CLINICAL VIGNETTE

Hodgkin Lymphoma in a Pregnant Patient

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Case Report

A 25-year-old female in the third trimester of pregnancy presented with dry cough and unintentional weight loss. She had noticed a lump on her right neck for 5 weeks. The patient denied having fevers, chills, night sweats, or recent exposure to sick contacts. On physical examination, she had a right supraclavicular lymph node measuring 2 cm. A fine needle aspiration of the right supraclavicular lymph node revealed an atypical lymphoid infiltrate with features suggestive of classical Hodgkin lymphoma. An incisional biopsy of the right supraclavicular lymph node confirmed the diagnosis of classical Hodgkin lymphoma, nodular sclerosis type. She had a single posterior/anterior view chest x-ray with adequate abdominal shielding, which showed a mediastinal mass measuring 16 cm in length and 7.8 cm in width. Concurrently, an abdominal ultrasound showed splenomegaly at 13.8 cm with no hepatobiliary abnormalities. Her CBC revealed a hemoglobin level of 10 g/dL and platelet count of 406 x 10^3/uL. A comprehensive metabolic panel showed slightly elevated total bilirubin of 1.3 mg/dL and alkaline phosphatase of 152 U/L concerning for cholestasis. Her ESR was markedly elevated at 89 mm/hr and LDH was elevated at 293 U/L. HIV and viral hepatitis serologies were normal. Based on limited imaging evaluation, she was clinically staged to have Ann Arbor IIIBx Hodgkin lymphoma (HL) with bulky mediastinal adenopathy.

The patient wants to know the recommendations regarding the management of her condition.

Discussion

Hodgkin lymphoma is a type of malignancy that arises from the lymphatic system first described by Dr. Thomas Hodgkin in 1832. There were some earlier descriptions of primary lymph node tumors by Marcello Malpighi in 1666, but Dr. Thomas Hodgkin was the first one to present a complete clinicopathologic description of primary tumors of the lymph nodes.[1] Hodgkin lymphoma (HL) accounts for approximately 10 percent of all lymphomas. It is the 24th most common cancer in the United States, and it is estimated that 9,050 new cases were diagnosed in the United States in 2015. It is more common in young adults with 31.5% of new cases diagnosed between the age of ages 20-34; the median age at diagnosis is 38.[2] The age range of HL diagnosis coincides with the female reproductive period. At such, HL is one of the most common cancers found during pregnancy along with breast cancer, cervical cancer, and melanoma.[3] The incidence is estimated to be between 1:1,000 and 1:6,000 deliveries.[4]

Pregnant patients with Hodgkin lymphoma present with similar findings to non-pregnant patients. Most patients present with peripheral lymphadenopathy, which is usually painless with a rubbery consistency. The most common involved sites are the cervical, supraclavicular, and mediastinal areas.[5] Associated constitutional symptoms include fever (>100.4F), night sweats, and unexplained loss of >10 percent of body weight over the past six months can be found in 20-50 percent of HL patients.

The diagnosis of Hodgkin lymphoma requires a complete pathologic evaluation of the involved tissue by an experienced hematopathologist. An excisional biopsy of an involved lymph node is recommended for an accurate diagnosis. Based on the appearance and immunophenotype of the malignant cells, HL is divided into classical HL and nodular lymphocyte predominant HL (NLPHL). Based on tumor cell morphology and its reactive cellular background, classical HL is subdivided into four subtypes: nodular sclerosis, mixed cellularity, lymphocyte rich, and lymphocyte depleted.[6] The incidence of these different subtypes of HL found in pregnant women is similar to that of non-pregnant women. Nodular sclerosis is the most common subtype of HL found in pregnant women.[7]

Appropriate staging for HL is essential because it provides prognostic information, and it determines the optimal treatment plan. Imaging studies typically employed during lymphoma staging represents a clinical dilemma during pregnancy due to concern for fetal radiation exposure leading to pregnancy complications including spontaneous abortion, fetus malformation, and mental and/or growth retardation.[8] It is generally accepted that prenatal radiation exposure to a cumulative dose of less than 0.05 Gy does not affect pregnancy.[9] This dose is equivalent to the radiation dose exposure from about 500 chest radiographs.[8] Hence, a single posterior/anterior view chest radiograph with adequate abdominal shielding can be performed as part of staging work up. If abnormalities are seen on chest radiograph, MRI of the chest can be done. For intra-abdominal staging, abdominal ultrasound or MRI of the abdomen is used for evaluation. Staging with MRI is generally considered safe during pregnancy. There is some concern about the potential acoustic

damage to the fetus and long-term safety regarding radiofrequency fields, but available studies so far show no harmful fetal effects. However, the use of gadolinium contrast is not recommended because gadolinium-chelate molecules may enter the amniotic fluid and may be harmful.[10] On the other hand, computed tomography (CT) scan exposes the fetus to larger radiation doses and therefore is generally avoided. Positron emission tomography (PET) scan is commonly used as part of the staging and treatment response evaluation. However, its use is not recommended in pregnancy because it results in pelvic irradiation, and the tracer fluorine-18 fluorodeoxyglucose is considered fetotoxic.[11] Bone marrow biopsy can be safely performed during pregnancy, if indicated.

Hodgkin lymphoma is curable in more than 80% of patients after primary treatment.[12] Treatments involve systemic chemotherapy with or without radiation therapy. The use of these treatment modalities during pregnancy can be a challenge for both patient and the treating physician. The decision to treat pregnant patients with HL immediately with chemotherapy needs to be weighed against the risk of treatment delay on maternal survival. The specific timing and type of therapy needs to be individualized according to disease stage, gestational age of the fetus, and patient preferences. For a long time, it was assumed that chemotherapy was dangerous to the fetus and would not be possible during pregnancy. A number of retrospective cohort studies have shown that there is an increased risk of spontaneous abortion, major malformations, and fetal demise during the first trimester.[13,14] Other studies have shown chemotherapy has been successfully administered to pregnant women during second and third trimester without major complications.[15,16,17,18] Based on available studies, for patients with a new diagnosis of HL during first trimester, deferral of chemotherapy to the second trimester is recommended. However if a patient's clinical status does not permit delay of treatment, elective termination of pregnancy needs to be discussed in a multidisciplinary format. For pregnant women with Hodgkin lymphoma during the third trimester, deferral of treatment until after delivery can be considered, if clinically feasible.

A common standard chemotherapy regimen for Hodgkin lymphoma is ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine). Based on available data, it is unknown which chemotherapy regimen offers the optimal risk-benefit ratio in a pregnant patient with a diagnosis of HL. The use of ABVD in pregnancy was investigated in case series and with no significant adverse fetal outcomes noted.[4, 14, 16, 17, 19] Other case series have also demonstrated good long-term clinical and neurological outcomes among children who were exposed to ABVD during the second or third trimester.[17,18,20] American Society of Hematology conducted a comprehensive literature review in 2008 and reported that there were limited available data to guide therapy. As such, they concluded that ABVD is a treatment of choice (Grade 1C recommendation) if multi-agent chemotherapy is to be used because it appears to be safe to fetal development.[19]

Conclusion

In summary, HL is one of the most common cancers found during pregnancy. Appropriate staging is essential for prognostication and selection of the appropriate treatment. Chest radiograph with adequate abdominal shielding, ultrasound, and MRI without contrast are acceptable imaging modalities during pregnancy. The specific timing and type of therapy needs to be individualized according to disease stage, gestational age of the fetus, and patient preferences. The patient must be informed of the risk and benefits of chemotherapy and have active participation in the treatment decisions. If treatment is required during pregnancy, ABVD is recommended based on current available data.

Clinical Case Follow-up

Our patient had presented with a new diagnosis of stage IIIBx HL with bulky mediastinal adenopathy during the third trimester of her pregnancy. She was initiated on treatment with ABVD with resolution of her presenting symptoms. She proceeded to deliver her infant without complications. Both the mother and the infant had an uneventful post-delivery clinical course.

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