Classical Hodgkin Lymphoma presenting in late pregnancy: A case report

Harpreet Kaur, MD[1], Bhavna, MD[1], Asmita Kaundal, MS[1], Pravesh Dhiman, MD[2], Manupriya Sharma, MD[3], Lokesh Rana, MD[4], Gaurav Jain, MD[4]

Department of Obstetrics & Gynecology, AIIMS, Bilaspur, HP., India, Department of Medical Oncology, AIIMS, Bilaspur HP, India, Department of Pathology, AIIMS, Bilaspur, HP, India, Department of Radiodiagnosis, AIIMS, Bilaspur, HP, India, Dr.Lal Path lab, Delhi, India

SUMMARY

Hodgkin Lymphoma (HL) is the fourth most common type of malignancy in pregnancy which accounts for around 3.2% of all the cases. Diagnosis is generally delayed in pregnancy due to physiological changes in pregnancy mimicking constitutional symptoms of lymphoma, hence high index of suspicion is required to diagnose such antenatal women in time to optimize the overall outcome. We present a case of 22-year-old Primigravida at 35 weeks period of gestation who presented to emergency with complaints of neck swelling for 5 days without any constitutional symptoms. The diagnosis of Hodgkin lymphoma was confirmed by lymph node biopsy. Induction of labour was done at 37 weeks with the uneventful birth of a healthy baby. After delivery CECT was done and stage III Hodgkin lymphoma was confirmed and patient was given 6 cycles of chemotherapy. Lymphoma in pregnancy presents a complex clinical scenario that requires careful consideration of both maternal and fetal factors throughout pregnancy. A multidisciplinary approach involving obstetricians, haematologist /oncologist, and neonatologists is essential to optimize the care of these patients and ensure the best maternal and fetal outcomes.

INTRODUCTION

Diagnosis of cancer during pregnancy is traumatic to the patient, and her family, and poses a challenge to the treating team. Cancer is diagnosed in 0.1%-0.7% of pregnancies and is the second most common cause of maternal mortality after pregnancy-related complications.[1] In pregnancy, usually, the diagnosis is delayed as the constitutional symptoms may mimic physiological changes of pregnancy. Lymphoma is the fourth most common type of cancer in pregnancy with Hodgkin's lymphoma (HL) being more common than non-Hodgkin lymphoma (NHL).[2] Management of lymphoma during pregnancy should be a multidisciplinary approach maintaining a fine balance of potential harmful effects of diagnostic as well as therapeutic intervention on fetal development without a compromise on the treatment. Whether to give chemotherapy during the antenatal period or delay till delivery and the type of chemotherapy depends on the extent of the disease, histopathological type, severity of the disease, and period of gestation at presentation.

CASE PRESENTATION

A 22-year-old Primigravida 35 weeks period of gestation presented to emergency with complaints of sudden onset neck swelling since last 5 days. There was no history of any fever, night sweats, cough, sore throat, weight loss, loss of appetite, or easy fatigability. A fine needle aspiration cytology (FNAC) taken at the regional hospital before her referral was suggestive of lymphoproliferative disorder and the patient was referred for further management to our institute. The patient was booked and supervised for the index pregnancy at a regional hospital and her antenatal period was uneventful till date. There was no significant past medical, surgical, or family history to report. On admission, her vitals were stable with normal general physical examination and no obvious pallor. There was a diffuse, nontender neck swelling with enlarged lymph nodes bilaterally. The largest lymph node was around 3x 3cm. The neck swelling was not moving with swallowing. There was no lymphadenopathy in the axilla or groin. Obstetrical examination revealed uterus corresponded with 32 weeks with flanks full, cephalic presentation with regular fetal heart rate. Her haemoglobin was 10.4g/dl, TLC 11.34x10^3/dl, platelets 3.55 lac/dl, and ESR 99mm/hour. TSH was raised 13.85 micro-IU/dl with normal T3, T4 and anti-TPO antibodies. Her serum urea was urea 11mg/dl, creatinine 0.5mg/dl, SGOT/PT/ALP 41U/L, 55U/L, 509U/L, LDH 414.2U/L, viral markers were non-reactive and coagulation profile was normal. USG for fetal well-being done at 16 weeks and 35 weeks and were normal for gestational age. USG neck was done which revealed a heterogeneously hypoechoic lesion in the supraclavicular region of size 6.7 x 4 cm with internal vascularity. Multiple enlarged lymph nodes with heterogenous echotexture with loss of fatty hilum seen in the bilateral cervical region at multiple stations. The thyroid gland appeared normal. USG chest was normal. Cervical lymph node biopsy was taken. Histopathology (HPE) confirmed the diagnosis of classical Hodgkin lymphoma [Fig.1]. Immunohistochemistry (IHC) showed CD15 +, CD30+, MUM1-ve and PAX5 weak +ve , ALK1-ve, CD 45-ve, OCT2-ve, CD3-ve, and CD20-ve pattern [Fig 2]. By time HPE report came, she was already 37 weeks, and after discussion in the medical tumor board meeting a decision for elective induction of labour was taken. Labour was induced with intracervical foley's catheter and tablet misoprostol 25 microgram simultaneously. She required 4 doses of misoprostol 25 micgrogram 4 hours apart . The patient had

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Corresponding Author: Asmita Kaundal
Email: drasmita_kaundal@yahoo.com

a full-term vaginal delivery of a girl child with a birth weight of 2320 grams with no gross congenital malformations. Apgar Score of 8,10 at 1 and 5 minutes. The patient was observed for 24 hours and underwent contrast enhanced computed tomography (CECT) neck, chest, abdomen for the staging and echocardiography (EHCO) as pre-treatment evaluation. ECHO was suggestive of mild MR, mild TR with normal biventricular function with mild circumferential pericardial effusion seen. CECT Neck, chest, and abdomen revealed the presence of an ill-defined soft tissue density mass lesion arising from the mediastinum and extending into apical and anterior segments of RUL having postcontrast attenuation value of 105 HU and measuring 7x7x10.2cm. The mass lesion extends into the pre-paratracheal region with compression of the trachea at the lower trachea and carina level. The lesion was seen to cause encasement of the ascending aorta and its branches, SVC, brachiocephalic vein, subclavian vein on the right side, and bilateral common carotid, however, no intraluminal extension/thrombus was seen. Mass was seen to displace the brachiocephalic vein, left common carotid artery, and left subclavian artery laterally causing mediastinal widening. Multiple enlarged peripherally enhancing bilateral axillary lymph nodes were noted, the largest on the left side measuring 4.2 x 2.3 cm seen in axial, sagittal and coronal view [Image 1 (a), (b), (c)]. Multiple enlarged peripherally enhancing lymph nodes were noted in cervical lymph node stations bilateral II, III, IV, and bilateral supraclavicular. Mild splenomegaly noted (Ann Arbor staging -III). She was planned for six cycles of ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) regimen chemotherapy by the medical oncology team. The patient and family were explained about the disease in detail, the possible risks and benefits of chemotherapy. Effect of chemotherapy on future fertility was discussed and available options for fertility preservation were discussed. Possible adverse effects of breastfeeding on the baby were discussed and milk suppression was given after discussion. The patient was then started on chemotherapy with an ABVD regimen which she tolerated well. She received 6 cycles of chemotherapy and her follow-up positron emission tomography-computed tomography (PET-CT) showed complete remission of the disease. Both mother and baby are doing well and are under follow up.

DISCUSSION

Lymphomas are the fourth most common type of malignancy in pregnancy after melanoma, breast cancer and cervical cancer.[1] Hodgkin lymphoma (HL) is more common than Non Hodgkin lymphoma (NHL).[2] Reported incidence of HL in pregnancy is around 1/1000-1/6000 deliveries. Symptoms of HL includes the development of palpable lymph nodes or constitutional symptoms like weight loss, night sweats, palpitations, and fatigue. Diagnosis is usually delayed in pregnancy as physiological changes of pregnancy mimic constitutional symptoms of lymphoma. Sometimes the patient may remain asymptomatic for a long period as in our case where swelling in the neck developed suddenly causing discomfort in neck at 35 weeks that brought her for evaluation. There were no constitutional symptoms in our patient.

Histopathology confirmation is must for the diagnosis. Imaging studies usually CT or PET combined with CT are required to stage patients with lymphoma. These tests cause significant radiation exposure to babies and are not recommended during pregnancy.[3] Chest X-ray with abdominal shield and ultrasound for abdominal assessment can be done. MRI without gadolinium administration can be used whenever required. Iodine-based contrast agents are contra-indicated during all stages of pregnancy.[4] In our case our patient presented at 35 weeks of pregnancy and by the time her diagnosis of HL was confirmed by histopathology she was already 37 weeks with no aggressive or high risk features requiring emergency management, hence delivery followed staging CECT was planned after discussion in the tumor board.

Mainstay of treatment for HL is chemotherapy. However chemotherapy can adversely effect the growing fetus. Hence, most crucial aspect in the management of HL is to decide on timing of initiation of chemotherapy and timing of delivery. It is good to prolong pregnancy to avoid preterm birth where-ever possible.[5] Teratogenic effect of chemotherapy administered to mother depends on period of gestation at exposure, dose of drug and type of drug given. Chemotherapy if administered between 2-8 weeks of pregnancy increases risk of congenital malformations and should be avoided. Treatment after thirteen weeks is considered safe and without teratogenic effect bur can be associated with preterm delivery, fetal growth restriction and low birth weight babies.[6] Most commonly used regimen for treatment includes bleomycin, doxorubicin, vinblastine and vincristine. This regimen is known to be safe when administered after first trimester.[7] Accurate assessment of prognosis is must to direct appropriate treatment at early phase. Moshe Y et al discussed about management of HL according to pregnancy stage and disease stage. During first trimester, termination of pregnancy after discussion and informed consent can be considered as one of the option in case waiting for few weeks can put the life of mother in danger. Vinblastine therapy or steroids only therapy can be considered in women who wants to continue pregnancy but treatment in necessary and cannot be postponed. In second and third trimester, early stage and advanced stage disease is treated with ABVP regimen for 4-6 months and 6-8 months respectively. In patients who are receiving chemotherapy during antenatal period their delivery should be postponed for 2-3 weeks following treatment for the bone marrow to regains its function. Lymphoma with supradiaphragmatic involvement can be treated with radiotherapy during pregnancy with adequate abdominal protection. Targeted therapy with Rituximab, a first-generation anti-CD 20 monoclonal antibody is known to cross the placenta, hence avoided during pregnancy. Management of advanced disease, visceral involvement, sub-diaphragmatic disease or disease with rapid progress remains controversial. As it increased the risk of abortion and congenital malformations with alkylating agents or multi-agent regimens such as MOPP (mechlorethamine hydrochloride, oncovin, procarbazine hydrochloride) & MOP (mechlorethamine hydrochloride, procarbazine hydrochloride), these drugs are to be best avoided during pregnancy.

Sometimes treated cases of HL present with relapse during pregnancy. Depending upon the time of appearance of symptoms after initial regimen relapse can be described as early (post ABVP <6 months) or late (beyond 6 months, especially if exposed to 2-4 cycles of ABVP only). In early relapse cases termination of pregnancy and treatment with second line regimen, high dose therapy or ASCT (Autologous stem cell transplantation), platinum and gemcitabine-based therapy can be considered. For late relapse cases ABVP during pregnancy, delivery and HDT/ASCT and alternate therapy with platinum /gemcitabine can be tried.[8]

Clinical features and prognosis are comparable in pregnant and non-pregnant patients and long term survival rate in patients in both groups is same. However, disease with advanced stage is common in pregnant women. Patients who are on chemotherapy in the postpartum period should be discouraged from breastfeeding, as most chemotherapeutic drugs can be excreted into breast milk and may cause potential risk to the baby.

The gold standard and first-line treatment in HL is the ABVD regimen showing a cure rate of 90% and is found to have very low gonadotoxic potential.[9] Some studies show that the ABVD regimen was associated with a significant fall in both ovarian follicle and endometrium thickness at 6 month follow-up time but it was followed by recovery at 12 months in both ovaries. So generally many young patients receiving this regimen are not offered fertility counselling. But 15-20% of cases are refractory to ABVP regimen or relapse on treatment or in need of salvage therapies that are usually more gonadotoxic and onco-fertility counselling is a must in those cases.[10] Embryo preservation is the oldest method of fertility preservation. Now oocyte preservation, ovarian tissue cryopreservation and its transplantation in females are being increasingly used.

CONCLUSION

Hodgkin lymphoma in pregnancy presents a complex clinical scenario that requires careful consideration of both maternal and fetal factors throughout pregnancy. With appropriate management, including the use of chemotherapy regimens deemed safe for pregnancy and close monitoring of fetal well-being, favourable outcomes can be achieved for both the mother and the baby.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

INFORMED CONSENT

Patient and her husband's consent was taken.

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Annexure 1: Summary of Cases of Hodgkin lymphoma diagnosed for the first time during pregnancy from 2009-2024

Authors	No. of cases	Age (years)	Parity	Trimester	Presenting symptoms	Type of HL	Stage	Treatment received	Treatment delivery	GA at (weeks)	Maternal Outcome	Fetal Outcome
Israel R et al.	01	26	NA	I	Persistent & Progressive Lymphadenopathy	MC	IIIA	NA	AVD (8)	10	CR	A
Iriyana N et al.	01	34	P2	II	Enlarge bilateral neck lymph node, supraclavicular, & Axillary lymph nodes	NS	IVA	II PP	ABVD (3.5)	PP: ABVD(6)	41 UN	CR
Chunag FL et al.	01	25	NA	I	Cough Unintentional weight loss Right supraclavicular 2cm lymph nodes	NS	IIIB	NA	ABVD	FT	CR	UN
Kasonkanji E et al.	01	26	NA	II	Painless progressive cervical lymphadenopathy	NA	NA	NA	ABVD(6)	FT	CR	UN
Cotteret C et al.	01	41	NA	III	Right supraclavicular adenopathy upto 3 cm	NA	IIA	III PP	Corticosteroids ABVD PP: ABVD	33	CR	PT
Delzotto J et al.	01	21	P0	II	Shortness of breath Facial swelling Lightheadedness Intermittent night sweats Syncopal event Enlarges the neck. Lymph node Swelling in the neck	NS	NA	II	Antenatal ABVD PP: ABVD + RT	28	CR	PT

NICU admission