CASE REPORT

A Lethal Case of Chronic Myeloid Leukemia in Accelerated Phase Presenting in Labor

Yajnaseni Banerjee[1], Arundhati Tilve[2]

Received on: 11 June 2024; *Accepted on*: 10 July 2024; *Published on*: 14 August 2024

Abstract

Background: Chronic myeloid leukemia (CML) is a hematological malignancy caused by the expression of the aberrant oncogene "BCR-ABL" attributed to t (9:22) Philadelphia translocation. The coexistence of pregnancy and CML is rare; less than 1 in 100,000. Managing a case of CML in pregnancy remains a clinical dilemma due to serious ethical and therapeutic implications which chemotherapy during pregnancy can pose for the fetus like various congenital malformations, abortion, and intrauterine growth restriction.

Case description: We present a case report of a 28-year-old female at 34.2 weeks of gestation with previous 2 lower segment cesarean sections in preterm labor. The patient was a known case of CML on Imatinib mesylate, who opted to discontinue chemotherapy in view of her ongoing pregnancy. She subsequently presented in labor in accelerated phase of CML, further complicated by placental abruption. Following an emergency cesarean section and ensuing disseminated intravascular coagulation (DIC), she ultimately succumbed to tumor lysis syndrome despite multidisciplinary critical care management.

Conclusion: The treatment of pregnant women with CML is challenging due to limited therapeutic options with sparse data regarding safety in pregnancy. Conception should be planned after achieving major molecular response and continuation of pregnancy and chemotherapy needs to be individualized after detailed counseling involving the obstetrician and the hemato-oncologist. Our case report, hereby, aims to emphasize the importance of preconceptional counseling, shared decision-making, and rigorous follow-up during pregnancy.

Keywords: Abruptio placentae, Accelerated phase, Case report, Chemotherapy, Chronic myeloid leukemia, Disseminated intravascular coagulation, Imatinib, Tumor lysis syndrome, Tyrosine kinase inhibitor.

Journal of South Asian Federation of Obstetrics and Gynaecology (2024): 10.5005/jp-journals-10006-2483

Introduction

Chronic myeloid leukemia (CML) is a chronic myeloproliferative neoplasm where a reciprocal translocation between the long arms of chromosomes 9:22 t (9:22) (q34,q11) results in the BCR-ABL fusion gene which encodes an onco-protein with tyrosine kinase activity. Chronic myeloid leukemia accounts for 30–60% of all adult leukemia making it one of the commonest adult leukemia in Indian population.[1] The median age of presentation in Indian population is almost 10 years lesser than that reported in European (median age is 55 years) or American (median age is 66 years) literature.[2] However, the prevalence of CML in pregnancy is less than 1 in 10,000.[3] With tyrosine kinase inhibitors (TKI) becoming the mainstay of treatment of CML, the situation gets challenging in pregnancy owing to the potential teratogenic effects of TKIs vs the risk of relapse or disease progression on cessation of treatment.[4]

[1,2]Department of Obstetrics & Gynaecology, Topiwala National Medical College & BYL Nair Charitable Hospital, Mumbai, Maharashtra, India

Corresponding Author: Yajnaseni Banerjee, Department of Obstetrics & Gynaecology, Topiwala National Medical College & BYL Nair Charitable Hospital, Mumbai, Maharashtra, India, Phone: +91 9372904841, e-mail: b.yajnaseni93@gmail.com

How to cite this article: Banerjee Y, Tilve A. A Lethal Case of Chronic Myeloid Leukemia in Accelerated Phase Presenting in Labor. J South Asian Feder Obst Gynae 2024;16(Suppl 2):S103–S105.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Case Description

A 28-year-old G3P2L2 female reported to the labor room with complaints of pain abdomen since the past 5 hours at 34.2 weeks of gestation. The patient had undergone two previous lower segment cesarean sections and had two living children aged 6- and 4-year-old, respectively. At the time of presentation, she was a diagnosed case of CML since last 1 year and was following up with the Department of Hematology. When the patient had first presented with on and off fever and progressively increasing fatigue, her peripheral smear was tested as a part of anemia work up. Owing to abnormal cells seen, a bone marrow aspiration was performed. When cytogenetic studies were performed, the report was positive for the presence of "Philadelphia chromosome." The patient was diagnosed with CML and was started on imatinib mesylate 400 mg/day. She achieved complete hematological response in 7 months. An image of her peripheral smear during remission phase is presented here (Fig. 1). However, she discovered that she was pregnant and discontinued imatinib by herself. She registered with the Department of Obstetrics and Gynaecology at 27 weeks where her routine antenatal investigations were done and an urgent hematology review was advised. Her malformation scan showed no gross congenital anomalies and her routine obstetric ultrasound (USG) showed normal growth of the fetus and adequate liquor. Unfortunately, the patient was lost to follow-up at

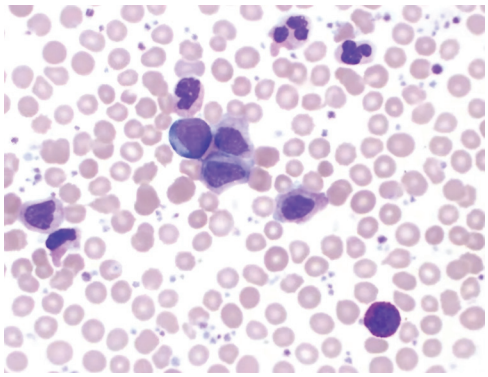

Fig. 1: Peripheral smear of patient in remission phase of chronic myeloid leukemia

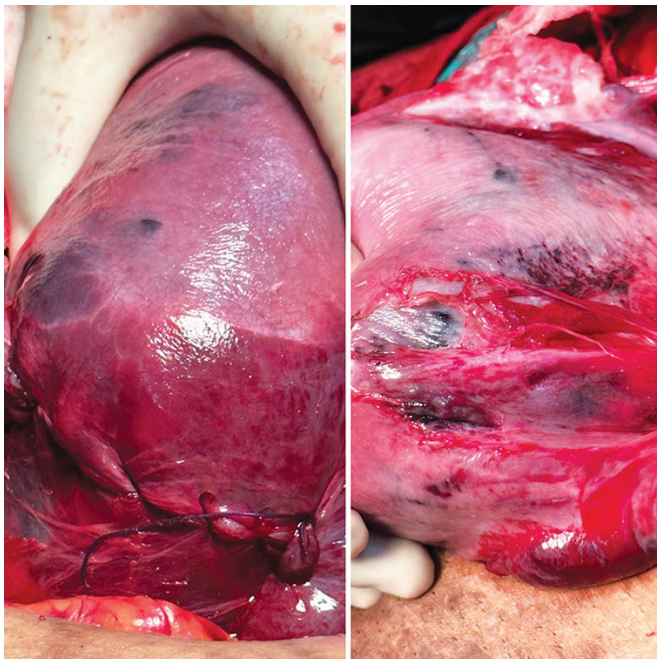

Fig. 2: Intraoperatively diagnosed Couvelaire uterus

both hematology and obstetrics for the next 3 months. When she presented to the labor room, she was already in preterm labor. Her complete blood count and peripheral smear on admission showed WBC count of 95,000/µL with 10% myeloblasts, 7% promyelocytes, 9% myelocytes, 6% metamyelocytes, 52% neutrophils, 10% eosinophils, 2% monocytes, and 3% lymphocytes. Hemoglobin was 9.5 gm/dL and platelet count 1.89 lakh/µL. Her renal and liver function tests and PT-INR were within normal limits. Hematology review was obtained and the patient was diagnosed to be in accelerated phase of CML based on the presence of 10% blast cells. Patient was advised to be restarted on imatinib 400 mg/day. Additionally, hydroxyurea was planned to be added at 2 gm per day immediately post-delivery. Clearance for emergency cesarean section was obtained with consultation of the hematologists. Intraoperatively, abruptio placentae was diagnosed with a retroplacental clot of 600 gm and Couvelaire uterus was noted (Fig. 2). Miraculously, a female child with an APGAR of 8 and 9 at 1 and 5 minutes of life weighing 1.8 kg was delivered. Uterus was closed in 2 layers using continuous non-interlocking technique with an absorbable suture. A total of 2 units of packed cell were issued along with 4 units of fresh frozen plasma (FFP). Subsequently, fresh bleeding was noted from peritoneal surfaces, subcutaneous tissue layer, and edges of the skin incision which raised the suspicion of disseminated intravascular coagulation (DIC). A total of 1 gm tranexamic acid was infused, 2 more units of PCV, 4 more units of FFP, and 4 platelets were arranged for transfusion. After a grueling 2.5 hours of surgery, patient was shifted to ICU for monitoring. Imatinib and hydroxyurea was started. Patient was apparently stable on postoperative day 1. However, on postoperative day 2, the hemoglobin had dropped to 6 gm/dL, WBC counts were 88,000/µL with 12% blasts, 70% neutrophils, 8% eosinophils, 2% monocytes, and 3% lymphocytes. Platelet count was 75,000/µL, and INR was 4. There was 700 cc of fresh blood in the intraperitoneal drain with an increase of abdominal girth by 5 cm. Bedside USG was suggestive of hemoperitoneum of 1 L with perihepatic and peri splenic hemorrhage. The patient's renal functional tests were suggestive of acute kidney injury (Sr. creatinine 3 mg/dL), liver function was deranged (total bilirubin - 4.5 mg/dL, ALT - 2000 IU/mL, AST - 1500 IU/mL, LDH - 3500 IU/mL), uric acid was 10 mg/dL and corrected calcium was 6.9 mg/dL. After a multidisciplinary meeting involving departments of internal medicine, hematology, nephrology, and gastroenterology, the patient was diagnosed to be in multiorgan dysfunction syndrome (MODS) secondary to tumor lysis syndrome. Aggressive corrective measures including lyophilized factor 7 (marketed as NovoSeven) to combat the patient's DIC was attempted. The patient succumbed early on postoperative day 4 despite all resuscitative efforts. Postmortem report showed diffuse microthrombi and plugs of cancerous hematogenous cells in liver, spleen, kidney, and lungs. The uterus showed no hemorrhage and was in postpartum status. The bone-marrow was hypercellular. The baby was in neonatal intensive care unit (NICU) for 2 weeks for low-birth weight but ultimately went home with her relatives and was called for cytogenetic studies after 3 months.

Informed written consent was taken from the patient's husband in accordance with the Declaration of Helsinki before submission of this case report.

Discussion

Chronic myeloid leukemia accounts for approximately 10% cases of pregnancy-associated leukemia yet there is no universal algorithm for management of such cases till date.[1] Drugs like tyrosine kinase Inhibitors, hydroxyurea, interferon alfa, and leukapheresis form the mainstay of treatment of CML in pregnancy despite the paucity of safety data with regards to the fetus.[5] Moreover, no option is proven to be superior over the other. The management depends on not only how far along the pregnancy is but also on the status of the disease. While immediate commencement of chemotherapy for a woman in accelerated or blast phase of CML seems prudent, early delivery may be considered after balancing the prematurity of the fetus against the benefit of starting extensive chemotherapy for the mother. For CML in accelerated phase during first trimester, the patient may be offered termination of pregnancy after requisite discussion with the obstetrician, hematologist and/or other disciplines.[6] The patient's reproductive goals, disease status, current therapy, and availability of other alternative therapies must be considered before a definitive treatment plan is made. In cases of complete molecular remission (CMR) or complete cytogenetic response (CCyR) for at least 2 years, few patients have reportedly stopped TKI with no adverse outcomes.[4] All such patients should be followed-up regularly with blood counts,

peripheral smear, and other necessary investigations. For patients not on any therapy, yet continued remission, intensive surveillance and restarting TKIs post-delivery could be considered in cases where remission is lost, leukapheresis in the first trimester and IFN-α and/or leukapheresis in the second and third trimesters can be considered.[4,6]

Conclusion

For a known case of CML, detailed preconceptional counseling and rigorous clinical, biochemical, and image-based monitoring may lead to a safe pregnancy for both the mother and fetus with positive outcomes for both. However, further research for safer and standardized treatment options is necessary to allow clinicians and patients to make informed decisions.

Orcid

Yajnaseni Banerjee https://orcid.org/0009-0009-6143-8675
Arundhati Tilve https://orcid.org/0000-0001-9565-9729

References

1. Pentheroudakis G, Orecchia R, Hoekstra HJ, et al. Cancer, fertility and pregnancy: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 (suppl 5):v266–v273. DOI: 10.1093/annonc/mdq198.
2. Bansal S, Prabhash K, Parikh P. Chronic myeloid leukemia data from India. Indian J Med Paediatr Oncol 2013;34(3):154–158. DOI: 10.4103/0971-5851.123711.
3. Prabhash K, Sastry PS, Biswas G, et al. Pregnancy outcome of two patients treated with imatinib. Ann Oncol 2005;16(12):1983–1984. DOI: 10.1093/annonc/mdi398.
4. Chowdhury TS, Jereen I, Chowdhury TA. Pregnancy with chronic myeloid leukemia: Case report and literature review. Int J Reprod Contracept Obstet Gynecol 2019;8(12):5046–5049. DOI: 10.18203/2320-1770.ijrcog20195369.
5. Apperley J. Issues of imatinib and pregnancy outcome. J Natl Compr Canc Netw 2009;7(10):1050–1058. DOI: 10.6004/jnccn.2009.0069.
6. Bhandari A, Rolen K, Shah BK. Management of chronic myelogenous leukemia in pregnancy. Anticancer Res 2015;35(1):1–11. PMID: 25550528.