Case 4-2008: A 33-Year-Old Pregnant Woman with Swelling of the Left Breast and Shortness of Breath

Lawrence N. Shulman, M.D., Rachel A. Hitt, M.D., and Judith A. Ferry, M.D.

A 33-year-old pregnant woman was admitted to the hospital at 30.7 weeks’ gestation because of swelling of the left breast, shortness of breath, and tachycardia. The patient had received prenatal care at this hospital since 9.7 weeks’ gestation. The blood type was O Rh-positive and the woman was immune to rubella. Test results for hepatitis B surface antigen, chlamydia and gonorrhea infection, rapid plasma reagin, cystic fibrosis–carrier status, and fetal aneuploidy were negative, and quadruple-marker screening confirmed low risks for fetal aneuploidy and neural-tube defects. At 18.6 weeks’ gestation, ultrasonographic examination revealed normal fetal anatomy and growth. Other laboratory-test results are shown in Table 1.

Four weeks before admission, at 26.1 weeks’ gestation, the patient noted swelling of the left breast. Examination by a certified nurse practitioner revealed an approximately 2-cm area of thickening in the upper outer quadrant. Follow-up with the patient’s obstetrician was scheduled. Two weeks later, 18 days before admission, the patient returned to the prenatal clinic because of marked increase in swelling of the breast during the preceding 2 to 3 days, associated with moderate pain. She did not have fever, discharge from the nipple, or respiratory symptoms. An area of fullness, 6 cm by 8 cm, was palpated in the upper outer quadrant of the left breast. Ultrasonography of the breast performed the next day revealed edema with mild skin thickening; increased blood flow was seen on color Doppler imaging. Mammography showed enlargement of the left breast in comparison with the right, diffusely increased tissue density and heterogeneity, and no suspicious microcalcifications, masses, or architectural distortions.

The patient was referred to a breast surgeon later that day. She described pain and heaviness of the left breast, for which she wore a brassiere 24 hours a day. On examination by the surgeon, there was no supraclavicular or axillary lymphadenopathy; the left breast was larger than the right, with slight erythema in the dependent portion, but no discrete mass. Cephalexin and oxycodone were prescribed. Three days later, at a prenatal clinic follow-up, the patient reported that the pain and swelling were the same or were reduced slightly. The left breast was...
unchanged in size. Laboratory tests were performed, and results are shown in Table 1. A specimen of blood was sent for laboratory culture, and the results were negative. The patient was referred to the breast clinic the same day; however, she left without being seen.

One week before admission, she returned for follow-up in the prenatal clinic. She was anxious and expressed concern about a possible diagnosis of cancer. On examination, the fetus was active; there was an ecchymosis overlying the swelling in the left breast. The patient was counseled

### Table 1. Results of Hematologic and Serum Chemistry Tests.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range, Adults†</th>
<th>5 Mo before Admission</th>
<th>2 Wk before Admission</th>
<th>On Admission</th>
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</thead>
<tbody>
<tr>
<td>Hematocrit (%)</td>
<td>36.0–46.0 for women</td>
<td>31.7</td>
<td>30.7</td>
<td>30.9</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.0–16.0 for women</td>
<td>10.7</td>
<td>10.3</td>
<td>10.6</td>
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<tr>
<td>White-cell count (per mm³)</td>
<td>4500–11,000</td>
<td>12,600</td>
<td>12,600</td>
<td>13,300</td>
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<tr>
<td>Differential count (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>40–70</td>
<td></td>
<td></td>
<td>89</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>22–44</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Monocytes</td>
<td>4–11</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0–8</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Platelet count (per mm³)</td>
<td>150,000–350,000</td>
<td>313,000</td>
<td>421,000</td>
<td>517,000</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>11.1–13.6</td>
<td></td>
<td></td>
<td>12.4</td>
</tr>
<tr>
<td>Prothrombin time (international normalized ratios)</td>
<td></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Partial-thromboplastin time (sec)</td>
<td>22.1–34.0</td>
<td></td>
<td></td>
<td>29.6</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (mm/hr)</td>
<td>1–25</td>
<td></td>
<td></td>
<td>131</td>
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<tr>
<td>Glucose (mg/dl)</td>
<td>70–110</td>
<td>104 (fasting)</td>
<td>106</td>
<td></td>
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<tr>
<td>Creatinine (mg/dl)</td>
<td>0.6–1.5</td>
<td></td>
<td></td>
<td>0.5</td>
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<tr>
<td>Bilirubin (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.0–1.0</td>
<td></td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Direct</td>
<td>0.0–0.4</td>
<td></td>
<td></td>
<td>0.2</td>
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<tr>
<td>Protein (g/dl)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>6.0–8.3</td>
<td></td>
<td></td>
<td>7.8</td>
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<tr>
<td>Albumin</td>
<td>3.3–5.0</td>
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<td></td>
<td>2.3</td>
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<tr>
<td>Globulin</td>
<td>2.6–4.1</td>
<td></td>
<td></td>
<td>5.5</td>
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<tr>
<td>Magnesium (mmol/liter)</td>
<td>0.7–1.0</td>
<td></td>
<td></td>
<td>0.6</td>
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<tr>
<td>Calcium (mg/dl)</td>
<td>8.5–10.5</td>
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<td></td>
<td>9.1</td>
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<tr>
<td>Alkaline phosphatase (U/liter)</td>
<td>30–100</td>
<td></td>
<td></td>
<td>192</td>
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<tr>
<td>Aspartate aminotransferase (U/liter)</td>
<td>9–32</td>
<td></td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/liter)</td>
<td>7–30</td>
<td></td>
<td></td>
<td>9</td>
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<td>Lactate dehydrogenase (U/liter)</td>
<td>110–210</td>
<td></td>
<td></td>
<td>1259</td>
</tr>
<tr>
<td>Troponin T (ng/ml)</td>
<td>0.00–0.09</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
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</table>

*To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for magnesium to milliequivalents per liter, multiply by 2. To convert the values for calcium to millimoles per liter, multiply by 0.250.

†Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. These ranges may therefore not be appropriate for all patients.
regarding the importance of a tissue diagnosis. Three days later, a core biopsy of the left breast was performed under ultrasonographic guidance. Over the course of the next 4 days, a nonproductive cough, shortness of breath with exertion, orthopnea, and swelling and tenderness of the right breast developed. The patient attributed the respiratory symptoms to allergies and self-administered loratadine; the symptoms did not improve, and she returned to the prenatal clinic.

She had not had fever, chills, dysuria, hematuria, or hematochezia, and fetal movements had been normal. On physical examination at this visit the blood pressure was 110/70 mm Hg, the pulse 156 beats per minute, and the oxygen saturation 99% while the patient was breathing ambient air. She was admitted to the hospital.

This was the patient’s second pregnancy. She had delivered her firstborn at full term by cesarean section because of breech presentation, without complications. Papanicolaou smears of the cervix had shown atypical squamous cells of undetermined significance, without evidence of human papillomavirus, on two occasions in the past year. She had anemia and sciatica with this pregnancy. She was allergic to penicillin. Medications included iron supplements, multiple vitamins with folate, and oxycodone. The patient was married and lived with her husband and child. She did not smoke or drink alcohol. Her father had coronary atherosclerosis and hypertension, two cousins had cystic fibrosis, and her mother, sibling, and child were healthy. There was no family history of cancer.

On examination, the patient appeared anxious. The temperature was 37.9°C, the pulse 157 beats per minute, and the blood pressure 137/80 mm Hg; the respirations were 22 breaths per minute, and the oxygen saturation was 98% while the patient was breathing ambient air. There was an anterior cervical lymph node 5 mm in diameter and no other signs of lymphadenopathy. The left jugular vein was distended nearly to the angle of the jaw. Both breasts were mildly tender, markedly enlarged, and firm, the left more so than the right. Ecchymoses were present in the upper outer quadrant of the left breast; there was no increased warmth, stippling, or retraction of the skin. The uterus was of appropriate size for gestational date, and the remainder of the examination was normal.

Results of laboratory tests are shown in Table 1. Electrocardiography showed sinus tachycardia. A contrast-enhanced computed tomographic (CT) angiogram of the chest performed to evaluate for pulmonary emboli showed no evidence of pulmonary embolus. A large anterior mediastinal mass, 5.1 cm by 13.7 cm, extended from the superior mediastinum along the right heart border to the level of the diaphragm. It encased and compressed adjacent vasculature, without obstruction. There was a right paracardiac lymph node, 2.0 cm by 2.5 cm, and a left axillary lymph node 1.6 cm in diameter. The breasts were asymmetric, the left larger than the right. There were no pulmonary nodules or consolidation, and the visualized portions of the upper abdomen were normal.

A test result was received.

**DIFFERENTIAL DIAGNOSIS**

**Dr. Lawrence N. Shulman:** This case calls for two differential diagnoses: causes of breast enlargement in pregnancy and causes of a mediastinal mass. May we see the breast images?

**Dr. Rachel A. Hitt:** Mediolateral-oblique projections of both breasts demonstrated asymmetry, with the left breast larger than the right. In addition, radiography revealed greater tissue density on the left breast than on the right (Fig. 1A). No mass, architectural distortion, or clusters of suspicious microcalcification were noted. Ultrasonography was performed in the region of clinical concern in the left upper central to outer breast. This showed diffuse heterogeneity of the underlying breast tissue with associated mild skin thickening (Fig. 1B). There was an increase in Doppler flow, consistent with increased vascularity (Fig. 1C).

**BREAST ENLARGEMENT IN PREGNANCY**

**Dr. Shulman:** I will begin with a discussion of the differential diagnosis of a pregnant patient with a swollen breast.

**MASTITIS**

The diagnosis of mastitis was initially considered, and antibiotics were given. Mastitis is sometimes associated with systemic signs of infection, which did not appear to be present in this patient. There was some improvement, which could possibly be
attributed to the antibiotics, but clearly the breast did not return to a state that was normal for pregnancy. Thus, mastitis is unlikely.

**Breast Cancer**

Breast cancer is a concern in this patient; about 1 to 2% of all cases occur during pregnancy. There are no data that suggest pregnancy causes breast cancer, and in fact, breast cancer is statistically more likely to develop in nulliparous than in parous women. Detection of a breast cancer on both physical examination and radiologic studies during pregnancy is challenging. The breasts become engorged and thus difficult to examine. When breast cancer is present, the breasts may become generally enlarged without palpable discrete masses. Imaging can be difficult to interpret because of the normal increase in density of the breast. Breast cancer in a pregnant patient is likely to be diagnosed at a more advanced stage than breast cancer in a patient who is not pregnant. Some breast cancers that are detected during pregnancy are estrogen-receptor positive; what role endogenous hormones play in the stimulation of the growth of these breast cancers is uncertain, but they may have an adverse effect on outcome in some patients. This patient’s presentation is consistent with a diagnosis of breast cancer arising in pregnancy.

**Venous Obstruction**

The breast was diffusely enlarged without dominant masses or architectural distortion, and ultrasonography showed increased blood flow on color Doppler imaging. I wondered whether obstruction of venous flow in the left chest and neck, possibly at the level of the innominate vein, could have produced passive congestion and swelling of the breast.

**Differential Diagnosis of a Mediastinal Mass**

Shortly before admission, shortness of breath and tachycardia developed. The serum lactate dehydrogenase level was elevated at 1259 U per liter. The presence of unilateral jugular venous distention raised the possibility of venous obstruction above the superior vena cava. Both breasts were mildly tender and markedly enlarged. Could we review the imaging studies?

*Dr. Hitt:* On admission, a contrast-enhanced chest CT showed a large anterior mediastinal soft-tissue mass (Fig. 2A), with compression but without obstruction of the great vessels. There was bilateral breast enlargement, more in the left breast than in the right. A reformatted coronal
contrast-enhanced chest CT (Fig. 2B) showed that the mediastinal mass extended from the superior mediastinum, along the right border of the heart to the level of the diaphragm. There was left axillary lymphadenopathy and collateral circulation within the left superior mediastinum.

**LYMPHOMAS INVOLVING THE MEDIASTINUM**

Lymphomas are the most likely cause of an anterior mediastinal mass. Mediastinal germ-cell tumors can occur in the anterior mediastinum, but almost exclusively in males. Hodgkin's lymphoma of the nodular-sclerosis type typically occurs as a mediastinal mass in women the age of this patient or younger, but it is often less extensive than what we see with this patient, and vascular compromise is relatively uncommon. Precursor T-cell lymphoblastic lymphoma typically occurs as a mediastinal mass, often with superior vena caval obstruction and pleural or pericardial effusions. However, this type of lymphoma is predominantly a disease of adolescent and young-adult men and is often associated with T-cell acute lymphoblastic leukemia. This patient has a normal platelet count and no abnormal circulating lymphoid cells, which argues against T-cell acute lymphoblastic leukemia.

Primary mediastinal large-B-cell lymphoma often manifests as bulky disease, with masses greater than 10 cm in diameter in 75% of patients. The majority of patients are between the ages of 20 and 50 years, as this patient is, with a slight female preponderance. Patients typically present with a large anterior superior mediastinal mass, often with extensive invasion of local structures within the chest, including the pleura, pericardium, chest wall, and lung parenchyma. Extrathoracic disease can be present, but involvement of lymph nodes and bone marrow is uncommon. Finally, diffuse large-B-cell lymphoma of the systemic type may involve mediastinal lymph nodes as well as extramediastinal nodes and extranodal sites. This patient's markedly elevated serum lactate dehydrogenase level is consistent with a diagnosis of advanced large-cell lymphoma, T-cell lymphoblastic leukemia, or advanced germ-cell tumor, and less consistent with a diagnosis of Hodgkin's disease.

If the mediastinal mass is lymphoma, does the patient have lymphomatous involvement of the breast or does she have both breast cancer and lymphoma?

**LYMPHOMAS INVOLVING THE BREAST**

Lymphomas that involve the breast can occur in one of three patterns. In primary lymphoma...
of the breast, the lymphoma is confined to the breast. The most common type is diffuse large-B-cell lymphoma, although Burkitt’s lymphoma, follicular lymphoma, and marginal-zone B-cell lymphoma of mucosa-associated lymphoid tissue may also occur. Breast involvement by lymphoma can be part of either an initial presentation of systemic lymphoma or a late manifestation in a patient with advanced lymphoma; this phenomenon is referred to as secondary breast lymphoma. The most common lymphoma to involve the breast secondarily is diffuse large-B-cell lymphoma. Burkitt’s lymphoma involving the breast, the ovaries, or both has been reported to occur in pregnant patients, and may involve both breasts.\textsuperscript{21,22}

A patient with primary breast lymphoma usually presents with a mass, which is identified by means of physical examination or screening mammography. The mammographic appearance is usually a mass, with or without spiculation.\textsuperscript{23} Diffuse involvement of the breast, as seen in this case, is more common with aggressive lymphomas than with indolent lymphomas.\textsuperscript{23}

**LYMPHOMAS IN PREGNANCY**

There is some literature on the association of pregnancy and lymphomas, including both Hodgkin’s lymphoma and non-Hodgkin’s lymphomas, particularly Burkitt’s lymphoma.\textsuperscript{21,22,24-27} Both Hodgkin’s and non-Hodgkin’s lymphomas occur in young women and may coincide with pregnancy. An immunosuppressive state of pregnancy predisposing to the development of lymphomas and a role for pregnancy hormones in escalating the risk have both been postulated, but without substantiation.

**MANAGEMENT OF LYMPHOMAS IN PREGNANCY**

If this patient has diffuse large-B-cell lymphoma, she has a potentially curable illness. Management of this disorder in pregnancy depends on the time in pregnancy at which it occurs. In the first trimester, the fetus is particularly sensitive to the effects of both chemotherapy and radiation, and treatment will usually result in intrauterine fetal death. However, a 3-to-6-month delay in treatment poses an unacceptable risk to the mother. Thus, termination of pregnancy is typically considered. Presentation during the second trimester in some ways poses the most difficult choices. There may still be a long period of time before the fetus can be delivered safely, and treatment effects on the fetus at this stage are not well understood.

When lymphoma is discovered during the third trimester, as in this case, there are at least three options: immediate delivery of the fetus, delaying all therapy until after delivery; treatment with corticosteroids until delivery, followed by definitive therapy after delivery; and initiating definitive therapy during pregnancy. These decisions need to be made in conjunction with the high-risk obstetrics team, the patient, and her family and will depend on the degree of fetal maturity and the extent of the maternal lymphoma.

If the patient is medically stable and there is no evidence of critical organ compromise, I favor treatment with corticosteroids, which have the potential to shrink lymphomas rapidly and also accelerate fetal-lung maturation. Localized radiation therapy has also been used in the past but is rarely used now.\textsuperscript{26} If corticosteroids are ineffective, definitive systemic chemotherapy can be initiated. The ideal treatment for advanced B-cell lymphoma is the combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Clinical experience with chemotherapy in the later stages of pregnancy is limited but suggests that the four latter agents can be safely administered.\textsuperscript{28-31} There is less experience with rituximab.

**TREATMENT FOR THIS PATIENT**

This patient was nearly at 31 weeks’ gestation, with tachycardia and shortness of breath, although her oxygen saturation was normal. The mass in this case extended along the right border of the heart, and supraventricular tachycardia could have been the result of pericardial irritation from an overlying tumor. On electrocardiography, sinus tachycardia was detected, which can be caused by compromise of venous return to the heart, the superior vena cava syndrome, or compression of the right atrium or right ventricle or both. Echocardiography should be performed.

If her cardiac status is stable, I might favor beginning treatment with corticosteroids and working with the obstetricians on the high-risk team to determine a safe time for delivery of the fetus. If corticosteroids are not effective, and if the fetus could not be safely delivered, then I would favor treatment with CHOP without rituximab. If definitive therapy is delayed until after delivery, the medical oncologists caring for the patient should be cognizant of the reduction in the glomerular filtration rate in the hours and days after delivery, which occurs as a physiolog-
ic phenomenon and may affect the recommended doses of chemotherapy drugs.

In conclusion, I believe this patient has diffuse large-B-cell lymphoma involving the mediastinum, left breast, and possibly the right breast. Burkitt’s lymphoma is a less likely diagnosis; although it can occur during pregnancy and involve both breasts, the mediastinal involvement in this case is not typical. Burkitt’s lymphoma might have grown more quickly during the weeks when the patient was under observation. I predict that the result of the core biopsy of the left breast, which was received around the time of admission, demonstrated large-B-cell lymphoma.

Dr. Nancy Lee Harris (Pathology): Dr. Specht and Dr. Greene, would you like to comment?

Dr. Michelle Specht (Surgical Oncology): When I initially saw this patient in the breast clinic, I was concerned about an inflammatory breast cancer. I told her, “We need to think about a biopsy,” and I think I scared her, because she didn’t come back right away. When she did return, I was somewhat reassured by the presence of fullness in the contralateral breast and thought perhaps that the process might all be pregnancy-related hyperstimulation. I requested a biopsy guided by ultrasonography, because of the high vascularity of the left breast. On the night the patient was admitted to the hospital, the pathologist called with the results of the biopsy interpretation.

Dr. Michael Greene (Obstetrics and Gynecology): When the patient was admitted, my differential diagnosis, which was based on the physical examination and the history, was either inflammatory carcinoma of the breast or lymphoma. We were very concerned about her shortness of breath and tachycardia and obtained radiologic studies to rule out a pulmonary embolus; this disclosed the large mediastinal mass, making the diagnosis of lymphoma most likely.

CLINICAL DIAGNOSIS

Lymphoma involving the mediastinum and breasts.

DR. LAWRENCE N. SHULMAN’S DIAGNOSIS

Diffuse large-B-cell lymphoma involving the mediastinum, left breast, and possibly the right breast.

PATHOLOGICAL DISCUSSION

Dr. Judith A. Ferry: The core-biopsy specimen of the left breast contained a diffuse infiltrate of cells with round nuclei of the same size as the breast epithelial cells, vesicular chromatin, prominent nucleoli, and pale cytoplasm (Fig. 3A). The tumor...
cells expressed the B-cell antigen CD20 (Fig. 3B) and the germinal-center marker Bcl-6 and were negative for cytokeratins, CD10, Bcl-2, CD30, anaplastic lymphoma kinase (ALK), histiocytic and T-cell antigens, and the Epstein–Barr virus. We also found that 80 to 90% of the cells were positive for Ki-67, a marker of proliferation. The cytologic and immunophenotypic features are not consistent with a diagnosis of Burkitt’s lymphoma and are diagnostic of diffuse large-B-cell lymphoma.

Dr. Lynne Bartholomew Goltra (Obstetrics and Gynecology): The results of an echocardiogram performed the next day were normal. Because of the patient’s orthopnea, the head of the bed was elevated by 30 degrees, and she was able to tolerate an epidural injection of anesthesia. An uncomplicated cesarean delivery on the third hospital day produced a live-born, male infant weighing 2.17 kg and with a 1-minute Apgar score of 5 and 5-minute Apgar score of 7. After the infant was delivered, we inspected the adnexa. The right ovary was normal, but the left ovary contained a mass, 8 cm by 10 cm, that was suspicious for lymphoma. In consultation with Dr. Neil Horowitz of gynecologic oncology, we informed the patient that although the ovarian lymphoma would probably regress with chemotherapy, we recommended proceeding with delivery.
therapy, there was an increased risk for ovarian torsion in the interim. Because of this, we recommended removal of her left ovary. The patient agreed, and we proceeded with an uncomplicated left salpingo-oophorectomy.

Dr. Ferry: There was a left ovarian mass, weighing 300 g (Fig. 4A). Microscopical examination revealed diffuse large-B-cell lymphoma, identical to that of the biopsy specimen from the breast (Fig. 4B).

The combination of pathologic and radiographic features and the pattern of spread are most consistent with a diagnosis of primary mediastinal (thymic) large-B-cell lymphoma. This lymphoma has clinical and pathologic features that distinguish it from other large-B-cell lymphomas. The normal counterpart is believed to be a B cell typically found in small numbers in the thymic medulla. When this type of lymphoma spreads beyond the thorax, it often involves unusual extranodal sites, including the gastrointestinal tract, kidney, ovary, adrenal gland, and central nervous system; there are reports of involvement of the breast.

Neoplastic cells typically lack surface immunoglobulin; some cells express CD30, as do cells in Hodgkin's lymphoma. The gene-expression profile is distinct from that of other diffuse large-B-cell lymphomas and similar to that of Hodgkin's lymphoma, with activation of the nuclear factor-κB and the Janus kinase–signal transducer and activator of transcription signaling pathways. Recently, cocexpression of both nuclear c-rel and tumor necrosis factor receptor–associated factor (TRAF), indicating activation of the nuclear factor-κB pathway, was shown to be diagnostic of mediastinal large-B-cell lymphoma, occurring in 50% of cases. Dr. Jeffery Kutok (Brigham and Women's Hospital) performed immunostaining in this case for c-rel and TRAF-1. Nuclear c-rel expression (Fig. 4C) was present, but TRAF-1 was absent.

Cytogenetic analysis revealed a strikingly abnormal karyotype, with 53 to 56 chromosomes found in different metaphases (Fig. 4D). The most conspicuous abnormality involved chromosome X, including three excess copies and five copies of an isochromosome of the long arm. In mediastinal large-B-cell lymphoma, chromosome gains are much more common than losses and involve chromosomes 2, 9p, 12q, and the long arm of chromosome X, as in this case. There was a possible abnormality at 3q27, the location of the Bcl-6 gene, and fluorescence in situ hybridization analysis of the Bcl-6 gene disclosed a rearrangement with an unknown partner. Bcl-6 rearrangement is rare but has been described in mediastinal large-B-cell lymphoma.

Dr. Harris: Dr. Hochberg, can you give us follow-up on this patient?

Dr. Ephraim Hochberg (Hematology/Oncology): R-CHOP chemotherapy was started after delivery. Radiologic and clinical evaluation confirmed that the lymphoma responded rapidly to the first cycle of chemotherapy. We recommended prophylaxis treatment to the central nervous system, because breast involvement, elevated lactate dehydrogenase levels, and the presence of multiple extranodal sites of disease all suggested a high risk of involvement of the central nervous system; the patient received high-dose methotrex-
ate therapy. She saw Dr. Peter Mauch of radiation oncology at the Dana–Farber Cancer Institute for consultation regarding radiation to the mediastinal mass; he thought that there was no role for radiotherapy in view of the initial advanced stage and the complete response to chemotherapy. Sixteen months after the diagnosis, the patient is in complete remission. There is a 65 to 70% chance of cure for this patient’s cancer. The baby is well.

Dr. Hitt: The positron-emission tomographic (PET) CT scan obtained at the time of initial diagnosis showed diffuse uptake of the radiotracer 18F-fluorodeoxyglucose in both breasts and in the anterior mediastinal soft-tissue mass (Fig. 5A). A post-treatment PET–CT scan demonstrated a decrease in radiotracer uptake and shows diffuse, irregular heterogeneity of the breast tissue (Fig. 5B).

**ANATOMICAL DIAGNOSIS**

Diffuse large-B-cell lymphoma, consistent with primary mediastinal large-B-cell lymphoma, with involvement of breast and ovary.

No potential conflict of interest relevant to this article was reported.

**REFERENCES**

29. Lipshultz SE, Lipsitz SR, Mone SM, et al. Female sex and higher drug dose as risk factors for late cardiotoxic effects of

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