ACUTE MYELOBLASTIC LEUKAEMIA IN PREGNANCY - CASE REPORTS.

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ABSTRACT

Leukaemia in pregnancy is a rare presentation and not often reported. This is the first report of acute myeloblastic leukaemia (AML) in pregnancy from this environment. The diagnostic and therapeutic management of pregnant patient with cancer are especially difficult because two persons are involved, the mother and the foetus. Clear guidelines for the management of these cases are, therefore, necessary. We present our experience on two Nigerian women confirmed to have AML in pregnancy with a view to suggesting possible management guidelines for future use.

KEY WORDS: Acute Myeloblastic Leukaemia, Pregnancy, Nigeria.

INTRODUCTION

Cancer complicating pregnancy is a rare coexistence with an incidence of approximately 1 in 1,000 pregnancies in the United States[1]. Cancer is the second leading cause of death in women during their reproductive years and complicates between 0.02% and 0.1% of all pregnancies [2]. However, no available clear guidelines for the management of these women have been specified. We report these two cases to highlight some of the problems of managing leukaemia coexisting with pregnancy and suggest possible management guidelines for future use.

CASE PRESENTATION:

Case 1:

A 32 year-old female civil servant, G3P2+0, 2 alive, presented to us with a 23-week old pregnancy associated with a 5-day history of chest and abdominal pains, fever and palpitations. She was found to be febrile (T^o = 37.5^{o}C), severely pale, not jaundiced, no peripheral lymphadenopathy, a pulse rate of 120/min, blood pressure of 140/80mmHg and heart sounds 1, 2, &3. She had tender hepatomegaly and splenomegaly of about 5cm and 8cm below the right and left costal margins respectively. Kidneys were not ballotable. Initial full blood count (FBC) showed: packed cell volume (PCV) 0.17, Platelet count 10.0 X 10^9/L, total white blood cell (WBC) count of 115.0 X 10^9/L, with neutrophils (N) of 21%, band forms of 11%, metamyelocytes of 8%, myelocytes of 13%, promyelocytes of 10%, myeloblasts of 35% and lymphocytes (L) of 2%. Bone marrow aspiration (BMA) cytology showed a hyper cellular marrow with all spectra of white cell

maturation with myeloblasts constituting about 40% of the total marrow nucleated cells. Most of the blasts showed monocytoid nuclear appearance with granulocytic and monocytic differentiation. Her liver function and renal function test results were within the reference range. No malaria parasites were seen. Facilities for cytogenetics, cytochemical staining and immunological tests were not available. A diagnosis of chronic myeloid leukaemia (CML) in myeloblastic transformation in pregnancy was made.

After detailed counseling with the patient, induction chemotherapy for acute myeloblastic leukaemia[5] was initiated with intravenous (iv) cyclophosphamide 650mg/m^2 days 1 & 8, iv vincristine 1.5/m^2 days 1 & 8, oral methotrexate 20mg/m^2 days 1 – 10, prednisolone 40mg/m^2/d days 1 – 10 and allopurinol 300mg/d days 1 – 14. Adequate supportive therapy (blood transfusion, fluid therapy and infection control) was given. At the end of the first cycle her total WBC was 26.4 X 10^9/L, blast count dropped to 19%, her PCV was 0.33, and platelet count was 39 X 10^9/L. A re-induction was commenced and she was discharged on request. However, at the end of the re-induction cycle she had a live male infant weighing 1.9 Kg by spontaneous vaginal delivery at 33weeks gestation. Then her PCV had reduced to 0.22, total WBC 26.0 X 10^9/L, platelets 30.0 X 10^9/L and myeloblasts 2%.

Her treatment became irregular because she became more uncooperative. Third cycle was eventually started after a month break. Three weeks into the 3rd cycle of chemotherapy, she developed a postpartum psychosis at 8 weeks after delivery. She was recovering from her psychosis when she died suddenly at 18 weeks from the date of diagnosis of leukaemia and 10 weeks post delivery. The immediate cause of death was unknown as relatives declined post mortem examination. Her last post transfusion blood count results before death was PCV 0.30, platelet 50.0 x 10^9/L, WBC 48.0 x 10^9/L; neutrophils 16%, eosinophils 2%, bands 12%, metamyelocytes 10%, myelocytes 28%, promyelocytes 27% and blasts 5%.

Case 2:

A 36 year-old woman was seen at a distant peripheral hospital in third trimester of pregnancy as a case of severe anaemia in pregnancy (exact gestational age unknown) of unknown cause. Initial PCV at the referring centre was 0.14. Two days after presenting to that hospital, she delivered a preterm live baby by spontaneous vaginal route. She had six units of whole blood transfused within one week before she was referred to us. On getting to our hospital she was found to be febrile (T^o =38.2^{0}C), severely pale, not jaundiced, moderately dehydrated, confused and restless. She had bilateral cervical lymphadenopathy, a pulse rate of 120/min, blood pressure of 140/70mmHg, heart sounds 1, 2 and 3; uterine size was 16weeks, and a tender hepatomegaly of about 10cm below the right costal margin. Her blood count showed PCV 0.09, Platelet <10.0 X 10^9/L, total WBC 28.0 X 10^9/L, with myeloblasts 52%, promyelocytes 20%, myelocytes 18%, N 5%, L 5%. The myeloblasts showed granulocytic and monocytic differentiation. Serum urea was 15.0mMol/L (normal range is 2.5 – 6.6mMol/L), potassium of 3.1mMol/L (3.5 – 5.5 mMol/L); other biochemical values were within the

reference range. A diagnosis of acute myeloblastic leukaemia (AML), FAB M4 subtype was made. She was still being resuscitated when she died after about 40hours of presentation.

DISCUSSION:

The occurrence of cancer in pregnancy is not a common phenomenon, with the incidence ranging from 0.07% to 0.1% of all malignant tumours [1]. However, as the trend for delaying pregnancy into the later reproductive years continues, physicians can expect to see more cases of cancer complicating pregnancy. The most frequently diagnosed malignancies in pregnancy are cervical cancer, breast cancer, malignant melanoma, lymphomas and leukaemias [1]. While some workers[1] ranked leukaemias as the third most common, others[6] ranked it(acute myeloblastic leukaemia, acute lymphoblastic leukaemia and chronic myeloid leukaemia) as the second most common malignancy in women in the childbearing age group. This disparity is possibly because breast and cervical cancers which come before leukaemia have almost equal occurrences [1].
Our two patients presented with severe anaemia (due to marrow failure), fever (from infection due to neutropaenia), splenomegaly and peripheral lymphadenopathy respectively (due to organ infiltration).

Acute myeloblastic leukaemia is defined by the presence of over 20% of blast cells in the bone marrow at clinical presentation[7]. Case 1 had 35% blasts in the peripheral blood and 40% in the bone marrow. Case 2 had 52% blasts in the peripheral blood. BMA could not be done before her death. Acute leukaemias are usually aggressive as seen in our patients. Actual incidence of leukaemia during gestation is not well known but it is estimated to range from 1 in 75,000 to 100,000 pregnancies [1]. Of the leukaemias acute variety is more frequent; among this variety, AML is diagnosed twice as often as lymphatic leukaemia[1, 8]. Our two patients had AML. Morphologic examination of well-stained peripheral blood and/or bone marrow cells is the main option for diagnosis of leukaemic disorders in Nigeria due to non availability of other diagnostic tools.

Cancer diagnosed during pregnancy poses a very difficult challenge to the patient, her family and the medical staff. The major problems encountered in case 1 were getting her to accept the diagnosis, which also delayed commencing treatment, drug compliance and the psychosis. The problem in case 2 was that of late presentation due to the distance between the referral centre and our hospital. This did not give her the opportunity of commencing therapy at all. Consequently she died much earlier than case 1. Both women delivered preterm, small for date live babies. Case 1 died after 18weeks of diagnosis. Case 2 died within 48hours of diagnosis. We believe that she died from bleeding due to severe thrombocytopenia. Her confusion and restlessness prior to death were probably due to severe hypoxia from anaemia or blood aspiration.

Clear management guidelines are necessary to avoid delays in treatment and improve outcome of both mother and baby in this type of cases. While it is difficult to make conclusive recommendations based on this limited number of cases, we suggest the following:

For early diagnosis of such diseases as haematological malignancies, we suggest regular full blood count (FBC) in pregnancy especially at booking, 28 and 38weeks and at delivery.

Good supportive care (appropriate blood transfusion, infection control, good feeding etc) is very vital.

Detailed counseling should form a major part of treatment guideline, with the final decision being made by the haemato-oncologist, the patient and the family.

Abortion may be recommended in the first trimester of pregnancy, in order to prevent cytotoxic drugs - induced congenital defects and allow for intensive chemotherapy. This decision should jointly be taken by the patient and the medical staff.

Treatment of acute leukaemia in pregnancy should be started immediately after diagnosis[1]. Systemic chemotherapy in second and third trimesters is not associated with teratogenic risk [1, 2, 6, 9] but may result in intrauterine growth retardation, prematurity and stillbirth [2]. As a result of this, we suggest that early delivery between 30 and 34 weeks gestation will allow intensive chemotherapy and better outcome. This may imply that such delivery should be undertaken where facilities for neonatal support are available.

Care should be exercised in the choice of cytotoxic drugs for combined chemotherapy. Of the drugs, antimetabolites (aminopterin, methotrexate, 5-fluorouracil, arabinosyl cytosine) and alkylating agents (busulphan, cyclophosphamide, chlorambucil) are the most common drugs reported to induce malformations [1, 2]. Vinca alkaloids and antibiotics seem to have no effect on the foetus. Etoposide is implicated in pancytopaenia and cisplatin in growth retardation and hearing loss[1].

It is hoped that these suggested guidelines would improve the outcome of both baby and mother in pregnancy- associated AML.

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