PERINATAL JOURNAL

Perinatal Journal 2011;19(2):94-98

e-Adress: http://www.perinataljournal.com/20110192010
***doi:** 10.2399/prn.11.0192010*

Non- Hodgkin Lymphoma Diagnosed During Pregnancy: A Case Report

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Abstract

Objective: Lymphomas, a heterogeneous group of disorders caused by malignant proliferation of lymphocytes. Hodgkin and non-Hodgkin lymphoma (NHL) is divided into two. Because of the rarity of NHL in pregnancy, the diagnosis and the management was presented with the literature.

Case: In the 5. gestational week; the symptoms of the patient were sore throat and a palpable mass in the neck. The biopsy was diagnosed as NHL. In the 28. gestational week, syclophosphamid, docsorubicin, vincristin, prednisone (CHOP) chemotherapy was started. In the 39. gestational week, 3,310 gr female baby was delivered. Left ventricular mild systolic dysfunction was revealed in the postnatal echocardiography of the baby. After birth, rituximab was added to the chemotherapy regimen.

Conclusion: The management of the NHL patients during pregnancy, performed with a multidisciplinary approach. Palpable cervical and submandibular masses during pregnancy, certainly should be considered in the differential diagnosis of lymphoma. That patients are showing fast cruise, must be diagnosed and treated as soon as possible.

Keywords: Non-Hodgkin lymphoma, pregnancy, chemotherapy.

Gebelikte tanı konulan Non-Hodgkin lenfoma: Olgu sunumu

Amaç: Lenfomalar, lenfositlerin malign proliferasyonu sonucu oluşan heterojen bir hastalık grubudur. Hastalık Hodgkin ve non-Hodgkin lenfoma (NHL) olmak üzere ikiye ayrılır. NHL'nın gebelikte nadir görülmesi sebebiyle tanısı ve yönetimi literatür bilgileri eşliğinde sunuldu.

Olgu: Beşinci gebelik haftasında, boğaz ağrısı ve boyunda ele gelen kitle semptomları ile gelen hastaya, yapılan biyopside NHL tanısı konuldu. Yirmisekizinci gebelik haftasında siklofosfamid, doksorubisin, vinkristin, prednizon (CHOP) kemoterapisi başlandı. Otuzdokuzuncu gebelik haftasında 3,310 g ağırlığında kız bebek doğurtuldu. Bebeğin postnatal yapılan ekokardiyografisinde sol ventrikülün hafif sistolik disfonksiyonu tespit edildi. Doğum sonrasında kemoterapi rejimine rituksimab eklendi.

Sonuç: NHL olgularının gebelik süresince ve sonrasındaki yönetimi multidisipliner yaklaşım ile gerçekleştirilmelidir. Gebelik sırasında ele gelen servikal ve submandibular kitlelerde lenfomalar ayırıcı tanıda mutlaka düşünülmelidirler. Hızlı seyir gösteren bu olgulara en kısa sürede tanı konulup tedaviye en yakın zamanda başlanmalıdır.

Anahtar Sözcükler: Non-Hodgkin lenfoma, gebelik, kemoterapi.

Introduction

Lymphomas are a heterogeneous group of disorders caused by malign proliferation of lymphocytes. According to the main histological classification, they are separated into two groups as Hodgkin and Non-Hodgkin lymphoma (NHL). Hodgkin disease is the most prevalent lymphoma type seen in pregnancy due to age distribution of patients.[1] But it is very rare to see NHL in pregnancy. Only 75 cases were reported between 1937 and 1985.[2] NHLs establish a very heterogeneous group in terms of hematologic tumors, clinical

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behavior, morphology, cell origin, etiology and pathogenesis. Though it is still not a perfect classification, REAL classification has been used since 1995.[3] NHL constitutes 4% of cancer cases newly diagnosed. It is 6th reason among reasons of newly diagnosed cancers in males and females. Prognosis is bad in a high level NHL and average life period is 1.5 years; but in a low level one, prognosis is better and average life period is 7.5 years.[4] They mostly surround peripheral lymphs and mediastinum.[4]

Lymphomas during delivery are high level. At the same time, they tend to surround organs mostly stimulated hormonally during pregnancy (such as breast, ovary, uterus etc.). Especially NHL has a bad progress in pregnancy since it is together with disseminated intravascular coagulation and aggressive tumors.

In our case, the patient who came to our clinic at her 5th gestational week with sore throat and palpable mass symptoms on neck was diagnosed as NHL in the biopsy. Her chemotherapy began on her 28th gestational week. Since NHL is rare during pregnancy, its diagnosis and management were presented together with the literature information.

Case Report

Thirty-three years old patient (G1, P 0) who did not have a similar complaint before applied to our clinic for the complaint of mass on her right cervical region. Cervical and submandibular lymph node was found in her physical examination. Lymph node biopsy was reported as lymphoma with diffuse major B cell (WHO/REAL). In the biopsy material, it was observed that cells displayed diffuse cytoplasmic staining by CD20 but no staining with CD30 and cytokeratin. In the cervical magnetic resonance (MR) examination of the patient, there were multiple cervical, submandibular and nasopharyngeal masses. Abdominal computed tomography which should be performed for staging purpose could not be done as the patient refused due to her pregnancy. Bone marrow biopsy was reported as normocellular. It was decided to apply 6 cures of CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) to the patient as 3 cures would be done during pregnancy and remaining 3 cures would be done after pregnancy.

On 28th gestational week, 750 mg/m^2 cyclophosphamide, 50 mg/ m^2 doxorubicin, 2 mg vincristine and 100 mg prednisone were applied as 1st cure chemotherapy. In the obstetric examination performed after chemotherapy of the patient, amniotic fluid volume was found on placenta posterior wall and as consistent with fetal development week. Umbilical artery Doppler was measured as PI: 086 and RI: 057.

Second cure was applied on 31st gestational week and it was found in the obstetric examination after chemotherapy that fetal development was consistent with gestational week. Umbilical artery Doppler was measured as PI: 083 and RI: 051. 3rd cure of chemotherapy was applied on 38th gestational week. In the obstetric examination performed after chemotherapy, amniotic fluid volume was found within normal volume and as located on placenta posterior wall. Umbilical artery Doppler was measured as PI: 088 and RI: 055.

Four days after last chemotherapy (on 39th gestational week), the patient applied to our obstetrics clinics since her spontaneous contractions began and single alive 3,310 gr baby girl (with 1st minute Apgar score 7.5, and 5th minute Apgar score 8) was delivered by spontaneous vaginal delivery. Baby and mother did not need intense care after delivery. In the postnatal echocardiography of the baby, slight systolic dysfunction of left ventricle was observed. It was decided by Pediatrics Cardiology Department to follow up the patient without providing treatment. One week after delivery, 4th cure of chemotherapy was applied to the mother. 375 mg/m^2 rituximab treatment was added to the CHOP regime. The follow-up of the patient who received totally 6 cures of CHOP chemotherapy and rituximab has still being performed in Internal Medicine Oncology Department.

Discussion

NHL constitutes 4% of newly diagnosed cancer cases. It is 6th among the reasons of newly diagnosed cancer in females and males.[4] The most frequent three NHL types in the USA are lymphoma with diffuse major B cell (31%), follicular lymphoma (22%) and minor lymphocytic lymphoma (6%).[4] In our case, the most frequently seen lymphoma type with diffuse major B cell was observed. NHL is not prevalent in fertile ages;

however, we only see it in the literature as case reports. Lymphomas in pregnancy are high leveled and aggressive. Also they tend to surround organs mostly stimulated hormonally during pregnancy (such as breast, ovary, uterus etc.). It is seen when literature is reviewed that though cases are diagnosed lately and progress aggressively, deliveries with healthy babies born mature are reported. In our case, a healthy baby girl was delivered by spontaneous vaginal delivery at her 38th gestational week.

In NHL treatment, the method to be preferred at delivery varies according to clinical staging and histopathological type. While "wait-and-see" approach can be used in slowly developing and low leveled NHLs, chemotherapy with single agent or local radiotherapy can be also applied.[5]

Lymphoma with diffuse major B cell is more aggressive and may cause life-threatening complications at early period. Since its prognosis is bad and display rapid progression, it is needed to treat by combined chemotherapy regime. CHOP is especially the most frequently preferred combined chemotherapy regime in lymphoma with diffuse major B cell. However, studies about the safe use of this regime in pregnancy are limited. Based upon the data including limited number of case series, no increase in the frequency of fetal malformation was observed in patients who were applied CHOP on 1st trimester.[6-13]

The effects of agents used in CT at NHL over pregnancy results are given in the Table 1 together with the case series.

Our case received totally 3 cures of chemotherapy during pregnancy as first one was on 28th gestational week. It is reported in the literature that disease may grow in postpartum period in some cases. In our case, no grow was observed in postpartum period.

Rituximab is a monoclonal antibody used in the treatment of lymphoma with diffuse major B cell. It is used by combining with CHOP regime. It is reported in the literature that it is used on limited number of cases for treatment of some autoimmune diseases during pregnancy. It was reported by the data obtained from these cases that using it on first trimester did not cause any increase in the frequency of fetal anomaly.[14, 15]

In another case, combined CT was applied with CHOP and rituximab on a 35 years old pregnant

Table 1. The effect of different combined chemotherapy diets on gestational results used on aggressive NHL treatment.[7-21]

Case series	Case number	Pregnancy result
NHL receiving CHOP treatment (on 2nd and 3rd trimesters)	4	Resulted with normal pregnancy progress.
Long-term follow-up results of children who were exposed to various chemotherapy protocols (children of mothers who received alkylating agent and anthracycline agent for NHL treatment on all three trimesters)	33	No congenital neurological or psychological anomaly was observed. Learning and education performances are normal.
Case series receiving combination chemotherapy treatment due to NHL on 2nd and 3rd trimesters (all of them include alkylating agent and anthracycline)	10	Stillbirth in 1 case. No congenital anomaly was observed.
Case series that received bleomycine, vinblastine, cyclophosphamide and prednisone chemotherapy (on 2nd and 3rd trimesters)	3	Resulted with normal pregnancy progress.
The case that received etoposide and cisplatin chemotherapy	1	Resulted with stillbirth at 25th gestational week.
The case that received cyclophosphamide, prednisone and rituximab (on 2nd trimester)	1	Resulted with normal pregnancy progress.
Our NHL (with diffuse major B cell) case that received CHOP chemotherapy on 2nd and 3rd trimesters	1	Resulted with normal pregnancy progress. In postnatal period, slight systolic dysfunction of left ventricle was observed.

and temporary complete deletion in fetal B cells and high rituximab values on cord blood were detected by postnatal examination.[16]

Wider case series are needed to confirm the safe use of rituximab during pregnancy. In our case, the patient and her family was informed in detail about treatment options and side effects. In the light of literature information, it was decided by multidisciplinary approach (Perinatology, Medical Oncology, and Pediatrics) to apply only CHOP treatment during pregnancy and to add rituximab to the treatment in postpartum period. Three cures of CHOP + rituximab were applied to our cases in postpartum 1st week. Remission was detected in the patient according to the physical examination and screening results performed after totally 6 cures of chemotherapy.

According to the limited number of case series in the literature, it was observed that CHOP chemotherapy had no significant effect on pregnancy results and fetal malformations. However, in the postnatal echocardiography of the baby, slight systolic dysfunction of left ventricle was observed but it was decided by Pediatrics Cardiology Department to follow up the patient without providing treatment.

Conclusion

Lymphomas are rare during pregnancy. Hodgkin lymphoma is more frequent than NHL.[17] The diagnosis is generally established lately.[18] The method to be preferred in the treatment varies according to clinical staging and histological type. Those with high leveled lymphoma, those with major tumor mass, and those with systemic symptoms should be treated by combined chemotherapy.[4]

There are limited numbers of data about the reliability of chemotherapy agents during pregnancy. Wider case series are needed to determine optimum treatment options to be used during pregnancy.

The management of cases during and after pregnancy should be performed by multidisciplinary approach which includes the Departments of Perinatology, Medical Oncology, and Pediatrics.

Lymphomas certainly should be considered in the differential diagnosis for palpable cervical and submandibular masses during pregnancy. These rapidly progressing cases should be diagnosed in the shortest time and treatment should be initiated as soon as possible.

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