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Acute lymphoblastic leukemia in third trimester

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I. Introduction

The occurrence of cancer and pregnancy is relatively rare, occuring in about 1 in 1000 pregnancies[1]. The most common tumors diagnosed during pregnancy are breast and cervical cancer followed by melanoma, leukemia and lymphoma.

Acute leukemia is uncommon during pregnancy. It affects approximately 1 in 75,000 pregnancies. A Total of 28% of leukemia cases diagnosed during pregnancy are ALL while AML and CML represent the remainder.

The management of a pregnant patient with malignancy is very challenging and requires a multidisciplinary approach.

II. Case Report

A 30yr old female G3P1L1A1with 36^{+1} weeks gestation came with complaints of fever, bruising and bleeding per vagina. The pregnancy until then had been uneventful and apart from a hyperthyroidism on treatment since 8 months.

she was referred from periphery i/v/o bleeding per vagina with anemia and thrombocytopenia. On admission her pulse-112bpm/min, BP-100/70mmhg,uterus-36 weeks size , mildly acting cephalic presentation, FHS- present, L/E - bleeding present. Petechiaeand ecchymosis noted over lower limbs and hands. Bedside obstetric scan was done n showed SLIUG 35wks with EFW 2.7kg with placenta posterior well aboveos,no retroplacental clots, laboratory investigation reports were as follows- HB- 6.2gm/dl ,TC-4180,platelets-2000, RFT&LFT-WNL.INR-1.17, TSH – 0.006, PBS – showed moderate microcytic hypochromic anemia with many large cells with oval nuclei, coarse chromatin 1-2 nucleoli with scanty agranular cytoplasm are seen – BLASTS.? LYMPHOBLASTS 50%

As she was already in latent labour , augmentation of labour was done with amniotomy followed by oxytocin drip, 1 pint PRBS and 4 pint platelets and 2 pint FFP transfused before delivery. She delivered spontaneous preterm vaginal delivery of an alive male baby of 2.2kg , and immediately after delivery 2pint FFP and 2pint platelets transfused, started on steroids, iv antibiotics , antifungal, Tab Prophythiouracil 50mg. Immediate postnatal period was uneventful. Next day 1pint PRBC was transfused . On day3 1pint PRBC and 4 pint platelets was transfused . On postnatal day5 Bone marrow aspiration was done and showed 80% blast cells, moderate coarse chromatin 0-1 nucleoli, scanty cytoplasm , other marrow elements were relatively suppressed - PRE B ALL , Karyotyping was 46XX(8). USG abdomen showed splenomegaly and hepatomegaly. Immunophenotyping by flowcytometry and immunocytochemical analysis was positive for CD34, HLA-DR, Tdt, CD10,CD19,CD79a and negative for CytCD3, CD1a, CD3,CD4, CD5, CD7 and CD8. RT PCR showed BCR – ABL1 Translocation positive, Patient was started on BFM95 protocol with vincristine, daunorubicine, L – asparaginase and continuation of prednisolone. BFM 95 protocol consists of induction, consolidation , re-induction and maintenance phase.

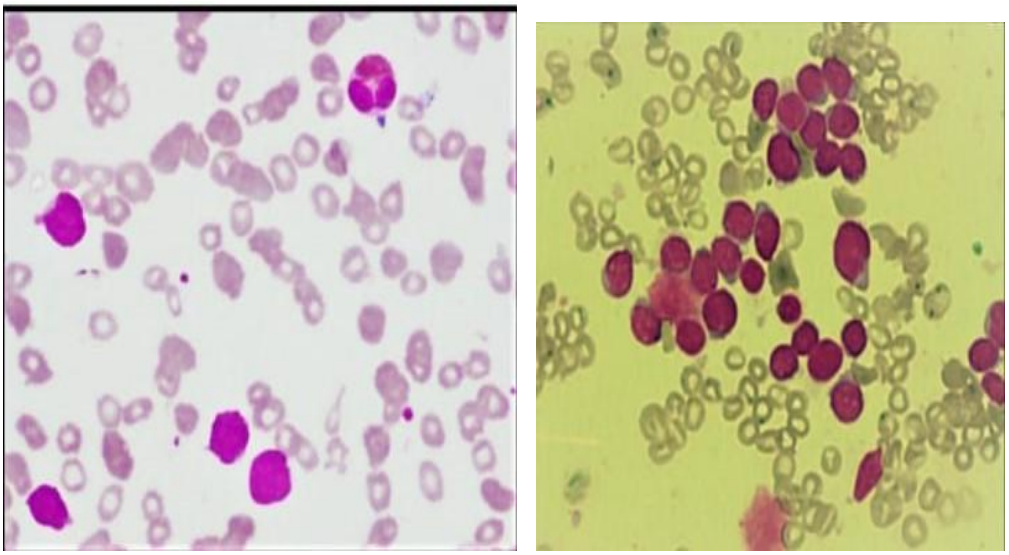

Figure: Peripheral smear of ALL showing small to medium sized blasts with high N:C ratio, irregular nuclear borders, clumped chromatin and scanty cytoplasm.

III. Discussion

Leukaemias are malignancies of the haematopoietic system, derived from transformed haematopoietic stem cells within the bone marrow. Leukaemia during pregnancy is acute in 90% cases and chronic in 10% cases. Among acute leukaemia in pregnancy 2/3rd are myeloid and 1/3rd are lymphoblastic. Among chronic leukaemia most common are myeloid[2].

Acute Lymphoblastic leukaemia (ALL) is a malignant disorder which originates in a single B or T-lymphocytes progenitor as a result of somatic mutation in a single progenitor cell at one of several discrete stages of development[3].

The diagnosis of acute leukemia is made by examination of the peripheral smear and bone marrow. Classification of the patients disease also require cytochemical stains, assessement of expression of immunological markers, cytogenetic analysis and molecular markers. The immunological markers are the major criteria to subdivide ALL into B-cell or T-cell lineage leukemias. Cytogenetic and molecular evaluation provide further identification of ALL subgroups.

Diagnosis of acute leukaemia during pregnancy need high index of suspicion and need prompt management with the proper chemotherapeutic regimen. Clinical judgement regarding the risk benefit ratio of using chemotherapeutic drugs ensures better mother and fetal outcome.

Diagnosis in pregnancy is most frequently done in 2nd and 3rd trimester; although disease may have been present earlier. This is because early symptoms are nonspecific. This emphasies the importance of early bone marrow examination in unexplained anemia in pregnancy.Effect of leukemia on pregnancy can be due to leukemia itself or due to chemotherapy induced. In first trimester, exposure to chemotherapy can result in congenital malformations or abortion. Second and third trimester exposure to chemotherapy has been associated with lowbirth weight, fetal growth restriction, premature birth, microchephaly and mental retardation[4].

Obstretricmanagement in first trimester is termination with proper counselling, but if in 2nd and 3rd trimester continuation of pregnancy can be done with proper fetal surveillance[5]. Anomaly scan and serial growth scan is to be done to detect malformation or growth restriction

Treatment of any malignancy during pregnancy represents a great challenge to the obstritician, patient and fetus. Treatment of acute leukemia during pregnancy remains an even greater challenge than treating a solid tumors or lymphoma due to requirement of using much higher doses of induction chemotherapy. Chemotherapy regimens varied, with most regimens including anthracyclines, vincristine, cyclophosphamide, cytarabine, and steroids[6].

Because of the rarity of intensive multiagent ALL chemotherapy during pregnancy, there are few well-controlled studies of its effects. However, despite the fetal toxicities of individual chemotherapeutic agents several retrospective and prospective studies of the long-term effects of in utero chemotherapy exposure suggest that standard combination chemotherapy for ALL—even during the first trimester—is not associated with any long-term serious consequences in the child. The most commonly reported adverse outcomes of pregnancy after first-trimester exposure are spontaneous abortion and intrauterine fetal death[7]; second- or third-trimester exposure is more commonly associated with intrauterine growth retardation and low birth weight.

Acute lymphoblastic malignancy requires urgent treatment, as life expectancy without therapy is less than 8 weeks. when cancer is diagnosed late in pregnancy, therapy should be delayed until after birth, provided there is no undue risk to the patient. In the case of aggressive malignancy for which treatment cannot be safely delayed (e.g., ALL or advanced-stage lymphoblastic lymphoma), fetal lung maturity should be assessed. If the lungs are mature, or if maturity can be sufficiently accelerated by steroid administration, elective premature delivery with all appropriate safety precautions should be planned. When premature delivery is not safe or is declined by the patient, standard induction chemotherapy (without asparaginase) should be started, with informed consent. Chemotherapy should be withheld after 35 week to allow the recovery of blood cell counts and to plan the timing for elective delivery.

Delivery can be done at haematological remission after the 1st treatment course[8]. Goal is to deliver after 34wk of pregnancy. If diagnosis is made in 3rd trimester ; delivery may be indicated before beginning of chemothrapy[9].

ALL in 36wks of pregnancy poses the health care team for specific challenge, in particular when immediate action, for example because of severe anemia and throbocytopenia, is warranted.Rapid tumor reduction was achieved with prednisolone monotherapy , blood and blood products transfusion and vaginal birth was initiated in a timed and controlled way, after which the patient was started on chemotherapy without delay.

IV. Conclusion

A delay in initiating therapy poses the greatest risk to the life of both the mother and fetus; therefore, emergent treatment must be provided regardless of the stage of gestation.

In acute lymphoblastic leukemia during pregnancy, maternal and fetal outcome can be favourable if promptly managed and delivered in appropriate case.

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