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Case Report

Anti-Neoplastic Drug Exposure in Pregnancy and Fetal Haemorrhage: A Rare Teratogenicity

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Abstract

Anti-neoplastic drugs are known to have teratogenic effects on the fetus. In this case report we are presenting a case of a patient who got operated for breast carcinoma, conceived while on chemotherapy and underwent termination of pregnancy in the second trimester. Fetal haemorrhage and ecchymosis lead to further evaluation of the case, which revealed fetal thrombocytopenia, a rare teratogenic effect of the anti-neoplastic drugs.

Keywords: Anomalous fetus, teratogenicity, fetal hemorrhage, fetal thrombocytopenia.

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INTRODUCTION

Pregnancy after chemotherapy is uncommon due to gonadotoxic effects of the chemotherapeutic agents. The common malignancies associated with pregnancy are carcinoma breast, carcinoma cervix, Hodgkin's lymphoma and blood cancers [1].

The main consequence of pregnancy following chemotherapy for neoplastic conditions is the birth of an anomalous baby. Congenital anomalies occur especially when a woman undergoes chemotherapy during first trimester or periconceptional period. Growth defects, small for gestational age and preterm labor may occur when antineoplastic drugs are prescribed at any gestational age [2-4].

In the present case, patient was operated for carcinoma breast two months before conception and was started on multidrug chemotherapy, during which she conceived and was unaware of her pregnancy. There was no maternal thrombocytopenia but the fetus presented with generalized and extensive ecchymosis, a rare manifestation due to administration of antineoplastic drugs in pregnancy.

CASE REPORT

Mrs. DV, 29 years, second gravida with five months period of gestation with a previous vaginal delivery came to the gynecology OPD for medical termination of pregnancy as she conceived while she was on chemotherapy for carcinoma breast and was not aware of the pregnancy.

Patient was operated for carcinoma right breast and was started on multidrug chemotherapy with Paclitaxel, Cyclophosphamide and Adriamycin. During 5th cycle of her chemotherapy, the patient came to know about her pregnancy.

On examination, her general condition was fair with normal vital parameters. Obstetric examination revealed a pregnancy of 20 weeks gestational age with a live fetus. The case was evaluated and all necessary investigations were done, her hemoglobin was 10 gm %, total leucocyte count was 8,700 per microliter, platelet count was 170,000 per microliter, coagulation profile showed that prothrombin time was 12 seconds and INR was 1.1, her serum TSH was 3.10 mU/L. Targeted imaging for fetal anomalies scan revealed a single 20 weeks live appropriate for the gestation age fetus with soft tissue swelling at joints.

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As the patient insisted on termination of pregnancy, she was counselled regarding the procedure and possible complications of mid trimester termination of pregnancy.

MTP was done with combined medical and surgical methods under antibiotic coverage with cefotaxime to prevent sepsis. The woman was given mifepristone 600 mg and six hours later mechanical dilatation was done with Foley's catheter introduced in to the extra amniotic space and bulb inflated with 30 ml of distilled water. Six hours after mechanical dilatation, oxytocin drip was started with 5 units in 500 ml of normal saline. A dead fetus and placenta was expelled in toto with intact amniotic sac within 10 hours of starting oxytocin drip. On cutting open the amniotic sac, blood-stained liquor was drained. The fetus weighed 360 grams and the placenta weighed 140 grams. On careful examination, fetus showed the following features,

Skin was shiny with prominent vascular architecture. Extensive ecchymosis and generalized petechiae were seen all over the body but more prominently on extensor surface of limbs and back (Fig 1). There was hypertrophy of soft tissues of the limbs (Fig 2). Umbilical cord was normal showing two arteries and one vein. Fetal side of the placenta was normal but maternal side showed retroplacental bleeding (Fig 3).



Fig-1: Generalized ecchymosis on the fetal back



Fig-2: Hypertrophied fetal limbs



Fig-3: Retroplacental bleed

Post abortal period was uneventful; cabergoline was given for suppression of lactation. Prophylactic antibiotic was given for 5 days. Cord blood sample was sent for analysis and was suggestive of fetal thrombocytopenia.

The fetus autopsy was done after taking written consent of parents to evaluate the teratogenic effects of the anticancer drugs. Autopsy report was suggestive of cutaneous hemorrhages and hemorrhages in subcutaneous tissue and skeletal muscles.

In this case fetal petechiae hemorrhages were due to fetal thrombocytopenia which was an adverse effect of antineoplastic drugs especially cyclophosphamide. But mother did not suffer from thrombocytopenia and its effects. Soft tissue appeared swollen due to hemorrhages beneath the skin and in the soft tissues.

DISCUSSION

The teratogenic effect of a drug depends on the dose, time of administration and cumulative exposure to the chemotherapeutic agent. The most vulnerable period is 2-8 weeks of pregnancy when organogenesis occurs but the hemopoietic system and CNS remain vulnerable to chemotherapeutic drug beyond the period of organogenesis [5]. In the present case, woman was exposed before and during pregnancy to antineoplastic drugs. She used Cyclophosphamide, Adriamycin and Paclitaxel for 5 cycles for carcinoma breast.

Cyclophosphamide causes fetal anomalies like hydrocephaly, microtia, facial asymmetry, club foot, micrognathia and fetal growth restriction [6]. Fetal subendocardial hemorrhages and petechial lesions on the epicardium were observed in few fetuses whose mothers were exposed to cyclophosphamide in the antenatal period. In some cases, infants developed neutropenia and thrombocytopenia by 3rd postnatal day after maternal exposure to cyclophosphamide therapy [6].

Adriamycin leads to a constellation of anomalies, including gastrointestinal, bone, renal, and cardiovascular defects. Esophageal atresia/ trachea esophageal fistula arises in isolation only 50% of the time; the remainder of cases present with other defects, most frequently with the VACTERL association of congenital anomalies [7]. Paclitaxel does not cause significant anomalies except that in a few cases congenital pyloric stenosis, preterm labor and fetal growth restriction was noted [8].

According to RCOG guidelines, women are generally advised to postpone pregnancy for at least 2 years after chemotherapy for breast cancer [9]. Women with a history of breast cancer should seek contraceptive advice, non hormonal contraceptive methods are recommended as hormonal contraception is contraindicated in women with current or recent breast cancer (World health organization and UK medical eligibility category 4) [10].

In this case the patient was not using an effective contraceptive method and was not aware of the teratogenic effects of chemotherapy. Effective contraception is required to prevent MTP for a fetal anomaly and its physical and mental stress, birth of an abnormal baby and the social burden.

CONCLUSION

There are only a few case reports and case series found in the literature about the fetal effects of antineoplastic drugs. As pregnancy and newborn pose a big ethical issue, prospective studies are difficult to conduct. A thorough TIFFA scan cannot exclude all the fetal defects like fetal coagulation defects and immunological aberrations. Each patient undergoing chemotherapy during pregnancy should not only be aware of the adverse effects of the drugs but also the teratogenicity of drugs.

In case of an accidental unplanned pregnancy, the woman should be counselled regarding fetal defects, growth defects and problems with second trimester MTP. Each case should be individualized and managed carefully by multidisciplinary approach.

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