

## T Cell Lymphoblastic Lymphoma/Leukemia in a Pregnant Woman with Initial Presentation of Superior Vena Cava Syndrome

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### Abstract

Acute lymphoblastic lymphoma/leukemia is a rare occurrence during pregnancy but serious condition if it is left untreated. Many risks both for mother and fetus will be encountered when these neoplastic diseases accompany to pregnancy. Here we reported a 25-year-old, 16-weeks-pregnant woman with initial presentation of superior vena cava syndrome and respiratory distress. Prompt intensive chemotherapy right after early termination of pregnancy restored pulmonary function and successful remission of very aggressive hematological malignancy. In conclusion, treatment of very aggressive lymphoma in a pregnant woman should be highly individualized based on maternal safety and fetal outcome, especially life threatening situation encountered.

**Keywords:** Lymphoblastic Lymphoma; Pregnancy; Superior Vena Cava Syndrome

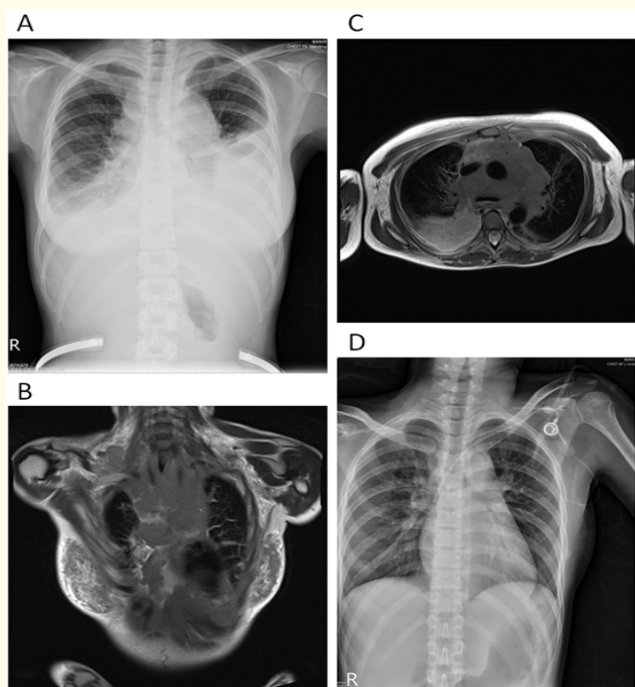
### Introduction

The diagnosis of cancer during pregnancy is not common and it might be raised in modern society due to late pregnancy. Breast, cervical cancer, melanoma and lymphoma are common malignancy diagnosed during pregnancy [1]. Lymphoblastic lymphoma is uncommon histologic subtype of non-Hodgkin lymphoma (NHL) and contributed to 2% of NHL cases. Although lymphoblastic lymphoma is highly aggressive NHL but it is curable if intensive chemotherapy offered [2]. To our knowledge, there is no available information regarding the incidence of lymphoblastic lymphoma in pregnant women but the estimated incidence of non-Hodgkin lymphoma is 0.8 case per 100,00 pregnancies [3]. However, only few reports were gathered on clinical outcome of lymphoblastic lymphoma in pregnant women and among lymphoblastic lymphoma patients with pregnancy, the prognosis remains poor and half of them died of lymphoma disease [4]. Here we reported a newly diagnosed T cell lymphoblastic lymphoma in pregnant women with initial presentation of superior vena cava syndrome critically.

### Case

A 25-year-old, 16-weeks-pregnant adolescent presented to divi-

sion of chest with a one month history of progressive shortness of breath. On physical examination, breathing sound was decreased bilaterally and puffy face with lymphadenopathy over right lower neck was noticed. Chest X-ray disclosed widened mediastinum and bilateral pleural effusion (Figure 1A). Blood test showed leukocytosis up to 17700/uL of white blood cells. She was admitted for further workup of superior vena cava syndrome. The pleural effusion of left side was drained and the character of pleural effusion was exudates in nature with elevated lactate dehydrogenase: 875 international unit/L. The test of tuberculosis was negative by GeneXpert using sample of pleural effusion. Magnetic resonance image of chest showed large mediastinal tumor and right lower neck to supraclavicular lymphadenopathy with major vessels encasement in addition to bilateral pleural effusion (Figure 1B and 1C). Pathologic diagnosis from excisional biopsy of enlarged lymph node of right neck was performed and tumor-tissue immunophenotypic marker were positive for CD1a, cCD3, CD4, CD5, CD7, CD8, CD10, TdT and negative for CD19 and DR (Figure 2A and 2B). T cell lymphoblastic lymphoma was diagnosed and daily methylprednisolone 40 mg intravenously was prescribed for alleviation of symptom of dyspnea.



**Figure 1:** Image at diagnosis and after cytotoxic therapy. (A) Chest X ray at diagnosis. (B) Sagittal section of magnetic resonance image at diagnosis. (C) Coronal section of magnetic resonance image at diagnosis. (D) Chest X ray after the first cycle of chemotherapy

Meanwhile diagnosis was made, termination of pregnancy was decided concerning outcome and critical condition of very aggressive nature of lymphoma in a pregnant woman. The bone marrow contained 95% small to medium sized atypical lymphoid cells with identical immunophenotype indicating extensive marrow involvement (Figure 2C and 2D). Cytogenetic study from bone marrow revealed 46, XX, del(6)(q23), t(7;10)(q36;q24). The final diagnosis was stage IV T cell lymphoblastic lymphoma/leukemia. Termination of pregnancy by misoprostol pharmacologically was delivered 14 days after initial admission. Course A of Hyper-CVAD chemotherapy regimen was applied 3 days after abortion using cyclophosphamide 300 mg/m<sup>2</sup> every 12 hours intravenously on D1, D2, D3; vincristine 2 mg intravenously on D4, D11; doxorubicin 50mg/m<sup>2</sup> intravenously on D4; and dexamethasone 40 mg/day orally on D1-4 and D11-14. The intrathecal chemotherapy consisted with methotrexate 12 mg on D2 and cytarabine 70 mg on D7. Chest X-ray 40 days after initiation of diagnosis and 26 days after initiation of chemotherapy disclosed almost resolution of bilateral pleural effusion and widened mediastinum (Figure 1D).

**Figure 2:** Histopathology of lymph node and bone marrow. (A) Low power field (40X) of lymph node in hematoxylin and eosin stain. (B) High power field (400X) of lymph node in hematoxylin and eosin stain. (C) Low power field (40X) of bone marrow in hematoxylin and eosin stain. (D) High power field of bone marrow (400X) in hematoxylin and eosin stain.

## Discussion

Systemic cancer treatment in pregnant women remains cautious to physicians and patients in term of both maternal and fetal safety. Delay in treatment in order to assure the birth of healthy neonate may lead to fatal outcome of the mother in highly aggressive malignancy. In contrast, administration of cytotoxic chemotherapy, especially in first trimester, could result in severe birth complications, even fetal death. Acute lymphoblastic lymphoma/leukemia is rare in pregnancy and the overall incidence of acute lymphoblastic lymphoma/leukemia is 1.3 per 100,000 with a slight male predominance [5]. Acute lymphoblastic lymphoma has a good prognosis in non-pregnant young patients and 80% of the cases have complete remission after intensive combined chemotherapy. And 40% of patients are cured by modern treatment strategies [6]. Cytotoxic chemotherapy in treating pregnant women with lymphoma remains uncertain and current clinical practice is based largely on case reports and limited case series. Ward and Weiss analyzed data on 42 cases with NHL during pregnancy from literature and stated a composite overall survival rate of 31% [7]. Before treatment, the staging process for lymphoma involved

radiological evaluation often using computed tomography of chest and abdomen. Chest computed tomography is much lower than the threshold dose for fetal side effects and should not be excluded from routine process. But abdominal or pelvic computed tomography is associated with higher fetal exposure to radiation upto 0.02Gy [8]. Alternatively, abdominal ultrasound or magnetic resonance image can be used to avoid exposure of ionized radiation.

Most chemotherapeutic agents have been documented to be teratogenic in animals but in human body, teratogenic effect of cytotoxic chemotherapy should be defined clearly. During this first trimester, chemotherapy may increase the risk of death of fetus, and major malformations since the fetus is extremely vulnerable from week 2 to week 8 of gestation during which organogenesis develops [9]. Second and third trimester exposure of cytotoxic chemotherapy is not associated with fetal malformations but it comes with the increased risk of fetal death, intrauterine growth retardation, lower birth weight and pre-term delivery [10].

In our case with presentation of respiratory distress, treatment should be initiated immediately after diagnosis even during the first trimester. The patient should be informed the aggressive nature of acute lymphoblastic lymphoma/leukemia and high risk of teratogenesis from cytotoxic therapy. Termination of pregnancy should be strongly recommended because therapeutic regimens for acute lymphoblastic lymphoma/leukemia usually contain high dose methotrexate which may induce the greater risk of teratogenesis in the first trimester and severe fetal myelosuppression in the second or third trimester [11,12].

### Conflict of Interest

All authors declared that they have no conflict of interest. Informed consent was obtained from this patient reported in this study.

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