Hodgkin's disease during pregnancy: a case report and review of the literature

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Summary

The simultaneous presence of cancer and pregnancy is rare but occurs, creating extreme scenarios in clinical practice. Hodgkin`s disease (HD), affects primarily young adults and therefore obstetricians may confront young women with this type of lymphoma during pregnancy. We report a case of a 27-year-old woman with HD who presented during the 28th week of gestation. After counseling the couple decided to continue with the pregnancy. The patient received conservative treatment with regression of the symptoms and rapid improvement of her general condition. At 36 weeks of gestation a healthy infant was born and the patient underwent chemotherapy after delivery with complete resolution of the disease.

Key words: Hodgkin's lymphoma; Pregnancy; Therapy.

Introduction

Hodgkin's disease (HD) is the most common hematological malignancy during pregnancy, corresponding to less than 1% of all malignancies [1]. This neoplasia affects mostly women in reproductive age and presents a peak incidence between 20-30 years of life. The frequency of HD in pregnancy is reported to vary between 1:1,000 and 1:6,000 deliveries [2-5]. Medical therapy of HD in pregnancy is a dilemma due to the nature of ethical and personal decisions that a couple has to make and it is strongly supported that each specific case should be individualized [5]. The treatment plan should include the least possible danger for the fetus without jeopardizing the mother's chance for cure.

Case report

A 27-year-old pregnant woman, primigravida, presented during the 28th week of gestation at our clinic with mild uterine contractions for the previous 24 hours. The patient also was suffering from intense cough, dyspnea, pleurodynia and fever up to 39°C for 48 hours. The medical and family history was insignificant. The clinical examination manifested absence of respiratory sound in the middle of the left mediastinum and profound cardiac sounds. Laboratory findings disclosed leukocytosis with lymphopenia, anemia, increased erythrocyte sedimentation rate (ESR) (67 mm/h) and c-reactive protein (CRP) (38 mg/dl). Chest X-ray and cardiac ultrasound (US), (Figures 1 and 2) showed a mass in the mediastinum, bilateral pleural infusion, pericardial effusion and distention of the cardiac cavities. Cardiotochography (CTG) disclosed uterine contractions (3/10). The patient was treated with tocolytics, corticosteroids, intravenous antibiotics and continuous oxygen flow with regression of the clinical symptoms and improvement of the laboratory results. On the second day of hospitalization, the woman presented a painless node in the right supraclavicular area. The histological examination of the excised lymph node revealed sclerosis-nodular HD (Figures 3 and 4) and the patient was staged II B. After counseling, the couple decided to continue with the pregnancy which was also being closely followed by oncologists. The patient remained in good health, did not suffer any other acute episodes and at 36 weeks of gestation she delivered a healthy newborn. She then underwent six cycles of chemotherapy with ABVD (doxorubicin+melomycin+vinblastine+decarbazine) without significant toxicity and follow-up reported complete regression of the disease.

Discussion

Malignancy during pregnancy is rare occurring in 0.07%-0.1%, with breast cancer, lymphoma and leukemia being the most frequent diseases [5, 6]. There is still not much information on the effects of cancer on pregnancy outcome. In developed countries, the trend to postpone family planning and conception until later in life might increase the incidence of cancer during pregnancy. The available data for HD is still limited thus its natural history, especially during pregnancy, is not yet well understood [7]. Risk factors for Hodgkin's lymphoma include adulthood, first-degree relative with the disease and infection with Epstein-Barr virus, while pregnancy is not considered a risk factor [3, 7] except for the hypothetical immunosuppressive effect on pregnant women. Physical examination, laboratory results and imaging methods in addition to the usual persisting symptoms such as unexplained fever, night sweats, weight loss, itchy skin, painless swollen lymph nodes in the neck, underarm, or groin can establish early diagnosis. Factors that affect prognosis of HD in pregnancy are associated with the stage of the cancer, patient's symptoms and wishes, and the age of the fetus. Due to limitations of the pregnancy status, lymphoma staging can be accomplished by further examinations such as bone marrow biopsy and radiological imaging. Initial staging in non

Revised manuscript accepted for publication June 30, 2005

Fig. 1

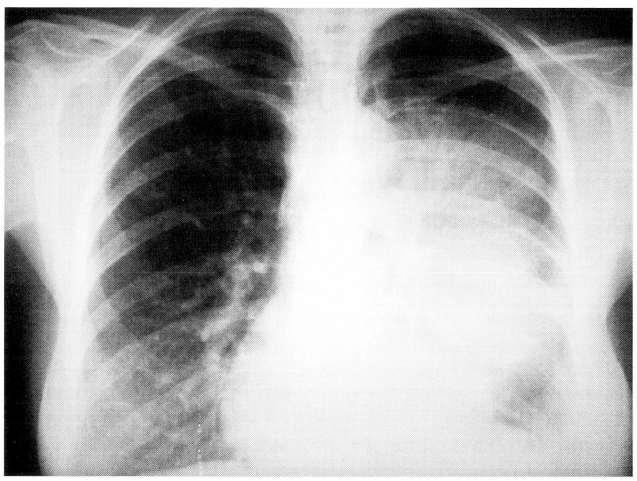

Fig. 2

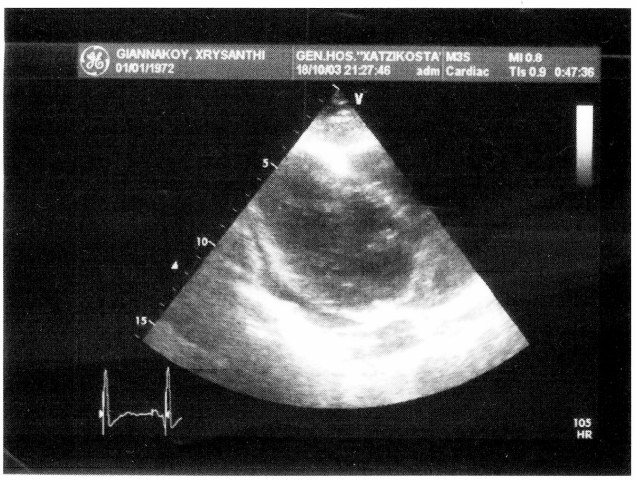

Fig. 3

Fig. 4

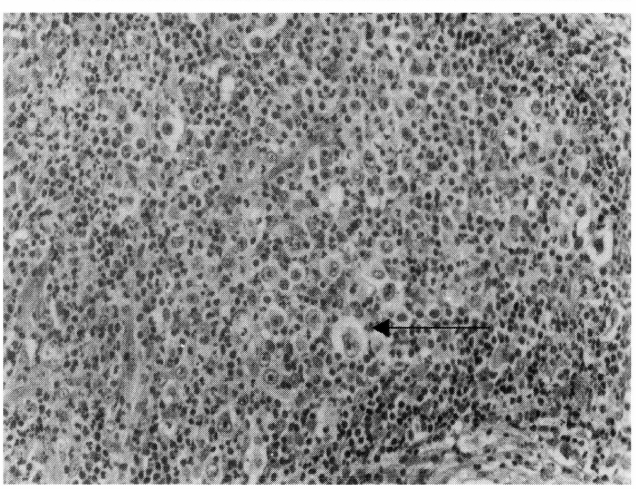

Figure 1. — Chest X-ray showing a mediastinal mass with pleural and pericardial effusion.
Figure 2. — Cardiac ultrasound showing the left ventricle and pericardial effusion.
Figure 3. — Histological examination of the excised lymph-node with the characteristic nodular morphology of Hodgkin's lymphoma (H&E, x 5).
Figure 4. — Microscopic appearance of the node with lacunar cells (arrow), (H&E x 40).

pregnant women includes chest X-ray and computed tomography (CT), while in pregnant women a two-view chest X-ray allows limited exposure of the fetus to radiation. Furthermore, a magnetic resonance imaging (MRI) scan is able to detect lymphadenopathy, evaluate the bone marrow and detect possible splenic involvement [8].

In clinical practice the intense challenge is to ensure optimal treatment for the mother by chemotherapy and radiation therapy without harming the fetus. Obstetricians, oncologists and radiotherapists have to deal with high-risk pregnancies and should agree on basic issues regarding therapy, and provide information on the relative risks of both treatments that are usually recommended for HD.

Half of the patients who present with supra-diaphragmatic manifestations have occult intraabdominal disease. Diagnostic imaging procedures are essential for treatment decisions, but are contraindicated in pregnancy [9]. Thus, the usual counseling for women in the first trimester presenting with HD is to proceed to therapeutic abortion [4, 9-11]. Rare exceptions can be acceptable if the disease is above the diaphragm, at early stage, and appears to grow slowly, or if some women strongly opt to continue the pregnancy. These patients should be under close follow-up, deliver as soon as possible and complete the treatment afterwards [9]. Alternatively, since these patients seldom develop new manifestations, they could receive radiotherapy with proper shielding [12]. Woo *et al.* reported no abnormalities in 16 babies delivered after their mothers had received supra-diaphragmatic radiation with five half-value layers of lead. Nevertheless, the patient has to be informed that the results of split-course treatment may be less effective than results from continuous treatment [13].

In a recent study for radiotherapy of Hodgkin's lymphoma in pregnancy, Mazonakis *et al.* [14] used a humanoid phantom to simulate pregnancy at the first trimester of gestation and a mobile shielding device of 5 cm of lead. Phantom exposures were made with a 6 MV photon beam. The measurements showed that radiation doses with this shield may be below or above the threshold value of 10 cGy depending on the distance separating the embryo from the field isocenter and the dimensions of the field applied. The author concluded that radiotherapy

in the regions of the neck or axilla may be safely performed even without shielding, while for irradiation of the neck-mediastinum or the mantle treatment, the embryo should always be shielded applying doses below 10 cGy.

Chemotherapy in pregnancy seems to be another bias. Many chemotherapeutic agents are considered highly mutagenic, could damage rapidly dividing cells and affect tissues with a high growth rate resulting in spontaneous abortion or malformations [15]. Former articles have reported that the risk of congenital abnormalities when chemotherapy is administered in the first trimester estimated at 10% for single agent chemotherapy and 25% for combined chemotherapy [16], while there is no evidence of increased risk of teratogenesis during the second and third trimester [17-19]. Nevertheless, an association between radiation exposure in utero and subsequent leukemia has also been reported [20]. Aviles and Neri [17] evaluated the acute and late side-effects in a large series of 84 children who received chemotherapy in utero for hematological malignancies. With a median follow-up of 18.7 years, they noted that no cancer or acute leukemia was observed and suggested that chemotherapy can be safely administered even during the first trimester if cure is considered reasonable. Regardless of this recent report the mother should be aware that every therapeutic cycle carries the risk of bone marrow depression, hemorrhage or sepsis and that if primary treatment fails the possibility for cure will be less despite intensive therapy [9]. In these cases, delivery of the infant should be timed to avoid adverse effects such as hemopoietic depression to the infant which is self limiting but increases the risk of infection and hemorrhage [21].

In the second trimester abortion is rarely recommended while almost never in the third trimester. The patients are followed-up carefully postponing therapy, if possible, until induction of labor usually between 32 and 36 weeks [19]. It is evident that ultrasonographic determination of the exact gestational age of the fetus is essential. If the lymphoma is advanced, patients usually receive steroids (to help lung development of the fetus and to fight tumor cells), supra-diaphragmatic radiation therapy and/or chemotherapy, usually alkaloids. In cases of chemotherapy, a single-drug regimen, usually vinblastine at 6 mg/m^2 intravenously every two weeks, is generally given with more extensive treatment once the baby has been delivered [18, 19]. Combined chemotherapy with ABVD appears to be safe in the second and third trimester [3, 4, 10, 11, 17, 22]. Breastfeeding after labor is not allowed because cytotoxic agents are found in maternal milk [1, 23]. In cases of respiratory compromise due to an enlarging mediastinal mass, a short course of radiation can be administered. Woo *et al.* [9], suggest that in pregnant women with stage I B or II B mediastinal presentations, radiotherapy should be tried prior to chemotherapy. In patients with stage I A or II A it might be possible to postpone treatment until after full-term delivery.

The clinical behavior of this neoplasm during pregnancy does not appear to be different from that outside of the setting of pregnancy. Furthermore, the prognosis and survival of pregnant women treated for HD seems to have similar rates to women treated while not pregnant and also similar rates to that in the general population [3, 4, 7].

In another study [24], reproductive outcomes and health of offspring were investigated in 340 patients with HD. Twenty-seven of them who had conceived after treatment were interviewed. No excess of stillbirths, low birth weight, congenital malformations or cancer occurred in the 49 offspring. The number of the study is still small and the results are in contrast with other reports [25]. Even if this recent evidence tends to be reassuring, the long-term effects of anticancer treatment on the children of these women are still unknown [24].

In our case, we did not have to face the dilemma of a therapeutic abortion since the woman presented during the 28th week of gestation. The diagnosis was established soon after with a nodular biopsy at the supraclavicular area. It was decided not to proceed with any aggressive therapy due to the complete regression of the symptoms with conservative treatment and due to the wishes of the patient. She was under close follow-up and delivered a healthy infant at 36 weeks of gestation. Chemotherapy with ABVD afterwards achieved complete remission of the disease. The follow-up of our case is in accordance with other reports, where it is noted that tumor progression during pregnancy is less rapid than in the postpartum period [19, 26]. Anselmo *et al.* [5], also noted that three of six (50%) women who started chemotherapy after delivery achieved the same outcome.

From the recent literature we have observed a trend for aggressive therapeutic options even in the first trimester of pregnancy [14, 17], although long-term sequelae remain largely unknown. Furthermore, retrospective studies and case reports are not yet feasible to make specific recommendations regarding the management of this type of lymphoma. Pregnant women are not likely to be at a higher stage of disease than their controls, nor suffer adverse effects from pregnancy on survival [3, 4]. Termination of pregnancy in the first trimester remains a strong option that has to be offered to the patient with very rare exceptions and after careful counseling. Still, our report indicates that Hodgkin's lymphoma in pregnancy, especially in the second or third trimester, will most probably have a favorable outcome for both mother and fetus.

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