Successful Pregnancy and Normal Delivery after Whole Craniospinal Irradiation in Two Patients

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Abstract. Background: Two cases of normal pregnancies and deliveries after whole craniospinal irradiation (WCSI) are described, and whether the ovaries can be left out of the WCSI field by identifying ovarian position using magnetic resonance imaging (MRI) is determined. Materials and Methods: The distance between the upper edge of the pubic symphysis and the central part of the ovary was measured on MRI in 17 women. Results: The right ovary was located 20.3-68.4 mm to the right of and 33.7-113.5 mm above the upper edge of the pubic symphysis; the left ovary was located 26.2-72.5 mm to the left and 25.8-106.6 mm above this edge. The lower border of the spinal field in WCSI should be the caudal border of the thecal sac, i.e., S2-S4. The line of this location, which nearly approximates normal ovarian position, should be employed in radiotherapy planning to avoid irradiating at least one ovary with its thecal sac. Omitting this area from the WCSI field in women of childbearing age with a good long-term prognosis, preserves potential fertility. Conclusion: It appears that the ovaries might be excluded from the WCSI field, using appropriate techniques, so as to preserve female fertility.

Whole craniospinal irradiation (WCSI) (irradiation to the entire central nervous system) is a radiotherapy technique in which irradiation is delivered to brain tumors that are likely to progress or disseminate into the subarachnoid space. It is mainly indicated for the treatment of medulloblastoma, ependymoblastoma, primitive neuroectodermal tumors and medulloblastoma which are embryonal tumors according to the WHO Classification of Tumors of the Nervous System (WHO 2000), and several other diseases. However, potential adverse effects associated with an extended irradiation field require sufficient investigation to appropriately select candidates for WCSI. While recent therapeutic advances have resulted in a growing number of long-term survivors, concerns have been raised about the development of radiation-induced late complications, especially impaired growth and fertility in young women. Fertility preservation has not been fully investigated as yet because cure of the disease has always been the first priority. Herein, we describe our clinical management of two women who experienced normal pregnancies and deliveries after WCSI. Furthermore, we identified the ovarian position using magnetic resonance imaging (MRI) to determine whether the ovaries could be left out of the irradiation field in WCSI.

Case presentation

Case 1. A 14-year-old girl. The patient had pain in both legs in July 1995, and presented to the Department of Orthopedics of our hospital on October 3 because of worsening pain. Exploration on admission led to a diagnosis of cerebral ependymoma at the third lumbar vertebra (L3). The patient underwent extirpation of the tumor on October 23 and thereafter was discharged home. MRI, performed at a follow-up visit in September 1997, revealed recurrences in the conus medullaris and spinal cord at the levels of Th4-5 and Th12-L1. The recurrent tumors were inoperable, and the patient received WSCI at a total dose of 30 Gy in 20 fractions (1.5 Gy/fraction) starting on November 5, followed by irradiation boosts to Th4-5 and Th12-L1 (16 Gy in 8 fractions) and the subtentorial region (40 Gy in 20 fractions). A simulation film of the lower border of the spinal field for
WCSI is shown in Figure 1. The pain had subsided at this time. MRI showed reductions in tumor sizes. The patient was managed with follow-up visits. The patient was found to be pregnant in April 2003 and gave birth to a healthy male infant in December at the age of 22 years. As of September 2004, both mother and child are well.

Case 2. A 31-year-old woman. The patient presented with motor disturbance of the right leg in June 1995. An investigation at the Department of Orthopedics revealed elevated HCG levels in blood and spinal fluid. An intramedullary tumor was detected at the Th3-4 level. Cytological examination of spinal fluid revealed a germ
cell tumor. Weekly intramedullary methotrexate injections were commenced with a diagnosis of HCG-producing intramedullary tumor. However, the tumor was not well controlled. She was thus referred to our department for radiation therapy. On June 3, 1997, WCSI was started with a total dose of 30 Gy (1.5 Gy x 20 fractions), followed by an 18 Gy boost, at a dose of 1.8 Gy per fraction, to Th3-4. A simulation film of the lower border of the spinal field for WCSI is provided in Figure 2. HCG levels normalized and the tumor disappeared on MRI after WCSI. The patient was found to be pregnant in September 2002, and gave birth to a healthy male infant.
in April 2003 at the age of 38 years. As of September 2004, both mother and child are well.

Materials and Methods

Ultrasound is reportedly an objective diagnostic imaging tool for determining ovarian position (1). A subsequent study carried out at the same facility showed T2-weighted MRI to be the most useful in localizing the ovaries (2). In the present study, we attempted to determine the positions of the right and left ovaries by pelvic MRI for 17 women of childbearing age (age: 24-46). A representative MRI is shown in Figure 3. The heights of our patients ranged from 156 to 166 cm, with a mean of 159.6 cm. Because pelvis size is thought to vary slightly, depending on a woman’s constitution, the ovarian position should be extensively evaluated based on the positions of the ovaries relative to the pelvis. However, measurements in 17 women showed the transverse diameter of the pelvis at the inner edge of the femoral head to be 125.5-143.3 mm (mean: 132.8 mm), suggesting that there may be little variation in pelvic skeletal size. In this study, therefore, we measured only the distance between the upper edge of the pubic symphysis and the central part of the ovary to

Figure 3. MRI showing the positions of the ovaries in a 33-year-old woman, 159 cm in height. The distance between the upper edge of the pubic symphysis and the central part of the ovary was measured to determine the ovarian position.
determine ovarian position. A large uterine leiomyoma was also present in 2 of the 17 patients.

Results

MRI scanning was undertaken in all 17 patients. In 2 of these patients, it was impossible to identify one of the ovaries on MRI scans. The distances between the upper edge of the pubic symphysis and the right and left ovaries are given in Table I. The right ovary was located 20.3-68.4 mm (mean: 41.0 mm) to the right of and 33.7-113.5 mm (mean: 61.4 mm) above the upper edge of the pubic symphysis; the left ovary was located 26.2-72.5 mm (mean: 41.0 mm) to the left of and 25.8-106.6 mm (mean: 61.5 mm) above the upper edge of the pubic symphysis. A pelvic radiograph from a 33-year-old woman (transverse diameter of the pelvis at the inner edge of the femoral head: 132 mm) is provided in Figure 4; the positions of the right and left ovaries (●) and mean position (●) are indicated. Upward and lateral deviations in ovarian position (♀) were noted in 2 patients who had very large uterine leiomyomas. The positions of the ovaries in all patients, except for these 2, were within 90 mm above and 50 mm to the left or right from the upper edge of the pubic symphysis.

Review of the irradiation fields in the 2 patients, in whom normal pregnancy and delivery were achieved (Figures 1 and 2), showed the lower border of the craniospinal irradiation field to correspond to levels S4 to S5 at the upper edge of the femoral head. This height implies that the mean ovarian position, as shown in Figure 4, is included in the irradiation field. In view of these observations, we speculated that the ovaries of these two patients were positioned somewhat lower than in most other cases.

Discussion

Although many patients who are potential candidates for WCSI have a poor prognosis, favorable therapeutic outcomes have also been reported, with 5-year survival rates of 90% or more for germinoma (3-5), 70-80% for medulloblastoma (6-8) and 40-80% for ependymoma (9-11). These malignancies are more likely to occur in younger patients and, when long-term survival can be expected, the development of radiation-induced late complications must be taken into consideration. There are many reports concerning growth impairment associated with childhood irradiation to the pituitary gland and skeleton (12-14), while few reports have focused on fertility preservation. Gonadal function following radiation therapy is reportedly affected by age, the presence or absence of combined chemotherapy, radiation doses and irradiation field (15-18). Pre-pubertal radiation therapy also reportedly has little effect on subsequent fertility and pregnancy (19). One report stated that a dose greater than 5 Gy to the ovaries may result in ovarian failure (15). In another study, total doses of 4 Gy were reported to cause permanent infertility in all women over age 40, but in only 30% of younger females (17), while another report recommended ovarian doses being kept below 1.5 Gy whenever possible (20). An approximately 30 Gy exposure, prescribed in WCSI, to the bilateral ovaries appears to be consistently associated with infertility. Since increased risk of abnormalities has not been observed in the offspring of long-term cancer survivors treated during childhood (18, 19, 21), fertility preservation is mandatory for women. Thus, the ovaries, if possible, should be excluded from the irradiation field when planning radiation therapy.

The lower border of the spinal field in WCSI should be the caudal border of the thecal sac, which corresponds to the second to fourth sacrae (S2 to S4) (22, 23). The location of this line nearly approximates to the usual position of the ovaries (Figure 4). The lower border of the irradiation field should be 90 mm or more from the upper edge of the pubic symphysis, which nearly corresponds to level S1, in order to leave the ovaries out of the irradiation field in patients who do not have uterine leiomyomas. Such a positional relationship is very subtle. However, if radiotherapy planning is designed so as to exclude at least one ovary, including the thecal sac, from the irradiation field in WCSI by localizing the ovaries on MRI scan, fertility preservation appears to be possible. An attempt has also been made to

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*These cases had very large uterine leiomyoma.
reduce ovarian doses using modified fields with a half beam block at the lower border of the spinal field (2).

More recently, chemotherapy has been combined with WCSI for many patients to improve therapeutic outcomes and reduce radiation doses. However, in terms of fertility preservation, chemotherapy should be avoided, if possible, and sufficient informed consent is mandatory for women with the possibility of becoming pregnant. In the 2 patients described herein, systemic chemotherapy was not administered. Alternative techniques for preserving fertility, such as ovarian transportation and cryopreservation of oocytes or ovarian slices, are also theoretically and practically possible, but have not yet been fully established (24-26). The introduction of stereotactic radiosurgery and

Figure 4. Pelvic radiograph showing left and right ovarian positions (○, ●) and mean position (●) in 17 women. Upward and lateral deviation of ovarian position can be seen in two cases who had very large leiomyomas (●).
three-dimensional conformal radiotherapy should also be investigated as local irradiation to increase the local control rate and preserve fertility.

Acknowledgements

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References