Non-Hodgkin's lymphoma complicating pregnancy: A case report

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Summary

A 40-year-old, gravida 3, para 2 woman was initially referred to our department at 31 weeks' gestation complaining of fever, night sweats, malaise in association with jaundice and pancytopenia. Cesarean section with excisional iliac lymph node biopsy was carried out following a period of expectant management. An 1,840 g healthy male infant with an Apgar score of 9 at 34 weeks of gestation was delivered. Histologic examination of the excised lymph node revealed non-Hodgkin's lymphoma (Histiocyte and T cell predominant B cell lymphoma). The patient was evaluated to have Stage II B disease. A chemotherapy regimen of CHOP/Rituximab was instituted with successful maternal-fetal prognosis.

Key words: Non-Hodgkin's lymphoma; Pancytopenia; Pregnancy.

Introduction

Non-Hodgkin's lymphoma has rarely been observed in association with pregnancy. In a 50-year literature review in 1989, only 75 cases associated with pregnancy were described [1]. Thus, experience in the diagnosis and management of pregnancy complicated by Non-Hodgkin's lymphoma is limited. Furthermore, patients with non-Hodgkin's lymphoma often have unusual manifestations and their diagnosis is frequently delayed [2].

We report a case of non-Hodgkin's lymphoma diagnosed in late pregnancy initially presenting with pancytopenia.

Case Report

A 40-year-old, gravida 3, para 2 woman was initially referred to our department at 31 weeks' gestation complaining of fever, night sweats, malaise in association with jaundice and pancytopenia. Her past medical and family histories were unremarkable. Physical examination revealed intermittent fever (39°C), moderate icterus, hepatosplenomegaly, and the uterus equivalent to 30 weeks' gestation. At obstetric ultrasonography a single fetus with estimated fetal weight of approximately 1,700 g (50th-90th percentile) was observed. Biophysical profile, umbilical and middle cerebral arterial Doppler studies were all normal without findings of redistribution. Multiple iliac and para-aortic lymphadenopathy with enlarged spleen and liver were also observed.

Her complete blood count revealed anemia (hemoglobin level of 8.7 g/dl), leucopenia ($1.9x10^3$/ul) and thrombocytopenia (19.200/μl). Blood smear confirmed hipocrome macrocystic anemia. Sedimentation rate was 28 mm/h (range: 0-20 mm/h). Serum albumin was 1.1 g/dl (range: 3.2-4.8), lactate dehydrogenase (LDH) was 708 U/l (range: 230-460 U/l), and uric acid was 7.8 mg/dl (range: 2-6 mg/dl). Liver function tests showed an aspartate aminotransferase level of 102 U/l (range: 5-40), alanine amino transferase of 132 U/l (range: 8-33), alkaline phosphatase of 231 U/l (range: 35-129 U/l), and direct bilirubine of 6.5 mg/dl (range: 0-0.3 mg/dl). Serum renal function tests and serum level of iron and iron binding capacity were all within normal limits. Beta-2 microglobulin and ferritin levels were found to be 5,887 ng/ml (range: 1,010-1,730) and 2,907 ng/ml (range: 5-148 ng/ml), respectively. Serum folic acid and vitamin B_{12} levels were all within normal limits. Urine analysis revealed normal findings except for bilirubinuria. Cytomegalovirus, Herpes simplex virus 1 and 2, toxoplasma, listeria, Hepatitis B-D, brucella, human immunodeficiency virus and parvo virus serology were all negative. Bone marrow aspiration revealed mild hypo- cellularity with a mild increase in erythroid/myeloid ratio without lenfoproliferative infiltration.

Expectant management with close monitorization of the fetus was planned until achievement of fetal pulmonary maturity. Betamethasone, 24 mg, was administered for induction of fetal lung maturation. On the 22nd day of hospitalization, a further increase in total bilirubine level (10.59 mg/dl) as well as worsening biophysical profile scores led to an emergency cesarean section at approximately 34 weeks of gestation.

An 1,840 g healthy male infant with an Apgar score of 9 was delivered. Abdominal exploration revealed hepatosplenomegaly with multiple enlarged iliac and para-aortic lymphadenopathy. A right iliac lymphadenopathy of 5 cm in diameter was also excised to enable tissue diagnosis.

Histologic examination of the excised lymph node revealed non-Hodgkin's lymphoma (histiocyte and T cell predominant B cell lymphoma with high CD 20 expression). The placenta was free of tumor. The patient was evaluated to have Stage II B disease according to the Ann Arbor Staging System. The postoperative period was uneventful. The infant was observed in neonatal intensive care unit for five days and then discharged without any significant problems.

On postpartum day 10, the first course of the CHOP/Rituximab (cyclophosphamide 750 mg/m², adriamycin 50 mg/m², vincristine 1.4 mg/m², prednisolone 100 mg, rituximab 375 mg/m²) chemotherapy regimen was instituted. The patient then was discharged from the hospital and an additional five courses of the same chemotherapy regimen was planned. After institution of the first course of chemotherapy, B symptoms and hyperbilirubinemia (which was attributed to enlarged paraaortic lymph nodes possibly causing bile duct obstruction) disappeared.

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Discussion

Non-Hodgkin's lymphoma complicating pregnancy is extremely rare as a result of the higher incidence of the disease beyond reproductive age [1]. Advanced maternal age in the present case may be evaluated to support this age distribution.

Prognosis for pregnant women affected by non-Hodgkin's lymphoma has been reported to be poor due to aggressive histology and disseminated disease. In review of 62 cases previously reported, only 32% survived without evidence of disease. Therefore, it is particularly important that the diagnosis is made as early as possible [2, 3]. Non-Hodgkin's lymphoma may present as a complex spectrum of symptoms and signs with peripheral lymphadenopathy being the most common clinical finding. Elevated temperature, night sweats and weight loss were categorized as B symptoms and are more common in high-grade lymphomas [4, 5]. Presence of B symptoms in the presented case necessitated an investigation for lymphoma complicating a third trimester pregnancy. However, absence of peripheral lymphadenopathy overted a histologic diagnosis until cesarean delivery. Both pancytopenia and hepatosplenomegaly were evaluated to be manifestations of a non-Hodgkin's lymphoma. Elevated lactate dehydrogenase, abnormal liver function tests, and increase in serum levels of beta-2 microglobulin are all poor prognostic factors associated with non-Hodgkin's lymphoma [6].

Although a poor prognosis is expected for pregnant women with non-Hodgkin's lymphoma, the influence of pregnancy on the course of the disease is uncertain. Since there is no current data that pregnancy can affect progression and the diagnosis is still uncertain, continuation of pregnancy until fetal pulmonary maturity was chosen in the present case [2, 3, 9]. With close monitorization of the fetus and the mother, three weeks could be saved. Cesarean delivery resulted in a healthy infant and also allowed a histologic diagnosis of non-Hodgkin's lymphoma. If the diagnosis is made in the first trimester, termination of pregnancy followed by systemic chemotherapy represents a rationale choice because of the possible harmful fetal effects of chemotherapy [4, 5]. If the diagnosis is made late in pregnancy as in our case, postponement of therapy until fetal maturity seems to be a reasonable option [8].

The Ann Arbor staging system is important in selecting a treatment choice. Bone marrow aspiration can be performed for both the staging and differential diagnosis of pancytopenia as in our case [7]. Abdominal ultrasonography, computed tomography (CT) scan of the neck, thorax and the abdomen and pelvis may be helpful for initial staging. However, pregnancy limits the widespread application of radiographic studies. Magnetic resonance imaging is a reasonable alternative to a CT scan [1, 6]. Radiotherapy is used for Stage I disease, whereas chemotherapy is recommended for most Stage II and all Stage III and IV tumors. The CHOP chemotherapy regimen is the standard of care as in the present case [6, 7]. We preferred to institute the CHOP/Rituximab chemotherapy regimen because of the poor prognostic factors and high CD20 expression in the malignant lymphoid cells.

In conclusion, non-Hodgkin's lymphoma complicating late pregnancy may be managed successfully with expectant management for fetal lung maturation even in the presence of pancytopenia. However, prolonged hospitalization with close monitorization is necessary. In case of evaluation of pancytopenia in pregnancy, non-Hodgkin's lymphoma should be kept in mind.

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