

# Hodgkin's lymphoma during pregnancy

A 34-year-old woman presented to her primary care physician with a chief complaint of a "neck lump" of 1-month duration, accompanied by night sweats, chills, and heart palpitations for several weeks prior to presentation. Two somewhat tender supraclavicular lymph nodes were found on physical exam, and CT scan of her neck showed two adjacent lymph nodes (12 × 12 mm and 9 × 9 mm) at the base of the posterior triangle on the left side. Superior mediastinal, para-aortic, precaval, and right cervical adenopathy was also reported on the study. Biopsy of a presenting lymph node showed only lymph node hyperplasia on pathology. She denied B symptoms, and her only other complaint was a 2-week history of a rash accompanied by pruritus. For 1 year after her initial presentation, her adenopathy waxed and waned.

Several months after her initial presentation, the patient became pregnant with twins after undergoing fertility treatment. She was referred to an oncologist for significantly enlarged right cervical lymph nodes and a left axillary lymph node that were now causing her pain. At 27 weeks' gestation, her white blood cell count was 17,500/μL, composed of 83% neutrophils. New-onset anemia and thrombocytosis also found at this time may have been caused by her pregnancy. Erythrocyte sedimentation rate and lactate dehydrogenase level were elevated, at 69 mm/hr and 172 U/L, respectively. At 28 weeks' gestation, the patient was seen in the oncology clinic.

## Diagnosis

A repeat lymph node biopsy of a

supraclavicular lymph node revealed Hodgkin's lymphoma (HL), nodular sclerosis type (Figure 1). The patient's staging workup included an MRI of the chest, abdomen, and pelvis that showed extensive bilateral supraclavicular, axillary, paratracheal, and mediastinal lymphadenopathy, with no lymphadenopathy found below the diaphragm (Figure 2). Her limited staging workup was consistent with stage IIA HL.

## Prevalence

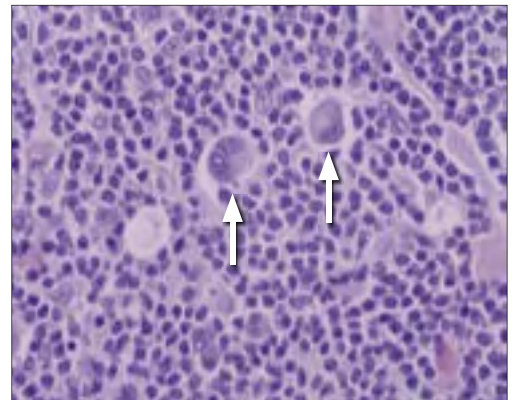
HL is not an uncommon malignancy during pregnancy. With its bimodal peak of incidence, women are affected during their reproductive years. The incidence of HL during pregnancy is 1:1,000–1:6,000 deliveries, with the peak incidence occurring at approximately age 20.<sup>1</sup> In women 15–24 years of age, HL is the most frequent malignant tumor encountered, accounting for 51% of the hematologic malignancies complicating pregnancy.<sup>2</sup> Single women have higher rates of the disease than married women, as do women with lower parity or late age at first full-term pregnancy.<sup>3,4</sup> Many studies suggest that HL presents with typical manifestations in the pregnant woman and does not have significant effect on pregnancy.<sup>1,5</sup> Pregnancy also does not seem to affect the stage of disease at presentation, the response to therapy, or the overall survival rate from HL.<sup>2</sup>

## Treatment

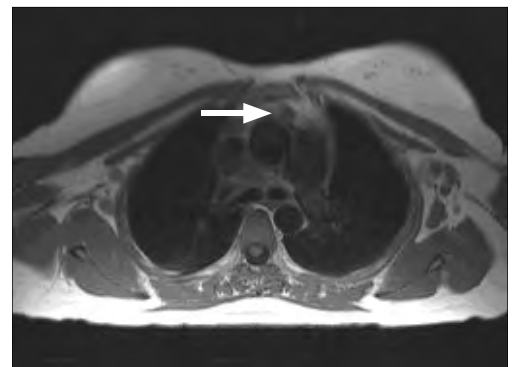
Regardless of the stage and the histology of disease, the risks and benefits of treatment in the prepartum period must be evaluated on a case-by-case basis. Chemotherapy for HL diagnosed in pregnancy is not a standard of care. Treating a patient during preg-

nancy may result in inadequate and incomplete treatment, whereas waiting until the end of pregnancy runs the risk of extension of the disease beyond curative treatment.<sup>6</sup>

Studies have shown<sup>1,3,7–10</sup> the adverse effects of chemotherapy when given during organogenesis, and it is generally acceptable to delay chemotherapeutic and radiation treatment during this time in gestation, except for in symptomatic, advanced-stage disease. Treatment during pregnancy is not recommended in the first trimester due to organogenesis and resultant



**FIGURE 1** Two lacunar-type Reed-Sternberg cells (arrows) characteristic of Hodgkin's lymphoma, nodular sclerosis type. Hematoxylin and eosin stain.



**FIGURE 2** MRI scan performed while the patient was pregnant. Note the large prevascular nodule (arrow). Axial spin-echo T1-weighted sequence.

malformation of the fetus. The pregnancy could be terminated, but therapy can be delayed until the fetus is safely delivered. During the third trimester of pregnancy, most patients can delay treatment and proceed to an early, safe delivery. For asymptomatic patients with nonbulky disease, observation may be appropriate, whereas for symptomatic patients with bulky disease, immediate therapy may be indicated. Symptoms and rapidity of growth, not bulky disease, are indications that the patient may need treatment.

Initiation of chemotherapy in the second and third trimesters of gestation remains controversial. Women who present with favorable histologic characteristics and early-stage disease can be followed carefully and chemotherapy delayed until after delivery. Lymphocyte-predominant and nodular sclerosis disease often presents at early stages, whereas mixed-cellularity and lymphocyte-depleted disease are seen more commonly in advanced stages.<sup>11</sup> Although patients with advanced favorable disease (based on the International Prognostic Index; with zero to three adverse risk factors) have a 60%–80% freedom from disease progression at 5 years with first-line chemotherapy,<sup>12</sup> patients at the very highest risk with advanced unfavorable disease (four to seven adverse factors) still showed a 42%–52% freedom from disease progression at 5 years with first-line therapy.<sup>12</sup>

Although the increased risk of spontaneous abortion, fetal death, and major malformations is well documented in fetuses exposed to chemotherapy in the first trimester,<sup>1,3,7–10</sup> exposure to chemotherapy during the second and third trimesters has less drastic but significant adverse effects. Intrauterine growth restriction and low birth weight have been observed after exposure to chemotherapy during the second and third trimesters, which may be contributed to by maternal nutritional deficiencies from the tumor or chemotherapy-induced

anorexia.<sup>7</sup> Dilutional and iron-deficiency anemia found during pregnancy combined with cytotoxic effects of chemotherapy may increase the risk of anemia.<sup>7</sup> Conversely, studies with long-term follow-up have not shown hematologic or immunologic abnormalities or impairments in learning behavior of children exposed to chemotherapy in the womb.<sup>5,7,8,13</sup>

Drugs with low molecular weight, high lipid solubility, and loose binding to plasma proteins promote transfer of drugs from mother to fetus.<sup>7</sup> Vinca alkaloids, which are highly protein bound; anthracyclines, which are high molecular weight agents; and corticosteroids have been found to have the least adverse effects on the fetus; alkylating agents and methotrexate have been shown to be the most teratogenic drugs commonly used in the treatment of lymphoma.<sup>1,7,8</sup> Steroids have an added advantage of hastening lung maturation in the fetus in preparation for an early delivery.

For the symptomatic patient with advanced-stage disease who requires treatment, vinblastine alone has not been found to cause fetal abnormalities in the second half of pregnancy.<sup>14</sup> Other multidrug regimens have not been reported to cause congenital malformations when given in the second or third trimester, after completion of organogenesis.<sup>10,14</sup> Treatment with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) has been reported to be relatively safe during pregnancy.<sup>7</sup> This regimen is also preferable for its low gonadotoxic effect, with less than 5% of patients experiencing amenorrhea, and hence is the treatment of choice for women who want to preserve fertility.<sup>3</sup> However, it is recommended that pregnancy be prevented for 2 years after complete remission due to the risk of relapse during this period.<sup>3</sup>

Gelb et al<sup>15</sup> reported their experience with 17 cases of HL diagnosed in pregnancy. Of them, 13 patients were diagnosed with nodular-scle-

rosis disease. Most presented with stages II–III disease, and the average duration of gestation at diagnosis was 22 weeks. Of 17 patients with HL, 10 received chemotherapy, and 8 of the 10 had mediastinal adenopathy. Most patients deferred therapy until after delivery and had no evidence of disease at the last follow-up visit, except for one death, which was not attributed to the disease. One patient had a spontaneous abortion before receiving chemotherapy, and one patient who received chemotherapy was found to have recurrent disease at 6-month follow-up. No congenital anomalies were found at delivery, and 88% of patients achieved a complete response to therapy.

### Patient outcome

Besides pruritus and painful adenopathy, our patient did not display any clinical signs of an aggressive disease course—no B symptoms, shortness of breath, chest pain, or systemic infection. Because she presented at 28 weeks' gestation and planned to deliver at 34 weeks' gestation, the risks and benefits of waiting 6 weeks to begin treatment of her lymphoma were evaluated. The results of her MRI placed her lymphoma at an early stage, and her nodular sclerosis histology was also favorable. Due to the stable nature of her disease, it was not believed that initiating chemotherapy before delivery was necessary, as a delay in therapy would not have a significant impact on her overall survival. After discussing these risks and benefits with the patient, she opted to delay treatment initiation until after delivery and completion of disease staging. She continued to have a normal gestation through her third trimester.

The patient underwent elective cesarean section at 34 weeks' gestation, delivering two healthy male babies. She was then able to complete staging of her lymphoma with a PET/CT scan, which revealed bulky bilateral cervical, supraclavicular, subclavicular, axillary,

and anterior mediastinal lymphadenopathy, demonstrating hypermetabolic activity consistent with stage II HL. ABVD chemotherapy was begun 2 weeks after delivery, and a total of 4 cycles were given over 13 weeks. A repeat PET/CT scan performed 1 week after completion of chemotherapy showed resolution of disease. One month after her repeat imaging, the patient began a 3-week course of mantle-field radiation therapy, with a total of 30.6 Gy delivered. She did well clinically, with minimal side effects from her treatment; all follow-up examinations and imaging studies have revealed no evidence of recurrent disease during the 12 months after completion of treatment.

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