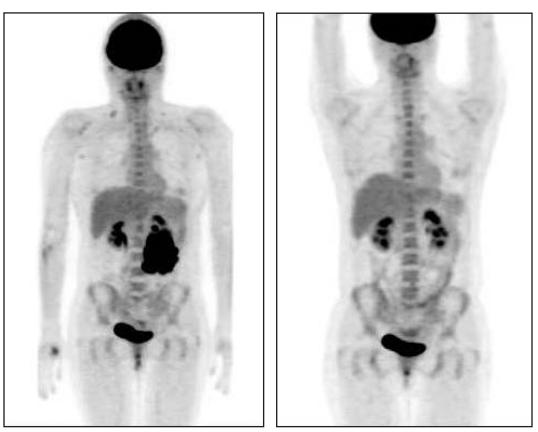

Figure 2. (left) Positron-emission tomography image obtained before treatment showing a large, lobulated lymphoma in the left abdomen.

Figure 3. (right) Positron-emission tomography image obtained after chemotherapy—2.5 months after the pretreatment image in Figure 2 (left)—showing no active residual lymphoma.

Discussion

Although the genetic hallmarks involved in FL have been extensively studied, the pathogenesis is not completely understood. In up to 90% of cases, there are breakpoint regions in chromosome 18 and reshuffled aspects of BCL-2.[5,6] A resulting translocation, t(14;18), leads to an increased expression of BCL-2, an oncogene that hastens apoptosis and leads to increased cell survival time.[7] FL develops from follicle B cells, including both centrocytes (smaller) and centroblasts (larger) types of cells.[8] Obtaining a tissue sample for histologic analysis is paramount in the diagnosis and grading of FL. Excision of an enlarged lymph node or core needle biopsy of a mass aids in the identification of FL. Fine-needle aspiration can miss the diagnosis of lymphoma and, if performed, should always be followed by a tissue biopsy.[9]

Establishing FL grade requires attention to the proportion of centroblasts present. Aggressive FL has more centroblasts, and the higher number of these cells, the higher the grade of the FL, with grade 3 being the highest assignable grade.[10] Blood tests and bone marrow analysis are also routinely done, in addition to immunohistochemistry of the biopsy sample. There is also the Follicular Lymphoma International Prognostic Index (FLIPI), which can be helpful when considering prognosis in FL. The FLIPI score can be calculated by assigning one point to each of these criteria: age >60 years, serum lactate dehydrogenase level above normal, a hemoglobin level of <12.0 g/dL, designation of stage 3 or intravenous FL, and the number of involved nodal areas >4.[11] A higher FLIPI score places the individual at higher risk of dying. A score of 0 to 1 is considered low risk, 2 is intermediate, and 3 to 5 is high risk. The patient described here had a FLIPI score of 2 (one point for the stage and the other for the number of lymph nodes involved). Staging of FL examines the number of involved lymph nodes and describes the anatomic extent of the disease.

The overall course of FL varies widely. Some patients have swift tumor growth and spread, leading to enlargement of lymph nodes and organs, causing discomfort and possibly obstruction. Others opt not to receive treatment and may live free of symptoms for years. Spontaneous regression of FL has also been observed.[12] FLIPI score and tumor grade are useful indicators for prognosis of FL and can aid in determining the course that the disease will take.

Treatment of FL is contingent on the stage of the disease. Radiation to the involved area is the treatment of choice in the early stages.[13] Stage 1 FL involves one lymph node region and potentially an extralymphatic site (stage 1E). Stage 2 has two or more lymphatic regions involved on the same side of the diaphragm and may also involve an extralymphatic site (stage 2E).[14] Radiation therapy is the treatment of choice for FL in stages 2 and 3, with 10-year survival reported to be between 60% and 80%.[15]

Chemotherapy is indicated in more advanced stages of FL. Stage 3 involves lymphatic regions on both sides of the diaphragm. Stage 3 can include involvement of the spleen (stage 3S), adjacent extralymphatic sites (stage 3E), or both (stage 3ES). Stage 4 disease involves one or more extralymphatic site(s) diffusely.[14] Treatment regimens of the more advanced stages of FL often include the monoclonal antibody agent rituximab. The use of this agent, along with combination chemotherapy, has shown to provide better control of the disease and increased survival.[16]

Understanding lymphoma as an entity can be daunting for patients. Testing, diagnosis, staging, grading, prognosis, and disease progression can be overwhelming and complicated.

Several chemotherapeutic agents are combined for the treatment of FL. The R-CVP (rituximab, cyclophosphamide, vincristine, and prednisone) combination can be used, as can this same set of medications with added doxorubicin (R-CHOP). There is no single standard of care when selecting the combinations of medications, and the treated patients comprise a heterogeneous group in which outcomes fluctuate and are complex to quantify.[17]

Patients should be monitored at regular intervals for relapse. A favorable response to treatment is initially widespread across cases of FL, but there is no cure for the disease. Relapse is common, as is the likely progression of FL.[18] It is important for patients with FL to be provided with information regarding their disease. Understanding lymphoma as an entity can be daunting for patients. Testing, diagnosis, staging, grading, prognosis, and disease progression can be overwhelming and complicated. Therefore, it is imperative that both the oncologist and those in primary care monitor for relapse and assist the patient in understanding the disease.

Conclusion

Although much of the diagnosis and treatment of FL will be carried out by oncologists, initially patients with FL will likely find themselves in the office of their primary care physician. The road that unfolds before the patient can include fear-provoking imaging, biopsies, tumor grade and immunohistochemistry assignments, staging, and treatments. Familiarity with the presenta-

tion, etiology, and treatment of FL will help clinicians better serve their patients.

The average age of patients at diagnosis of FL is 63.5 years. The case described here involves a 38-year-old woman. This disparity highlights one aspect of the variable presentation of FL. Inconsistencies also exist from individual to individual in respect to the progression and course of FL.

Treatment options and combinations for FL are many. None are curative. Patients diagnosed with FL require monitoring at regular intervals and support from both their specialists and their primary care physicians. More information for patients, their families, and their clinicians can be found at www.cancer.org, www.cancer.gov, and www.lls.org/. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Leap the Nile

When thou examinest the obstruction in his abdomen
and thou findest that he is not in a condition to leap the Nile …
say thou to him: "It is the Blood that has got itself fixed and does not circulate."

— Ebers Papyrus, *circa 1550 BC, Egyptian medical papyrus*