Indexed by : DOAJ Google Crossref Dimension sinta GARUDA

J.Biomed.Transl.Res
e-ISSN: 2503-2178

JOURNAL OF BIOMEDICINE AND TRANSLATIONAL RESEARCH

Case Report

B-Acute Lymphoblastic Leukemia L2 In Second Trimester of Pregnancy

Iraisa Rosaria[1*], Dwi Retnoningrum[1]

[1] *Clinical Pathology Department, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia*

Article Info
History
Received: 25 Nov 2020
Accepted: 23 Apr 2021
Available: 30 Apr 2021

Abstract

Background: Acute lymphoblastic leukemia (ALL) in adults tends to have a poor prognosis and even more challenging to treat during pregnancy due to the mother and the fetus's safety issue. Despite commonly found in 2nd and 3rd trimester, ALL found during 2nd trimester needs more comprehensive management on maintaining the pregnancy while chemotherapy cannot be delayed.

Case Presentation: A 36-year-old woman at 27 weeks of gestation visited the hospital with multiple cervical lymphadenopathy and major weight loss for the last six months. Bicytopenia with leukocytosis was found, along with an increase in LDH, Ferritin, and low albumin level. Bone marrow biopsy had confirmed the diagnosis of ALL-L2. Positive immunophenotyping results on HLA-DR, CD10, CD19, CD20, which support the lymphoid Line-B subtype. The patient was treated with Vincristine 2 mg/IV weekly and 100 mg of oral prednisone for six weeks and maintain the pregnancy. Successful delivery was carried out at 32 weeks of gestational age by lower segment cesarean section due to premature rupture of the membrane. A baby girl was born weighed 1700 gram, APGAR Score 8/9/9, and has no disability on clinical or hematological features at the moment.

Conclusion: ALL in pregnancy is very rare and extremely aggressive disease unless promptly treated. In this case report, it was a first pregnancy in advanced maternal age mother with high social value baby and can be treated successfully using single regimen of chemotherapy during pregnancy even though at the first time administered to hospital the mother come with critical clinical presentation. Leukemia in pregnancy is challenging and still need further study to increase the safety and better treatment outcome.

Keywords:
ALL in pregnancy; ALL-L2; Line-B Lymphoid; Immunophenotyping ALL
Permalink/ DOI: https://doi.org/10.14710/jbtr.v7i1.9542

INTRODUCTION

During pregnancy, 90% of leukemia cases are an acute process and chronic in the other ten, with two-thirds of the cases, are myeloid.[1] Leukemia in pregnancy is commonly diagnosed in the 2nd and 3rd trimesters, although the disease may pre-exist. This emphasizes the importance of early bone marrow examination for unexplained anemia in pregnancy. Early diagnosis is needed to monitor the patient's and her baby's condition closely.[2]

ALL is rare in adults and rarer in pregnancy. Philadelphia chromosome (Ph)-positive ALL represents the major cytogenetic abnormality in adults (20-30%) and is associated with a poorer prognosis than Ph-negative ALL.[3,4] Chemotherapy exposure in the first trimester may lead to congenital malformations or abortion. Second and third-trimester chemotherapy exposure is associated with low birth weight, stunted fetal growth, spontaneous abortion, preterm birth, microcephaly, and mental retardation.[5]

* Corresponding author:
E-mail: iraisarosaria.mv@gmail.com
(Iraisa Rosaria)

Recently, the prognosis of Ph-positive ALL has improved markedly after BCR-Abl targeted tyrosine kinase inhibitors (TKI) were introduced. With upfront TKI, approximately 90 % of patients achieved complete remission (CR).[6] However, the safety use of TKI for pregnancy is still under debate because of the low molecule that can transferred transplacental cause severe adverse effects and teratogenic effects have been reported, makes TKI in pregnancy should be avoided if possible.[7] Before starting chemotherapy in pregnancy, the mother's potential benefits should be considered against the mother and fetus's potential risks. Besides, the chemotherapy procedure is not easily accepted by pregnant women education on potential benefits and risks should be discussed to achieve the treatment goal.

CASE REPORTS

A 36 years old female primigravida at 27 weeks of gestation presented to the emergency room with progressive weakness in the last week. The complaint was accompanied by swelling on both upper eyelids, enlarged multiple neck-lymph nodes, heartburn, and fatigue. The patient experienced a significant weight loss of 24 kg in the last six months. Laboratory tests are presented in Table 1.

Peripheral blood count shows Eosinophils 0%, Basophils 0%, Stab 2%, Segment 26%, Lymphocytes 20%, Monocytes 7%, Myelocytes 4%, Metamyelocytes 2%, Blast 6% and Atypical Mononuclear Cell of 33%. Peripheral blood examination indicates the loose distribution of erythrocytes, mild anisocytosis (normocytes, microcytes), and mild poikilocytosis (ovalocyte, pear-shaped cell). The estimated platelet count is decreased, and the giant platelet is positive but predominantly normal. The leukocyte count is increased, shift to the left, vacuolize neutrophils (+), atypical lymphocytes (+), with the impression: acute hematological malignancy. Bone marrow aspiration (BMA), and cytochemical staining were suggested for further examinations. BMA (Figure 1,2,3) showed an increase in lymphocyte activity by 91% with 64% of lymphoblast, large cell size with a wider cytoplasm, 1 to 3 nuclei together with suppression of granulopoiesis and erythropoiesis, and a decline in megakaryocytes confirmed the diagnosis of ALL-L2. Positive immunophenotyping results on HLA-DR, CD10, CD19, CD20, which according to the FAB criteria, support the Line-B lymphoid subtype (Figure 4).

The patient was given two bags of packed red cell leukocyte-depleted transfusions and four bags of concentrate platelets before starting the chemotherapy regimen. Obstetric ultrasound was performed and indicated a single live intrauterine fetus, breech presentation with an estimated fetal weight of 758 gram, FHR: 150 times per minute, not in labor, negative HIS, and reactive cardiotocography (CTG).

The chemotherapy regimen was following the Indonesian Protocol of Acute Lymphoblastic Leukemia 2013.[8] The chemotherapy began with an induction phase consisting of Vincristine 2 mg/IV weekly and 100 mg of oral prednisone for six weeks. The phase is suggested to eradicate detectable leukemia cells in peripheral blood and bone marrow, moreover, returning the normal hematopoiesis. Despite mild nausea and vomiting, the patient's appetite increases and weight gain; no alopecia nor febrile neutropenia were reported during chemotherapy.

Fetal monitoring was performed with CTG and FHR before and after chemotherapy. Pregnancy was maintained, and planned termination was set at 34 weeks of gestation because of chemotherapy hematological toxicity in the last 4 weeks of pregnancy. The fetus was finally delivered at 32 weeks of gestation by section cesarean (SC) due to premature rupture of the membrane. An alive baby girl weighed 1700 grams was born, APGAR Score 8/9/9. There were no defects, either clinically or hematological features, at the time. The patient shall continue the chemotherapy regimen to the consolidation phase. However, it is unfortunate that the patient lost to follow-up thus both treatment and surveillance are impossible to be done.

DISCUSSION

ALL is rare in adults and even more uncommon in pregnancy. In the previous study, the incidence of acute leukemia reported a single case per 75000 pregnancies, with only 28% cases of ALL.[9] The management of all cancer types in pregnancy is a huge challenge for physicians, mothers, and the fetus. The long-time follow-up is also needed on the children whose mothers receiving chemotherapy during pregnancy. Those difficulties are more profound in developing countries such as Indonesia. Lost to follow-up often happens because of various reasons, ranging from adverse effects, lack of health insurance coverage, beliefs and cultural considerations, to a confusing health system.

Our patient represents a great challenge in treating leukemia during pregnancy. Higher risk of other pregnancy complications on her age (36), remarkable weight loss during pregnancy, and bycitopenia indicated that closed monitoring should be performed to reach the treatment goals. The risk of bleeding and infection increased on the delivery and higher risk of premature rupture of the membrane. The consequence of leukemia in pregnancy can be lead by leukemia itself or lead by chemotherapy-induced.[10] The timing of fetal exposure to chemotherapeutic agents is one of the main factors of pregnancy outcome.

According to the morphology FAB of bone marrow smears in this patient, the cell distribution was suggestive of ALL-L2, which consists of larger lymphoblast cells but vary in size; chromatin is coarser with one or more nucleoli. Immunophenotyping is performed using bone marrow blood samples to differentiate between T-cell or B-cell leukemia. Adjusting the CD markers owned by our health facilities in these patients, it was found HLA-DR (+), CD10 (+), CD19 (+), CD20 (+) so that it supports the L-Line B lymphoid image. CD19 antigen appears earliest during B cell ontogeny and is expressed in almost all cases of B-lineage ALL.

The currently available guideline in Indonesia for ALL refers to the Indonesian Acute Lymphoblastic Leukemia 2013 protocol. However, the consideration of pregnancy condition in ALL is still not specified. ALL chemotherapy regimes usually have a higher dose compared to solid tumor. The prognosis of patients made through age, cytogenetic assessment, white blood cell count, and the duration to reach CR. It is advisable to start the chemotherapy when the cure is very likely regardless

of gestational age because the outcome of delayed therapy is way worse.

ALL is a heterogeneous disease at the genetic level. Chromosome analysis is used to prognostic consideration, and a predictive biomarker to provide subtype, outcome, and drug response information. In ALL, existing of Philadelphia chromosome is important to determining chemotherapy regimen, as TKI highly improved the CR of ALL with the positive mutation. However, in our case, the cytogenetic and molecular examination was not performed due to several reasons. The chromosomal examination would not differ the chemotherapy regimen because the safety issue of TKI on pregnancy has not been established. The pro and cons of TKI on pregnancy have been debated for quite some time; TKI was reported to causes adverse events and congenital malformation in several literatures. Still, many critics also came for its validity. In this case, TKI was decided not to deliver to the patient, and further follow-up treatment showed an improved overall condition.

At that time the family refused to do chromosome analysis because it wont make big changes in therapeutic regimen for saving mother and the baby, considering the regimen that had been used is single chemotherapy : vincristine, to lower the side effect of chemotherapy but still should be considered later for continuing the regimen of chemotherapy in order to achieved a complete remission.

CONCLUSION

ALL is not a common occurrence during pregnancy. Treatment is challenging for doctors, patients, and the unborn fetus. In this case report, induction chemotherapy was performed while maintaining the pregnancy as it entered the 2nd trimester. The baby was delivered at 32 weeks by CS on obstetric indications. Complications in pregnancy, including infection and bleeding, should be predicted at delivery because of anemia, neutropenia, and thrombocytopenia in the patient. This report aimed to provide insight into clinical judgment and decision-making with a risk-benefit assessment in future similar cases. In this case the patient was having a first pregnancy in advanced maternal age mother with high social value baby and can be treated successfully using single regimen of chemotherapy during pregnancy even though at the first time administered to hospital the mother come with critical clinical presentation. The suggestion of follow-up chromosome analysis/cytogenetic examination is still needed for the continuation of the therapeutic regimen. The patient and family should better understand the prognosis, potential recurrence, child monitoring, and the next possible pregnancy outcomes to avoid losing treatment follow-up.

ACKNOWLEDGMENTS

The author would like to thank dr. Dwi Retnoningrum, Sp.PK for her enthusiasm, knowledge and attention to detail have been an inspiration in developing this case report from my first encounter to the final draft. The author would like to thank dr. Herniah Asti Wulanjani Sp.PK as well for the advice, support, and unexpectedly shared the invaluable information about the hematological presentation in this case.

REFERENCES

1. Fracchiolla NS, Sciumè M, Dambrosi F, Guidotti F, Ossola MW, Chidini G, et al. Acute myeloid leukemia and pregnancy: Clinical experience from a single center and a review of the literature. BMC Cancer. 2017;17(1):1–8.
2. Ticku J, Oberoi S, Baidas S, Friend S, Busowski J, Langenstroer M. Acute lymphoblastic leukemia in pregnancy: A case report with literature review. Ther Adv Hematol. 2013;4(5):313–9.
3. Bl K, Padma M, Lokanatha D, Kumari P, C OR. Research article landscape of additional chromosomal abnormalities in philadelphia chromosome positive Acute Lymphoblastic Leukemia : 5 years experience of a regional cancer center in south east asia. 2019.
4. Seol CA, Cho YU, Jang S, Park CJ, Lee JH, Lee JH, et al. Prognostic significance of recurrent additional chromosomal abnormalities in adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Cancer Genet [Internet]. 2017;216–217:29–36. Available from: http://dx.doi.org/10.1016/j.cancergen.2017.06.001
5. Report C, Khandaker S, Munshi S. A Rare Case of Acute Lymphoblastic Leukaemia in Pregnancy-Unique Maternal-Fetal Challenges. 2014;8(10):10–3.
6. Jiao Q, Bi L, Ren Y, Song S, Wang Q, Wang Y shan. Advances in studies of tyrosine kinase inhibitors and their acquired resistance. Mol Cancer. 2018;17(1):1–12.
7. Balsat M, Etienne M, Elhamri M, Hayette S, Salles G, Thomas X. Successful pregnancies in patients with BCR-ABL-positive leukemias treated with interferon-alpha therapy during the tyrosine kinase inhibitors era. Eur J Haematol. 2018;101(6):774–80.
8. Ikatan Dokter Anak Indonesia. Protokol Pengobatan Leukemia Limfoblastik Akut Anak - 2013 (Indonesian Childhood ALL - 2013 Protocol). Ikat Dr Anak Indones. 2013;2013:1–36.
9. Zaidi A, Johnson L-M, Church CL, Gomez-Garcia WC, Popescu MI, Margolin JF, et al. Management of Concurrent Pregnancy and Acute Lymphoblastic Malignancy in Teenaged Patients: Two Illustrative Cases and Review of the Literature. J Adolesc Young Adult Oncol. 2014;3(4):160–75.
10. Baltazar C, Lopez S, Pertida P et al. Leukemia during pregnancy. Obstet Gynecol Int J 2017, 6(6): 00225.