Annals of Clinical Case Reports

Case Report
Published: 25 Jan, 2022

Multidisciplinary Management and Antenatal Care of a Third-Trimester Pregnancy Complicated with a Hasty Breast Burkitt Lymphoma with Atypical Symptoms

Zhong Hua[1#], Iqra Ijaz[2#], Muhammad Naveed Shahzad[3,4#], Duanyi[5], Hu Gaoyun[6], Faiza Nawaz Satti[7], Fu Xiao Dong[1] and Lubna Ejaz Kahloon[7]**

[1]Department of Obstetrics, First Affiliated Hospital of Southwest Medical University, PR China

[2]Sichuan Provincial Center for Gynecological and Breast Diseases, Southwest Medical University, PR China

[3]Department of Hematology, Stem Cell Laboratory, The Affiliated Hospital of Southwest Medical University, PR China

[4]Department of Medicine, Holy Family Hospital, Pakistan

[5]Department of Pathology, First Affiliated Hospital of Southwest Medical University, PR China

[6]Department of Radiology, First Affiliated Hospital of Southwest Medical University, PR China

[7]Department of Obstetrics and Gynecology, Holy Family Hospital, Pakistan

[#]These authors contributed equally to this work

OPEN ACCESS

***Correspondence:**

Fu Xiao Dong, Department of Obstetrics, First Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan, PR China, Tel: +86-830-3160283; Fax: +86-830-3160283; E-mail: sirinihao@163.com

Lubna Ejaz Kahloon, Department of Obstetrics and Gynecology, Holy Family Hospital, Rawalpindi, Pakistan, Tel: +92-3455540343; E-mail: drlubnaejaz@gmail.com

Received Date: 31 Dec 2021

Accepted Date: 20 Jan 2022

Published Date: 25 Jan 2022

Citation:

Hua Z, Ijaz I, Shahzad MN, Duanyi, Gaoyun H, Satti FN, et al. Multidisciplinary Management and Antenatal Care of a Third-Trimester Pregnancy Complicated with a Hasty Breast Burkitt Lymphoma with Atypical Symptoms. Ann Clin Case Rep. 2022; 7: 2110.

ISSN: 2474-1655

Abstract

Pregnancy with Primary Breast Burkitt Lymphoma (PBBL) is a highly aggressive Non-Hodgkin's Lymphoma (NHL), currently reports as sporadic cases. Here is a case of a 34-year-old lady, with gestational age of 28 weeks, who presented with an abrupt appearance of Burkitt Lymphoma (BL) treated in a tertiary care hospital. The initial unusual presentation with an enlarged protruding right eyeball was quite a puzzle. Non-resolving Unilateral (U/L) proptosis and sustained mastitis led to a Multidisciplinary Team (MDT) discussion for the management of the pregnant patient. Ultimately through a chain of investigations, the culprit was detected and most importantly the patient agreed to receive the antenatal combined chemotherapy with R-CHOP regime instead of labor induction or postponing treatment until term delivery. Afterward, during the early chemotherapy period at 32^{+} weeks, a healthy premature baby was delivered smoothly by the vaginal route, weighing 1,510 g with a good Apgar score. Later in the course, postnatal Intrathecal Chemotherapy (ITC) was administered as the patient's sensorium was affected due to lymphoma infiltration to the Central Nervous System (CNS). The patient's symptoms were relieved quite a bit as soon as the therapy ensued. But unfortunately, due to an aggressive refractory malignancy, it could not be controlled and the patient survived a year after the diagnosis. We believe that MDT plays a pivotal role in establishing the diagnosis and tailoring treatment of such rare, complicated and challenging obstetrical cases. Therefore this aspect should always be taken into account as early as possible for speedy decision-making for obstetrics cases with atypical Signs and Symptoms (S/S).

Keywords: Lymphoma; Pregnancy; Antenatal chemotherapy; Multidisciplinary analysis

Abbreviations

BL: Burkitt Lymphoma; PBBL: Primary Breast Burkitt Lymphoma; NHL: Non-Hodgkin's Lymphoma; MDT: Multidisciplinary Team; CNS: Central Nervous System; B/L: Bilateral; USG: Ultrasonography; MRI: Magnetic Resonance Imaging; IHC: Immunohistochemistry; DWI: Diffusion-Weighted Imaging; CT: Computed Tomography; NICU: Neonatal Intensive Care Unit; PET-scan: Positron Emission Tomography scan; G-CSF: Granulocyte-Colony Stimulating Factor; MIP: Maximum Intensity Projection; HIV: Human Immunodeficiency Virus; OS: Overall Survival

Introduction

Lymphoma in pregnancy is rare with an incidence of 1 in 6,000 births [1,2]. PBBL is an extremely rare, highly aggressive tumor, growing in pregnancy with an incidence rate of 0.04% to 0.5%. Average-age of onset is 55 years but seldom seen at age <35 years. Stages I & II have good prognosis of about 90% if treated timely, but in more advanced stage when CNS is involved survival reduces

to as low as 0% to 30% [1-22]. Literature reports 21 cases of PBBL associated with pregnancy, 16 were diagnosed during pregnancy [3-15] and 5 in lactation [4,16,17], with mean age of 29.9 years (ranging 15 to 42). Out of 16 cases diagnosed during pregnancy, 11 were in 3rd trimester, whereas 4 and 1 in 2nd and 1st trimester, respectively. The reported OS among 21 cases was <1 month in 9, <6 months in 4 and one case had 10 month survival. Whereas, 6 were disease free at 12+ months after aggressive treatment. Pregnancy complicated with Lymphoma is extremely challenging to manage, partly by fact that it's thought to be untreatable, and partly by the patient's fear of antenatal-chemotherapy being harmful to her baby. We report the first case from China, for PBBL diagnosed in the 3rd trimester. Our patient mindfully accepted to undergo antenatal-chemotherapy. Initially, R-CHOP regimen was started, and meanwhile, a premature healthy baby was delivered. Later, postnatally ITC was added for CNS infiltration and more potent drugs including R-DA-EPOCH regimen were used for this nasty cancer. R-CHOP regimen is considered safer in 2nd and 3rd trimester except for increased risk for preterm delivery [18]. Thus, current recommendation for treatment of BL depends on the time of presentation in pregnancy, nature of the disease, and patient preference [19].

Case Presentation

A 34-year-old pregnant patient ($G_4P_2A_1$) was admitted to our inpatient in 28th week of gestation with unresolved Bilateral (B/L) swollen breasts and extensive right proptosis for three weeks. The initial outpatient treatment opted for mastitis and inflammatory pseudotumor, and remained futile. Therefore, inpatient admission was advised to assess her thoroughly to catch the culprit. On clinical examination, vital signs were normal, there was obvious right proptosis without tenderness, and B/L breasts were diffusely swollen, without redness or palpable lump. The gravid uterus was palpated with fetal touches, along with a hard density mass mimicking the fetal head, on the left side of the uterus. Mild physiologic edema was noted on the lower extremities. Patient gave the history of viral hepatitis 10 years ago which was effectively treated and two Cesarean-Sections (CS) 10 and 7 years ago and had two healthy daughters. At admission, her hemoglobin level was 100 g/L, white cell count 7.6 × 10^9/L and platelet count was 280x10^9/L. The viral markers suggested chronic HBV carrier status, but HIV & Epstein Barr Virus (EBV) were negative. The obstetric-Ultrasonography (USG) showed an intrauterine single alive fetus and an uneven hypoechoic mass measuring 15.2 cm × 9.8 cm (clear boundary and regular shape) was observed on the left side of the uterus, probably a uterine fibroid. The breast color Doppler USG, showed B/L inflammatory changes along with axillary accessory breast tissue, importantly swollen axillary lymph nodes with size of 1.3 cm × 0.6 cm on right and 1.2 cm × 0.5 cm on the left. The result of the binocular (magnetic resonance imaging) MRI. Treatment for symptomatic relief went in vain, besides only aggravating her signs and symptoms. Therefore, it prompted MDT discussion (Obstetrics and Gynecology, Infectious Diseases, Breast Surgery, Neurology, Ophthalmology) for management and to dig out for unknown disease. Relevant examinations proposed by each department were carried out to detect the root cause of her condition. Breast MRI was suggested but as it needs prone positioning, alas to rely on USG, wherein findings remained the same. However, current obstetric USG showed increased size of left sided mass to 16.7 cm × 11.6 cm and, another mass with regular shape measuring 12.2 cm × 9.0 cm seen on right of the uterus, both masses appeared with unclear boundaries and abundant blood flow signals. It was opted to take a biopsy of the right axillary mass under local anesthesia with patient's consent. The microscopic histopathologic and Immunohistochemistry (IHC) results of the core biopsy confirms the diagnosis of BL. To know more precise characteristics of the masses, abdominal MRI was performed; chest CT-scan was ordered to see the metastatic status and chemotherapeutic consideration. As it was quite clear what the patient was going through, hence the MDT, now including a hematologic oncologist recommended, preferably postponing the cesarean section if patient agrees and to start the combined chemotherapy immediately. The patient was risk-stratified as high intermediate based on the International Prognostic Index score.

Once everything was made clear to the patient about her diagnosis of BL and treatment options, she chose antenatal chemotherapy. The prophylactic treatment of entecavir was given prior to commencement of chemotherapy. Pretreatment with dexamethasone and Polyene phosphatidylcholine was given and R-CHOP regimen was started. As soon as the therapy was initiated, the patient responded well, proptosis and breast swelling reduced remarkably.

Chemotherapy became a challenge when the patient developed short lived psychosis just before baby's birth, anticipating that lymphoma had infiltrated CNS causing Lymphomatous meningitis. Pregnancy-related symptoms were aggravated (shortness of breath, palpitations) due to ongoing chemotherapy. Meanwhile the patient developed neutropenia after the 2nd-chemo cycle, and went into labor and vaginally delivered a premature (32+2 weeks) alive and healthy baby weighing 1,510 g with Apgar score 8 and 10 at 1 and 5 min respectively, without any apparent anomaly. The baby was transferred to Neonatal Intensive Care Unit (NICU) for prematurity. ITC was added on day 1 followed by R-CHOP regimen for positive CSF report (presence of white blood cells, cue protein, and lactate dehydrogenase 71.0 U/L) clarifying the infiltration. ITC worked well and psychosis symptoms disappeared quickly. When patient developed Tumor Lysis Syndrome (TLS) after 2nd cycle, she was rehydrated, urine alkalinization with sodium bicarbonate, febuxostat to lower uric acid, furosemide for diuresis, and hypertonic sugar with insulin to promote potassium transfer to cells, were administered to further prevent the occurrence of TLS. For raised liver enzymes, reduced glutathione injection and human serum albumin were added. The post chemotherapy myelosuppressive period of neutropenic fever, was managed with antibiotics, blood products and recombinant human Granulocyte-Colony Stimulating Factor (G-CSF) to rescue leukocytes. However, as the patient's condition remained unchanged with subsequent chemo, the bone marrow biopsy was taken. Further, a more potent drug Etoposide was added to the regimen for refractory PBBL. Later in the course of aggressive therapy when the patient did not show any improvement, Positron Emission Tomography (PET-CT) examination was performed, which revealed the distant spread sign of failed treatment. Patient requested to stop chemotherapy except only for the symptomatic relief. By now she had completed 11 cycles of systemic chemotherapy and 25 ITC injections but unfortunately being very aggressive nature of the malignant tumor is metastasized abruptly making it difficult to control and required further chemotherapy. Patient was encouraged to continue treatment but she abandoned and died due to multi organ failure after 6 weeks, with an overall survival of 12+ months.

Comments

Lymphoma type and S/S during pregnancy are not different from

non-pregnant women. Currently, there is no evidence that pregnancy accelerates development of lymphoma, but some say, its pathological type in pregnancy seems more malignant therefore gives poor prognosis. Misdiagnosis is common, often due to atypical clinical manifestations or considering otherwise physiological pregnancy-related changes making it difficult to distinguish from hyperhidrosis of lymphoma so delaying diagnosis [23]. Some risk factors induce the occurrence of malignant lymphomas, such as infections including EBV, HIV, ionizing radiation etc [20]. Our patient had a history of infection with HBV, was adequately treated but it's highly suspicious whether this chronic infection was a predisposing factor of this attack? BL affecting pregnant women requires prompt diagnosis and should be managed immediately with an aggressive therapeutic approach. Ideally, for patients with limited early disease, pregnancy should be terminated and radiotherapy be started when diagnosed in the first half. While in the second half, combined chemotherapy can be started antenatally, and radiotherapy be added after the fetus is born [23]. Our case presented in the 3rd trimester, diagnosis was delayed for 3 weeks due to atypical symptoms but multidisciplinary approach helped greatly. Even though termination of pregnancy by cesarean-section was an option to ensure timely aggressive treatment, as the prognosis of the premature newborn is good, but our patient preferred antenatal-chemotherapy. On the other hand, to avoid fetal exposure to radiation, several imaging examinations are restricted, so it further delays the diagnosis and the best time for therapy is missed. Therefore, it is suggested that for pregnant women with unexplained fever, fatigue, bleeding tendency or abnormally increased blood cells, and progressive anemia, further relevant tests, even bone marrow testing should be considered. Quality of prenatal examinations should be improved for early detection of disease to ensure timely treatment. In past, it was believed if pregnancy with lymphoma is diagnosed, labor should be induced immediately, the main reasons were, and active treatment with low molecular weight cytotoxic agents in the 1st trimester has potentially negative effects on the fetus [23]. Complications predictable for 2nd and 3rd-trimester are fetal or neonatal death, preterm delivery, low birth weight, and severe bone marrow suppression secondary to disease and treatment endangers mother and fetus at any time [18]. But so far there is no conclusive evidence that induction of labor is beneficial for prognosis. Therefore, if the condition itself is not critical, it is worth taking the pregnancy to the middle and late stages of pregnancy under close monitoring [18]. Our patient exhibited significant respiratory depression and altered sensorium, but her condition stabilized when ITC was started. Therefore, the author personally prefers to terminate pregnancy once the organ dysfunction occurs in middle and late stages of pregnancy. Despite the possible complications the overall advantage of the treatment is clear; hence the current recommendation is to administer chemotherapy with continuation of pregnancy.

Conclusion

Managing lymphoma in pregnancy poses significant diagnostic and treatment challenges. Additionally, treatment related decisions require a balance of feto-maternal risks posed by tumor and its therapy on a case-to-case basis.

References

1. Rizack T. Management of hematological malignancies during pregnancy. Am J Hematol. 2009;84(12):830-41.
2. Pereg D, Koren G, Lishner M. The treatment of Hodgkin's and non-Hodgkin's lymphoma in pregnancy. Haematologica. 2007;92(9):1230-7.
3. Bannerman RJBMJ. Burkitt's tumour in pregnancy. Br Med J. 1966;2(5522):1136.
4. Shepherd J, DJJBS Wright. Burkitt's tumour presenting as bilateral swelling of the breast in women of child-bearing age. Br J Surg. 1967;54(9):776-80.
5. Armitage JO, Feagler JR, Skoog DPJJ. Burkitt lymphoma during pregnancy with bilateral breast involvement. JAMA. 1977;237(2):151.
6. Jones D. Burkitt's lymphoma: Obstetric and gynecologic aspects. Obstet Gynecol. 1980;56(4):533-6.
7. Illes A. Bilateral primary malignant lymphoma of the breast during pregnancy. Orv Hetil. 1996;137(24):1315-7.
8. Fadiora S. Generalised Burkitt's lymphoma involving both breasts-a case report. West Afr J Med. 2005;24(3):280-2.
9. Miyoshi I. Burkitt lymphoma of the breast. Am J Hematol. 2006;81(2):147-8.
10. Cordeiro A. Burkitt's lymphoma related to Epstein–Barr virus infection during pregnancy. Arch Gynecol Obstet. 2009;280(2):297-300.
11. Savvari P. Burkitt's lymphoma in pregnancy with bilateral breast involvement: Case report with review of the literature. Onkologie. 2010;33(8-9):461-4.
12. Serikawa T. A case report of fatal tumor lysis syndrome after chemotherapy in a pregnant patient with Burkitt's lymphoma. J Obstet Gynaecol Res. 2011;37(8):1141-4.
13. Hurley P. Burkitt lymphoma in pregnancy: Two cases of successful treatment and continued fertility; with a review of the literature. Clin Lymphoma Myeloma Leuk. 2013;13(6):e10-4.
14. Testa AC. Burkitt's lymphoma of the breast metastatic to the ovary diagnosed during pregnancy. Ultrasound Obstet Gynecol. 2013;42(3):364-6.
15. Foreste V. Gigantomastia during pregnancy due to Burkitt lymphoma. Eur J Breast Health. 2020;17(1):76-9.
16. Durodola JI. Burkitt's lymphoma presenting during lactation. Int J Gynaecol Obstet. 1976;14(3):225-31.
17. Nomizu T. Burkitt's lymphoma of the bilateral breasts presenting during lactation. Gan No Rinsho. 1986;32(9):1023-7.
18. Lee EJ. Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy for diffuse large B-cell lymphoma in pregnancy may be associated with preterm birth. Obstet Gynecol Sci. 2014;57(6):526-9.
19. Mattia AR, Ferry JA, Harris NL. Breast lymphoma. A B-cell spectrum including the low grade B-cell lymphoma of mucosa associated lymphoid tissue. Am J Surg Pathol. 1993;17(6):574-87.
20. Zagouri F. Cancer in pregnancy: Disentangling treatment modalities. ESMO Open. 2016;1(3):e000016.
21. Linet MS. Lymphoma incidence patterns by WHO subtype in the United States.
22. Jeanneret-Sozzi W. Primary breast lymphoma: Patient profile, outcome and prognostic factors. A multicentre rare cancer network study. BMC Cancer. 2008;8:86.
23. Evens AM. Lymphoma occurring during pregnancy: Antenatal therapy, complications, and maternal survival in a multicenter analysis. J Clin Oncol. 2013;31(32):4132-9.