

## Hodgkin's Disease in Pregnancy

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**Key words:** Hodgkin's disease, pregnancy, chemotherapy, in vitro fertilization, abortion

*IMAJ 2004;6:502-503*

Hodgkin's disease during pregnancy poses a therapeutic as well as ethical dilemma. We present a case and brief review of the literature, and discuss the steps taken in decision-making.

### Patient Description

A 26 year old pregnant woman was admitted to the emergency room with a non-tender cervical mass in the left posterior triangle that appeared 2 weeks before admission. Despite an initial antibiotic therapy trial, this mass rapidly progressed to involve the left anterior triangle. There was no history of fever, night sweats, pruritis, weight loss or rash. The patient did not have a history of past exposure to animals or birds and had not traveled in a suspicious endemic area. On presentation, she was in the 23rd week of her first pregnancy, following 2 years of in vitro fertilization trials due to infertility.

On physical examination, she was in good general condition, afebrile, anicteric and without dyspnea. Blood pressure was 105/70 mmHg, heart rate 78/min and respiratory rate 14/min. A supraclavicular, non-tender and mobile left cervical mass of 2 x 2 cm was observed. In the left anterior

triangle a non-tender, fixed mass of 5 x 4 cm was also found, and small submandibular nodes 2 x 2 cm were palpable. The rest of the physical examination did not yield any other gross pathologic findings.

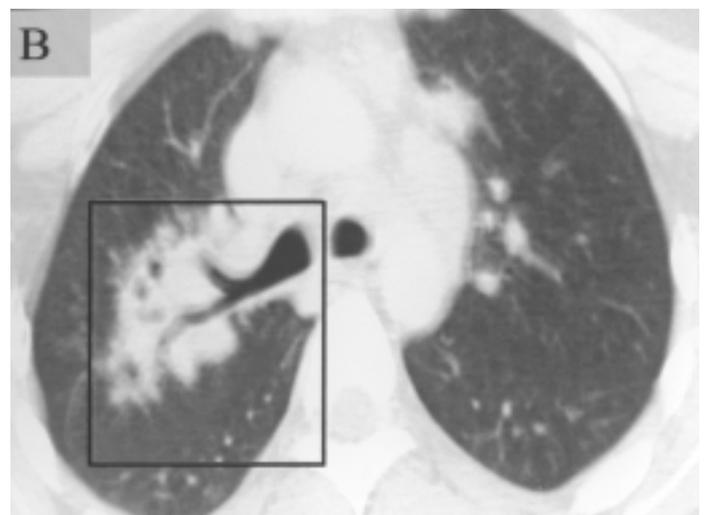
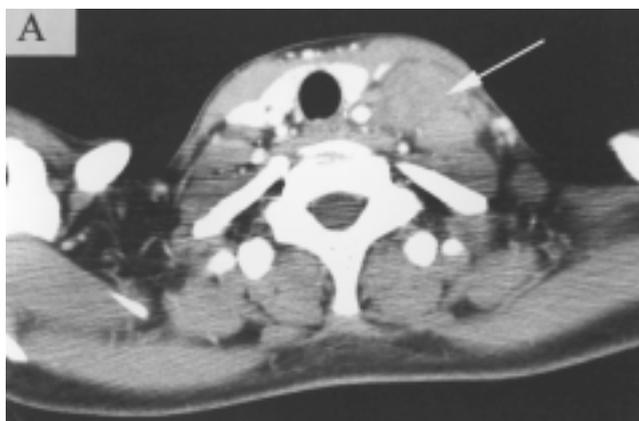
Laboratory evaluation showed a white blood cell count of  $14,200 \times 10^9/L$ , 82% of which were granulocytes and 13.5% lymphocytes. Plasma hemoglobin concentration was 13.5 g/dl and the platelet count  $236,000 \times 10^9/L$ . The erythrocyte sedimentation rate was 20 in the first hour. Serum albumin level was 3.4 g/dl, while electrolytes, lactate dehydrogenase, renal and liver function tests were within normal limits. Cervical sonogram and computed tomography revealed cervical lymphadenopathy with an incomplete non-thrombosed occlusion of the left jugular vein [Figure A]. Mediastinal lymph node enlargement with a suspected right lung infiltration was also noted [Figure B]. Abdominal ultrasound was interpreted as normal. Fine needle biopsy and open biopsy of the posterior cervical node showed nodular sclerosis compatible with Hodgkin's lymphoma. No evidence of bone marrow involvement was found on biopsy.

In light of the rapidly progressive course

of the disease, accompanied by malignant signs already at the initial presentation, accurate clinical staging and treatment in accordance seemed pressing. Termination of the pregnancy was contemplated in order to offer the patient suitable staging modalities and initiate an aggressive treatment protocol, thus providing the patient with the best chance of cure. Following abortion, positron emission tomography scan showed increased uptake in the left neck, upper mediastinum, lung tissue, lingula, spleen and right sacroiliac joint. Abdominal CT scan revealed spleen and sacrum involvement. Notably, after abortion, the patient suffered from high fever and night sweats. Subsequently, her disease was staged as IV-B and she was started on an escalated BEACOPP protocol treatment for aggressive Hodgkin's lymphoma.

### Comment

Hodgkin's disease peaks at the age of 20-30 years, with a second peak at age 70. The incidence of Hodgkin's lymphoma during pregnancy ranges between 1:1,000 and 1:6,000 [1]. During pregnancy, CT scan is an undesired option for staging due to high radiation exposure of the fetus [2]. Clinical



**[A]** CT revealed lymphadenopathy leading to an incomplete non-thrombosed occlusion of left jugular vein (arrow). **[B]** Mediastinal lymph node enlargement with a suspected right lung infiltration was also identified (triangle).

staging relies more on ultrasonic examination and magnetic resonance imaging, which is considered a safer modality during pregnancy [3]. Furthermore, there is an absolute contraindication to use either PET or Gallium scan in pregnancy [3]. If conception occurs after the initiation of treatment for Hodgkin's disease, the attending physicians might prefer therapeutic abortion due to the high risk of malformation to the fetus. On the other hand, for Hodgkin's diagnosed during pregnancy, such an option is less easy. Furthermore, the age of the pregnancy itself largely affects the decision on management. For Hodgkin's disease diagnosed early in pregnancy, an abortion is mostly chosen. Yet, a wait-and-see strategy with local involved-field irradiation (neck field) together with appropriate shielding of the uterus might fit an early, limited but not aggressive disease (stages IA or IIA) [4]. During the third trimester, such an option can be contemplated even for higher stages, provided the disease is not too aggressive.

The problem is more challenging for Hodgkin's disease diagnosed during the second trimester. The question here is whether to treat such patients, thus risking teratogenicity to the fetus or, on the other hand, postpone treatment till after delivery. Anselmo et al. [2] presented six cases of Hodgkin's patients diagnosed at different ages of pregnancy (15–24 weeks) and at different stages of disease (I–IV). Three patients underwent chemotherapy during pregnancy, while the other three were treated only after delivery (about week

32). All patients, whether treated during pregnancy or after delivery, achieved complete remission. The data presented suggest that ABVD-like chemotherapy can be safely administered during the second trimester [2]. Woo and collaborators [5] examined the outcome of 16 pregnant women treated by radiotherapy for clinical stages IA and IIA. One patient was in the first trimester, 10 in the second and 5 in the third. Four to five half-value layers of lead were used to shield the uterus during radiotherapy. All patients delivered full-term, healthy children. Ten years of follow-up revealed that all children had normal mental and physical development and no secondary malignancies were noted. The 10 year overall survival of women with Hodgkin's disease was 71% [5]. Yahalom [3] reviewed 47 cases of Hodgkin's lymphoma during pregnancy reported in the literature between 1960 and 1989. Twenty-five percent of them were in the first trimester, while 45% and 30% were in the second and third trimester, respectively. Twenty-five percent of the patients received no treatment during pregnancy, most of whom were in the third trimester. Another 25% underwent abortion, all of them in the first trimester. Radiotherapy was given to 49% of the patients (5 were in the first trimester, 13 in the second and 5 in the third). A 10 year follow-up revealed no difference in the pregnancy outcome between those who received treatment and those who did not. The reported 10 year disease-free rate was 77%.

Our patient had an aggressive and progressive course, with a diffuse and fast deteriorating disease. Re-staging post-

abortion showed extensive extranodal involvement, indicating an aggressive disease demanding an aggressive protocol. The finding suggests that in an effort to preserve pregnancy we might sometimes end up underestimating the maternal staging and treatment. To date, no superior therapeutic protocol exists to cope with the question of Hodgkin's disease during pregnancy. Aggressive protocols such as BEACOPP offer high cure rates but have not been thoroughly evaluated in pregnancy and they might be toxic for the fetus. Less toxic protocols such as ABVD might be an alternative in the less aggressive disease.

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PET = positron emission tomography

## Capsule

### Inhibiting HIV-1 integration

Among the main modes of therapy used for treating infection with human immunodeficiency virus-type 1, two have proved successful in obstructing the viral life cycle by interfering with virally encoded reverse transcriptase and protease enzymes. A third and rather more elusive target has been the viral integrase, which is required for incorporation of viral DNA into the host genome. Hazuda and co-workers successfully used a novel

integrase inhibitor to protect macaques from infection with a hybrid simian and human immunodeficiency virus. When the monkeys were either acutely or chronically infected with the virus, the inhibitor strongly suppressed viral loads while allowing significant T cell immunity against the virus.

*Science* 2004;305:528

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