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Cancer and Pregnancy

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Cancer associated with pregnancy arrests the attention of all physicians. A mother who has the misfortune of developing cancer is burdened by two proliferating systems, the disease and the fetus. One demands elimination or control; the other, preservation.¹¹² Cancer is becoming a more frequent cause of maternal death because many obstetrical factors that previously were responsible for maternal deaths are not as prevalent today.²⁵

The following review presents current medical practice when the more common types of cancer are associated with pregnancy. The reader is referred to a recent more extensive article on cancer and pregnancy.¹³¹

BREAST

Cancer of the breast is still the major cause of death from cancer among women.⁷⁴ One in 35 patients with carcinoma of the breast will have pregnancy as a complication, but if the cancer is during the childbearing years, the figure is 1 in 3.¹²⁰

The disease is found by the patient in approximately 90% of cases.⁷⁶ Immediate biopsy of a suggestive tumor is indicated.^{19, 33, 75, 76}

Holleb and Farrow reviewed 266 patients with carcinoma of the breast in whom the carcinoma was associated with pregnancy as a simultaneous, postpartum, or subsequent event.⁴¹ They observed 28 women in the first

trimester of pregnancy, 24 of whom were treated by radical mastectomy. Four patients were excluded because they refused treatment or received roentgen therapy only. The five-year survival rate was 25% for the radical mastectomy group in the first trimester of pregnancy. The axillary nodes were involved in 79% or 19 patients, and the five-year clinical cure rate for this group was 21%. Only 21%, 5 patients, had negative nodes, and here the clinical cure rate rose to 40%.⁴⁹ One-half of the patients were allowed to deliver normally, and one-half had therapeutic abortions.⁴⁹ In their group of 24 patients, the interruption of pregnancy did not seem to affect the clinical cure rate. The overall five-year clinical cure rate was better in the group which delivered normally compared with those patients whose pregnancy was interrupted, 33% versus 17%.⁴⁹

Peters reported 70 cases of cancer of the breast associated with pregnancy that were treated by use of radiotherapy in conjunction with mastectomy.⁹² In this group she reported 8 patients in whom prophylactic therapeutic abortion was performed for carcinoma coincident with pregnancy. None of the previously mentioned women survived over 4 years.⁹²

White recorded 12 patients operated upon for breast cancer and then became pregnant within 4 years. Eight of these patients had disease localized to the breast and 4 had axillary node involvement. Seven of the 8 patients with local disease survived 10 years or

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more.¹²⁰ In Stage II cancer of the breast the fate of the patient depends more on the state of the disease than on the condition of the pregnancy.⁴⁸

If cancer is discovered during or after pregnancy, radical mastectomy and axillary lymph node dissection should be carried out promptly.^{21,48,49,73-120} Postoperatively radiation therapy can be given to the involved tissues.⁹² The pregnancy should not be interrupted nor should castration be performed.^{40,92,73} Pregnancy after therapy for cancer of the breast should be delayed for at least 3 years and longer if the axillary lymph nodes contain cancer.

CERVIX

Cervical carcinoma coexisting with pregnancy occurs once in every 2,000 to 6,000 women.^{44,57,64,72,103,115}

All women should have a cytospin of the cervix performed during pregnancy.^{4,50,55,57,105} Preinvasive carcinoma of the uterine cervix can be made on biopsies of pregnant patients and the lesions are not changes due to pregnancy.^{41,53,72,77,91} Conization of the cervix during pregnancy for the diagnosis of preinvasive or invasive cervical cancer can safely be performed.^{12,32}

Patients with carcinoma in situ can have a vaginal delivery providing there are no obstetrical contraindications.^{24,53,78} There is insufficient evidence to prove that pregnancy or delivery per se causes progression of the lesion.⁵³

Fletcher, et al. reviewed 74 cases of carcinoma of the cervix associated with pregnancy or diagnosed up to 1 year postpartum.³⁵ All patients were given radiation therapy and divided into 2 groups according to whether they were treated before supervoltage radiation therapy or with supervoltage radiation therapy. Before supervoltage

radiation therapy 30 patients were treated with 40.5% five-year survival and after supervoltage therapy was instituted, 44 patients were treated with a 55.5% five-year survival. The increased survival rate was most marked for Stage I cases with all 18 patients treated still alive.³⁵ Fletcher, et al. gave to Stage I and Stage II cases a dose of 4,000 rads to the whole pelvis.³⁵ In the first trimester of pregnancy abortion usually occurred after 2,000 to 3,000 rads were given. When external irradiation was completed at 4 weeks, the usual intracavitary radium therapy was used. In the second trimester, abortion usually occurred before 4,000 rads were delivered. When external irradiation was completed, the uterus had involuted enough to proceed with the normal radium therapy. There were 4 instances in which abortion did not occur by the time 4,000 rads had been delivered. In those cases vaginal radium only was used and a hysterectomy performed.³⁵ In the third trimester, with a viable fetus, a high cesarean section was done and whole pelvis irradiation was started 3 or 4 days afterward. The uterus was sufficiently involuted after 4,000 rads were delivered to carry the normal intracavitary radium therapy.³⁵ In the immediate postpartum period 4,000 rads were given to the whole pelvis. The uterus was fully involuted at the end of external irradiation and radium therapy was performed without difficulty.³⁵

Kinch compared 75 pregnant patients with cancer of the cervix treated by irradiation with 402 patients in a comparable age group of 35 or under and discovered an almost identical five-year survival rate of 44% as compared with 45%.⁵⁵ In 28 patients with Stage I carcinoma of the cervix in pregnancy, a five-year survival of

64% was obtained which was almost identical with that in the comparable 402 nonpregnant women. He concluded there was no general worsening of the prognosis when the lesion was complicated by pregnancy.⁵⁵

Sadugor, et al. believe women with cancer of the cervix during pregnancy should be treated without regard for the fetus up until viability was certain since any appreciable delay might decrease the mother's chance of survival. If diagnosis was made after viability they performed a cesarean section without hysterectomy and started the patient on radiation therapy in about 2 weeks. The results of their irradiation treatment for 78 women with cancer of the cervix in all stages associated with pregnancy was a 26.9% five-year survival. This was contrasted to 3,173 women with a comparable percentage in each stage of cervical cancer and a five-year survival of 27.5% was disclosed.¹⁰³

Kistner, et al. performed radical hysterectomy and pelvic node dissection alone in 13 women as the treatment for cervical cancer in pregnancy with 7 women surviving 5 years.⁵⁷

Most authors state that the clinical stage of invasive cancer during pregnancy was the single most important prognostic criterion.^{44,50,55,64,115} The predisposing factors to the rapid spread of invasive cervical cancer in pregnancy were late diagnosis and the effects of vaginal delivery.^{35,55} Cytologic follow-up postpartum of patients with preinvasive carcinoma of the cervix discovered during pregnancy with indicated cold conization of the cervix is carried out if additional children are desired.^{4,53,68,24} Patients with invasive cancer of the cervix discovered before the seventh month of pregnancy or postpartum should undergo definitive therapy.^{35,103} External irradiation can be administered, and fol-

lowed by intracavitary radium therapy after spontaneous abortion.^{35,55,103} Radical hysterectomy and pelvic node dissection in Stage I cancer of the cervix is another mode of treatment.^{57,61} Women with a pregnancy approaching fetal viability and invasive cancer can have therapy briefly delayed until viability. Patients with a viable fetus and invasive cancer of the cervix should be delivered by a classical cesarean section and radiation therapy started after operation.³⁵

HODGKIN'S DISEASE

The incidence of Hodgkin's disease is approximately 1 in 6,000 deliveries⁸³ and in women with Hodgkin's disease the incidence of pregnancy is approximately 18%.¹¹²

The cardinal symptom in the typical case was painless enlargement of the cervical lymph glands.⁴⁶ The diagnosis is based on histologic study of an excised gland.^{46,83,112} The women are permitted to go to term and delivery of healthy infants is usual.^{46,83,99,114,116}

Barry, et al.¹¹ observed 347 patients with Hodgkin's disease and compared those whose illness was associated with 1 or more pregnancies with those whose illness was not. The median survival was just under 5 years. Fertility was not impaired with Hodgkin's disease.^{11,46,54,99,110} Barry and others have discovered active disease during pregnancy to be most frequent above the diaphragm; this was treated with ionizing radiation, shielding the abdomen.^{11,46,99,112} The median survival time in Barry's study was 90 months in the group with pregnancy associated with Hodgkin's disease and it compared favorably with findings for the age-corrected nonpregnant control group (median survival 52 months). The onset of Hodgkin's disease during pregnancy does not adversely af-

fect survival.¹¹ The frequency of exacerbations of the disease was not increased by pregnancy, as the expected rates in the control subjects and pregnant patients were similar.¹¹ Pregnancy did not have a detrimental effect on survival as 54 women in the entire Barry study survived 10 years and 22 of the 54 were pregnant a total of 34 times in association with Hodgkin's disease.¹¹ Other authors have also made this observation.^{46,67,83,99,112,116}

It is desirable not to administer cytotoxic drugs in the first trimester of pregnancy because of the risk to the fetus.^{26,47,112,113,46,83}

Women desirous of pregnancy with Hodgkin's disease should be urged to wait until they have had quiescence of disease for at least 2 years.¹¹ Patients with active disease should be advised against pregnancy, not because of any adverse effect of pregnancy on the mother or danger to the fetus, but because of the poor prognosis in the mother.

LEUKEMIA

Good prenatal care is indicated in pregnant women with leukemia.³⁶ The treatment of chronic leukemia is usually external radiation therapy with shielding of the pregnant uterus.¹⁰⁸ Pregnancy does not appear to have an adverse effect on chronic leukemia.¹⁰⁸ In a disease such as acute leukemia with few survivors, the aim of therapy is to maintain the pregnant patient's general condition at least until a healthy infant is obtained.^{36,62,63,70,79,85,130} The rapidly effective steroids are the drugs of choice during all trimesters with folic acid antagonists and antimetabolites being reserved for periods during the second and third trimesters when steroid control fails or for the postpartum period.^{63,130} Most authors have observed that in-

fants born of leukemic mothers will do as well as normal controls provided that antimetabolites are not administered and radiation therapy to the uterus is not given during the first trimester of pregnancy and the fetus goes beyond the age of viability.^{30,36,62,63,79,84,87,130}

MELANOMA

George, Fortner and Pack³⁸ report a five-year survival in 27 of 54 (50%) and a ten-year survival of 8 of 19 (42%) women pregnant coincident with melanoma. Fifteen of 32 women (47%) followed 5 years survived and 9 of 23 (39%) survived 10 years in the group pregnant after melanoma. In the control or nonpregnant group in the ages of 16 to 43, 56 of 112 (50%) survived 5 years and 21 of 47 (45%) survived 10 years.

White et al.¹²⁶ compared 30 patients whose pregnancies occurred 1 year before the diagnosis of melanoma and 5 years after diagnosis with 31 patients not pregnant during this period. The five-year survival in the pregnant group was 73.3% and in the nonpregnant group 58.8%. They conclude that the five-year survival of melanoma in pregnant women is as good as, or better than, five-year survivals in nonpregnant women. They also state that the stage of disease at the time of diagnosis and treatment was of great importance in determining five-year survival, but the pregnancy did not seem to exert any influence.¹²⁶

Pack and others state that the demonstrated good prognosis for pregnant patients with melanoma establishes a basis for carrying out the same early, adequate surgical treatment for them as for their nonpregnant counterparts.^{14,38,70,80} The pregnancy is not interrupted.

OVARY

An enlarging ovary 6 cm. or more in diameter should be inspected to exclude cancer.^{17,65} The complete excision of ovarian cancer tissue is indicated at any stage of pregnancy.^{15-17,39} The use of external radiation therapy or intra-abdominal radioactive compounds should be delayed after operation until fetal viability.^{15,27} Cesarean section can then be performed or it can be combined with a primary definitive surgical operation.^{39,42,58} Interruption of pregnancy does not appear to have any beneficial effect on maternal prognosis.²⁷

THYROID

The diagnosis of thyroid cancer is made by tissue examination of an enlarged gland.^{15,43,47,81,102} The treatment is immediate thyroidectomy followed by external radiation therapy to the involved area. The pregnancy is not interrupted. Radioactive iodine to inactivate functioning thyroid metastases should not be used after 12 weeks of gestation because it traverses the placenta and may concentrate in the fetal thyroid.^{43,102} After viability of the infant cesarean section can be performed to allow earlier use of radioactive iodine.

SUMMARY

Primary cancer has been reported in most regions of the body during pregnancy. The obstetrician is in an unparalleled position to diagnose cancer. His patient is making her first visit to a physician or the first visit since the birth of her last child for a complete physical examination. The early diagnosis of cancer in a pregnant woman, as in a nonpregnant woman, is usually associated with an increase in survival. In addition to earlier diagnosis, the improvement in surgical techniques, radiation therapy, and chemotherapeutic agents have opened a new era in oncology.

The occasional case report of cancer and pregnancy is of value but precedent in therapy should not be determined until sufficient clinical material has been followed for 5 or more years. As greater numbers of group studies of pregnant women with cancer are published, the concept that pregnancy does not influence the cancer emerges. Treatment is directed at destroying the cancer if it is considered curable, preserving the fetus if the cancer patient is terminal, and compromising with both situations when palliation is indicated and the fetus needs to become more mature before it is delivered.¹⁵

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