

Unintended pregnancy during radiotherapy for cancer

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SUMMARY

Background A 27-year-old woman with upper mediastinum stage IIA Hodgkin lymphoma was treated with six cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine chemotherapy. Two months later she received a total of 4,250 cGy to the upper mediastinum and left clavicular region over a 1-month period. One week after completion of radiotherapy she was found to be 13-weeks pregnant. Her physician advised her to terminate pregnancy. She contacted a teratology information service for further information regarding the risks of radiation exposure for her fetus.

Investigations Estimation of fetal radiation exposure, literature review and synthesis of published cases and effects of fetal radiation exposure.

Diagnosis Estimated fetal radiation dose between 5 and 18 cGy.

Management Counseling on the possible risks to the fetus as a result of radiation exposure.

KEYWORDS fetus, Hodgkin lymphoma, outcome, pregnancy, radiotherapy

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Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Identify the radiation dose threshold associated with an elevated risk for fetal malformation.
- 2 Specify the period of pregnancy when the fetus is at highest risk from radiation therapy.
- 3 List the factors that influence the dose of radiation therapy during pregnancy.

Competing interests

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THE CASE

A 27-year-old woman (woman A), who had delivered a healthy child 2 years earlier, was diagnosed with upper mediastinum stage IIA Hodgkin lymphoma. She was treated within a month after diagnosis with six cycles of doxorubicin (adriamycin), bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy. Two months after completion of chemotherapy, she received radiotherapy to her upper mediastinum; 250 cGy in 15 fractions and 100 cGy in 5 fractions (total 4,250 cGy) over a 1-month period. One week after the end of the radiotherapy course, she suspected that she was pregnant. Ultrasonography confirmed a 13-week pregnancy, and her physician advised her to terminate the pregnancy for fear of serious adverse effects to the fetus during embryogenesis because of her daily radiation exposure for 4 weeks (weeks 8 to 12 of gestation). Abdominal shielding was not

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used during radiotherapy. The fetal radiation dose was estimated to range between 5 cGy and 18 cGy. This dose was estimated by the medical physicist of the radiotherapy department where the woman received treatment, on the basis of the woman's body size, location and dose of radiation, and pregnancy duration. She contacted a teratology information and counseling service for further information regarding the risks of radiation exposure for her fetus. The patient elected to continue her pregnancy, and at approximately 18 weeks of gestational age, level III ultrasonography showed unilateral borderline dilatation of a lateral ventricle. A follow-up head MRI scan 1 week later showed no ventricle dilatation and no other intracerebral abnormalities. Additional ultrasound scans during the course of pregnancy were also unremarkable. At term she gave birth to an apparently healthy infant. The infant developed normally up to 22 months and—to our knowledge—is not in a specific follow-up program. The mother's health was good at 22 months postpartum, with no recurrence of Hodgkin lymphoma.

DISCUSSION OF DIAGNOSIS

The available information on radiation-induced embryonic damage in humans is mainly extrapolated from animal studies, follow-up of individuals exposed to atomic bomb radiation in Japan, and data from women who were exposed to natural radiation, as reviewed by the International Commission on Radiological Protection (ICRP).¹

The main adverse events described following fetal radiation exposure are prenatal death, malformations, neurodevelopmental disorders and childhood cancer.¹ Prenatal death is more frequent than malformations when exposure occurs at weeks 0–2 after conception, and vice versa when exposure occurs at weeks 3–8 after conception.¹ The risk of malformations has been estimated at 5% per 10 cGy above a threshold level of 10–20 cGy fetal exposure, mainly based on the Japanese bombing cohort data.¹ When fetal exposure is lower than 10 cGy, this risk does not seem to exceed the baseline risk of malformation in the general population (1–3%).² The risk for adverse neurodevelopmental outcome is most apparent when exposure occurs between 8 and 25 weeks of gestation.³ In the Japanese atomic bomb cohort, a decrease in intelligence quotient (IQ) of 21 points (95% CI, 12–30) per 100 cGy fetal exposure was observed for women

exposed during 8 to 15 weeks of gestation, and a decrease of 13 points (95% CI, 3–24) during 16 to 25 weeks of gestation.³ Reassuringly, the mean IQ score and the mean school performance of those exposed *in utero* to doses under 10 cGy were similar to nonexposed controls.³ The current available data are, however, insufficient to determine if a clear threshold value exists for neurobehavioral damage. Considering the small number of women who are exposed to intermediate or high doses of radiation and continue pregnancy, it is unlikely that sufficient data will ever become available.

Prenatal radiation exposure has also been associated with an increased risk of cancer during childhood.⁴ Results of international studies have suggested a cancer risk of 60 per 1,000 children, which is 40% above baseline cancer risk.⁴ As the overall incidence of childhood cancer is low, the small numbers of patients with cancer in these studies preclude solid estimates of the relative risk of cancer after fetal radiation. Reaching a clear understanding of the dose–response relationship between fetal radiation exposure and radiation-induced cancer is, therefore, not possible at present.¹

In summary, on the basis of available human data, there is no evidence that fetal radiation levels of 5–10 cGy present a measurable risk to the embryo or fetus.¹ By contrast, fetal exposure above 50 cGy has been clearly associated with less favorable outcomes, while intermediate exposure (10–50 cGy) might negatively affect some cases.³

In most centers, early-stage Hodgkin lymphoma is treated with a combined treatment modality that consists of chemotherapy and radiotherapy.⁵ Although standard radiation doses (2000–4000 cGy) are commonly given for Hodgkin lymphoma,⁵ fetal exposure might vary among individuals because of the following variables: target dose, size of radiation field, teletherapy machine used and its radiation leakage, distance from the edge of the radiation field to the fetus and the use of shielding—abdominal shielding can reduce fetal dose by 30–60%.⁶ With proper shielding, the dose to the fetus will be lower than the threshold dose for adverse fetal outcome.

TREATMENT AND MANAGEMENT

As 50% of all pregnancies are unplanned, women do occasionally conceive during radiotherapy for oncologic disease. The treating physician in

Table 1 Patient and newborn characteristics.

Case	Disease	Gestational age at exposure (weeks)	Total dose (Gy)	Estimated fetal dose (cGy)	Pregnancy outcome
A	Hodgkin (stage IIA)	8–12	42.5	5–18	Good at 22 months
B	Non-Hodgkin	2–6	40.0	>20	Therapeutic abortion
C	Hodgkin (stage IIA)	3–7	40.0	Maximum 10.5	Good at 28 months

this case advised the patient to terminate pregnancy for fear of serious adverse fetal outcome. This practice reflects physicians' perceptions of the high risk of teratology from radiation.⁷ In the same period, two other patients with radiation exposure during unintended pregnancy contacted the same teratology information and counseling service and were also advised by their physicians to terminate pregnancy.

The following discussion presents a practical paradigm to deal with such cases. Firstly, to determine the potential effect of radiation on the fetus, the medical physicist involved in the women's radiotherapy was asked to estimate fetal radiation exposure. Of note, the estimated fetal radiation exposure varied significantly among the three women who contacted the counseling service (Table 1), despite exposure to a similar dose of radiotherapy with no abdominal shielding. In woman A, the estimated exposure ranged from 5 to 18 cGy, during weeks 8–12 of gestation. As this fetal dose might have exceeded the safety threshold of 10 cGy, her fetus might have a slightly increased risk of a lower IQ and childhood cancer. In woman B, exposure at weeks 2–6 of gestation was estimated to be above 20 cGy, with additional radiation exposure from several X-ray, CT, and gallium scans during the first trimester. For this fetus, considering the exposure period, an increased risk of birth defects and childhood cancer (and less of an effect on neurodevelopmental outcome) was most likely. In woman C, because of the low dose and timing of exposure (10.5 cGy at weeks 3–7 of gestation), an increased risk of fetal adverse effects seemed to be limited to a very marginal increased risk of birth defects and childhood cancer, with an effect on neurodevelopment unlikely. Secondly, the association of lymphoma with pregnancy is not, by itself, a known risk for adverse fetal effects.^{8,9} Of the few case reports

that have been published of first trimester fetal exposure to radiation for treatment of non-Hodgkin lymphoma, neonatal outcome was favorable at the time of follow-up.^{10,11} Finally, fetal exposure to chemotherapeutic agents does not seem to affect neurodevelopmental outcome.¹² Although these data are reassuring, sample size was small and the design was not optimal in the available studies, and, therefore, more research is needed before a definite conclusion can be drawn. Only woman B received chemotherapy (cyclophosphamide), in addition to celecoxib, during weeks 12–17 of gestation. The other women received chemotherapy before conception.

During the assessments of woman A and C, no evidence of increased adverse fetal outcome was apparent. These women decided to continue pregnancy, and both delivered apparently healthy newborns at term. Both of these infants developed normally and have no other health problems at 22 and 28 months of age, respectively. Woman B decided to terminate her pregnancy. This decision was based on the combined risk of radiation and chemotherapy during pregnancy and the anticipated unfavorable maternal outcome.

CONCLUSIONS

These cases illustrate that unplanned pregnancy during radiation therapy for cancer may be encountered in clinical practice. The increased risk of poor fetal outcome after fetal radiation exposure is dependent on the fetal dose received. Careful evaluation of estimated fetal exposure should, therefore, be performed in each individual. Results of such evaluation should be discussed with the woman and the family, in the context of the underlying disease and other concurrent therapy (e.g. medication), to allow her the opportunity to make an informed decision on the fate of her pregnancy.

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Competing interests

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