CASE REPORT

Pregnancy Complicated by Hodgkin's Disease

S A W Fadilah, PhD*,, C F Leong, MPath**,***, M Y M A Jamil, MOG****, S K Cheong, FRCPA**, R Rozilaila, BSc.****

*Department of Medicine, **Clinical Haematology and Stem Cell Transplantation Services, Hospital Universiti Kebangsaan Malaysia (HUKM), Kuala Lumpur, Malaysia, ***Department of Pathology, ****Department of Obstetrics and Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM), Kuala Lumpur, Malaysia.

Summary

Hodgkin's disease (HD) in association with pregnancy is rarely reported. Thus, the data in the management of pregnancy complicated by HD is limited. We report here the management of advanced HD in pregnancy that was treated successfully with chemotherapy.

Key Words: Hodgkin's disease, Pregnancy, Teratogenic, Chemotherapy, Radiotherapy

Introduction

Since the peak incidence of Hodgkin's disease (HD) is in the age range from 20 – 40 years, it is not surprising that it may coincide with pregnancy, occurring in 1:1000 to 1:6000 deliveries and making it the fourth most common cancer diagnosed during pregnancy[1]. Pregnancy does not adversely affect the outcome of HD, nor does HD appear to adversely affect pregnancy[2]. Although the prognosis does not appear to be adversely affected, pregnancy does impose significant limitations in the management of HD. Exposure of the developing foetus to teratogens should be avoided where possible but delay in treatment may be deleterious to the mother. Consideration may need to be given to termination of pregnancy when the patient presents within the first trimester with advanced disease. Chemotherapy can probably be safely given in the second and third trimester, but radiotherapy should be avoided late in pregnancy due to close proximity of the pregnant uterus to the lower border of the treatment field[3].

Case Report

A 24-year-old Malay woman presented in May 2002 with cervical and mediastinal lymphadenopathy for one month due to HD of mixed cellularity variety (Ann Arbor stage IIA). The patient defaulted treatment and presented again in December 2004 with a 5-month history of breathlessness and severe weight loss. Her last normal menstrual period was 24 weeks before admission. Examination revealed a cachectic woman in severe respiratory distress. There were pallor, bilateral cervical, supraclavicular, axillary and inguinal lymphadenopathy, and dilated veins over the upper chest and right upper limb. The breath sound was markedly reduced bilaterally. Hepatomegaly and a gravid uterus consistent with 18 weeks gestation were evident. Foetal movement and foetal heartbeat were present. Chest radiograph with abdominal shielding revealed a huge anterior mediastinal mass (Fig. 1). A 2D-echocardiogram showed pericardial effusion. Ultrasound of the abdomen confirmed a viable foetus weighing 0.87 kg with no foetal abnormality. The haemoglobin was 8.2 g/dl, white cell count 14.8 x 10^9/l and platelet count 410 x 10^9/l. The erythrocyte sedimentation rate (99 mm/hr) and serum lactate dehydrogenase (831 U/l) were elevated. Serum protein was 51 g/l (normal range (NR) 63 – 83), albumin 24 g/l (NR 35 – 50) alkaline phosphatase 146 U/l (32 – 104), and alanine transaminase 91 U/l (<40). There was also hypoxaemia (pO_2 70 [85 – 100] mmHg) that resolved

This article was accepted: 20 February 2006

Corresponding Author: Fadilah S Abdul Wahid, Department of Medicine, Faculty of Medicine, Hospital Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia

following a short course of dexamethasone. The patient and her family requested for termination of pregnancy owing to the concern of an abnormal baby and worsening of maternal health. However, the patient agreed to continue with the pregnancy after being reassured of a high possibility of a successful outcome of both mother and foetus following chemotherapy. She received ABVD chemotherapy consisting of a two-day course of doxorubicin, bleomycin, vinblastine and dacarbazine without dose modification and granisetron antiemetic starting from 25 weeks gestation, thereafter 3 – 4 weekly. There was no significant adverse effect associated with the chemotherapy. Her blood counts after the third course of chemotherapy (three weeks prior to delivery) were normal. The mediastinal mass (Fig. 2) and peripheral lymphadenopathy resolved after three cycles of chemotherapy. Serial ultrasound revealed a healthy foetus that was small for date. Pregnancy progressed to 38 weeks gestation when she delivered a healthy baby boy weighing 1.65kg with a good Apgar score (1 min 9, 5 min 10) by caesarean section. The baby was admitted to the intensive care unit for observation and discharged well with normal blood counts a week later. The patient was discharged four days after delivery and was advised against breastfeeding. Three weeks later, the patient received the fourth cycle of ABVD chemotherapy. Both the mother and her baby remained well ten months after delivery (at the time of writing this report).

Discussion

Although pregnancy does not adversely affect survival of both the mother and the foetus[2], it imposes significant limitations on the ability to stage and effectively treat the patient. Consideration must be given not only to the immediate health of the mother and foetus but also to the long term health of the foetus if exposed to potentially teratogenic drugs or radiation. Hence, the decision to initiate therapy in a pregnant patient is usually a difficult one and may be complicated by heightened emotions, ethical issues and religious beliefs.

The clinical behaviour and histological subtypes of HD in pregnancy are not different from that of non-pregnant women of similar age[2]. However, the usual investigations have to be modified to minimise the risk to the developing foetus. Since tomographic scans and isotope studies are not recommended during pregnancy and since, the current trend is to administer chemotherapy even in early stages (Stages 1 and II) of HD, a limited initial staging work-up is suggested. It should include blood tests, bone marrow biopsies, chest radiograph with abdominal shielding, abdominal ultrasound and possibly magnetic resonance imaging (MRI). Ultrasound, which is without known adverse foetal effects, may be helpful for assessing foetal age and the presence of lymphadenopathy, and lesions in the liver and spleen. MRI is preferred to tomographic scans as it does not expose the foetus to ionising radiation and therefore appears to be free from genetic hazard.

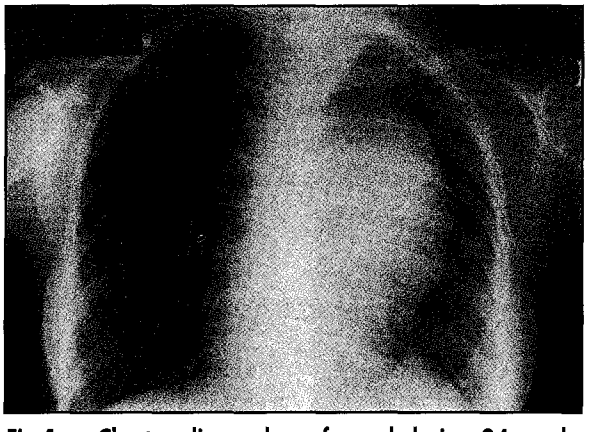

Fig 1: Chest radiograph performed during 24 weeks period of gestation

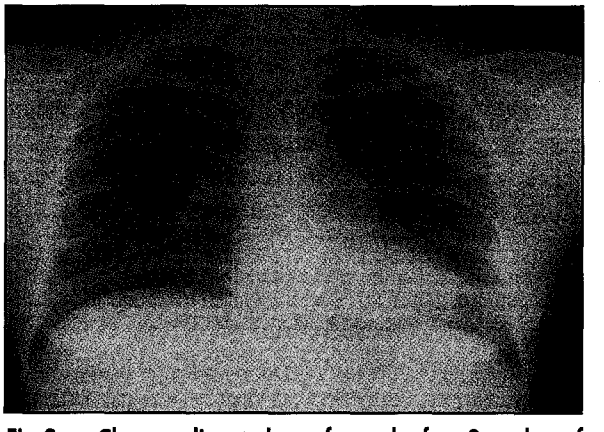

Fig 2: Chest radiograph performed after 3 cycles of ABVD chemotherapy

In general, it is recommended that chemotherapy be avoided during the first trimester of pregnancy if possible and to postpone radiotherapy until after delivery[2]. Significant exposure to cytotoxic agents during the first four weeks of gestation may result in spontaneous abortion. The risk of birth defects increases if the exposure occurred during 5 – 12 weeks of gestation, when organogenesis takes place. The estimated risk of malformations when a single agent is administered during the first trimester ranges from 7.5% to 17%, the teratogenic risk being estimated to increase when combination chemotherapy is used[1]. By week 12 of gestation, organogenesis is complete with the exception of the brain and gonads. Exposure to these drugs during the second and third trimesters is not associated with teratogenic effects, but may further result in intrauterine growth retardation, prematurity and stillbirth[1]. Thus, close monitoring of foetal wellbeing throughout the pregnancy is mandatory. The poor growth of the foetus in the case presented could be attributed to the poor nutritional state of the mother and the exposure of the foetus to chemotherapy.

If the diagnosis of HD is made in the first trimester, termination of pregnancy may be considered if there has been exposure to teratogens, or if there is the necessity for aggressive treatment between 5 and 12 weeks. If the pregnancy continues, treatment should be deferred where possible, until the second trimester at least, otherwise supradiaphragmatic radiotherapy or single agent vinblastine appears to be the safest option. Once the first trimester is over, switching to the least teratogenic combination chemotherapy regimen may be considered. The recommended protocol is probably ABVD[3].

Localised supradiaphragmatic disease presenting during the late second and third trimester may be closely observed, postponing treatment until the pregnancy is completed. Labour should be induced as soon as a viable infant can be delivered, usually at 32 – 34 weeks. If progressive disease threatens either mother or foetus, supradiaphragmatic radiotherapy or chemotherapy may be commenced. Infradiaphragmatic or advanced bulky disease presenting during later pregnancy should be treated with combination chemotherapy followed by radiotherapy after delivery.

Since chemotherapy is associated with transient bone marrow depression, delivery should be planned accordingly. A woman should not give birth within three weeks of chemotherapy, instead delivery should take place when maternal blood counts are optimal. Neonatal cytopenia have been noted after exposure to chemotherapy so blood counts should be monitored on the newborn baby. Mothers receiving chemotherapy are best advised not to breastfeed during treatment as these agents administered at a therapeutic dosage reach significant levels in the breast milk[3].

Our patient presented with advanced HD associated with superior vena caval obstruction. We have outlined a successful practical approach to the management of HD in midtrimester pregnancy.

Acknowledgments

We would like to thank Dr Andrea Ban Yu-Lin, Dr Bahariah Khalid and Mrs Eunice Choong for their excellent assistance in the management of patient.

References

1. Sadural E, Smith LG: Haematological malignancies during pregnancies. Clin obstet Gynaecol 1995; 38: 53-46.
2. Lishner M, Zemlickis D, Degendorfer P, Panzarella T, Sutcliffe SB, Koren G. Maternal and foetal outcome following Hodgkin's disease in pregnancies. Br J Cancer 1992: 65: 114-7.
3. Fisher PM, Hancock BW. Hodgkin's disease in the pregnant patients. Br J Hosp Med 1996; 56: 529-32.