

HODGKIN'S DISEASE AND PREGNANCY

Report of 4 Cases

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DOES pregnancy cause exacerbations of Hodgkin's Disease? In 1888, when Wright¹ reported the first known instance of Hodgkin's disease complicating pregnancy, and until 1948 when Summers and Reid² gave their account, this question has been debated and several individual cases have appeared in the literature. Perrier³ described 5 instances and Gilbert⁴ 7 pregnancies in 5 patients. Our report concerns 4 proven cases of Hodgkin's disease observed at the Cleveland Clinic between 1930 and 1949, and associated with known pregnancy during the course of the disease.

Case Reports

Case 1. A woman, aged 21, was first seen at the Clinic on July 24, 1930. Her chief complaint was dyspnea. Six months previously she had had pleurisy with effusion following a cold. She had undergone numerous thoracenteses but the fluid had reformed so rapidly that her dyspnea was relieved only for a day or so after aspiration.

Our examination disclosed adenopathy in the left supraclavicular and axillary lesions. The entire chest on the left side was flat to percussion and the heart displaced to the right. A roentgenogram showed complete opacification of the left side of the chest with displacement of both heart and mediastinum into the right thoracic cavity. A diagnosis of Hodgkin's granuloma was made by biopsy of an axillary node.

Thoracentesis of about 2000 cc. daily was required (between July 24, 1930 and August 12, 1930) in order to relieve dyspnea. The fluid was a cloudy yellow and contained numerous lymphocytes. Roentgen therapy was given to the anterior and posterior mediastinum, and to the left supraclavicular and left axillary regions.

The patient was free of symptoms for 3 years until 1933 when she returned complaining of back pain. There was no dyspnea, although a partial hydrothorax was present in the left side of the chest. No enlarged nodes were demonstrable. Her chest on the left was again irradiated anteriorly and posteriorly.

The patient was not heard from until June, 1937, at which time she had been delivered of a full term baby at another hospital. This was 7 years after her first admission to the Clinic and 4 years after the last treatment. The pregnancy had been presumably uneventful; however, during her stay in the hospital a mass in the left axillary region was discovered. Roentgen therapy was given with apparently satisfactory results.

Six months later the patient entered the same hospital complaining of dyspnea, fatigue, reappearance of a mass in the left axilla, and severe pruritus of the legs. The symptoms were of 2 months' duration. She was described as obese and pale. A firm non-tender mass was attached to the left lower chest wall and a roentgenogram disclosed probable extension into the left lower lung. An electrocardiogram revealed

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inverted T waves in Leads 1, 2 and 3. This supposedly indicated infiltration of the pericardium and/or myocardium. Roentgen therapy was given over the tumor area and the patient was discharged.

Improvement was slow but the mass in the axilla gradually subsided; the patient improved and eventually became well enough to do housework. Roentgenogram in October 1938 showed considerable decrease in the size of the left thoracic mass.

She was again admitted to the hospital in April 1939 after a gradual relapse over a period of several months. She was semistuporous, orthopenic, and had generalized edema. The veins in her neck were engorged and no breath sounds were audible in the left side of the chest. A large firm mass in the left upper quadrant appeared to be attached to the skin and did not move on respiration. The electrocardiogram showed auricular fibrillation and low ARS waves. Supportive treatment, digitalis, and mercurial diuretics were administered without improvement and the patient died.

At autopsy a large grayish-white mass was found which exhibited irregular areas of necrosis, largely replacing and invading the left upper lung; the left hilar region was invaded and the pulmonary artery was surrounded by neoplastic tissue. There was encroachment on the wall of the left atrium with actual invasion of the muscle in several places; several nodules measuring 1.5 cm. were present on the endocardial surface. The coronary sinus in the left auriculoventricular groove was occluded by a tumor growing within the lumen. No pericardial effusion was present.

A second large hard mass, difficult to remove, was located in the left upper quadrant; it had invaded the lower ribs and dorsal vertebrae, the muscles in the back and subcutaneous tissue. The mass measured 28 by 15 cm. and weighed 2800 Gm. The splenic flexure of the colon was encased in neoplastic tissue and the left adrenal gland was largely replaced by tumor. The liver, spleen and kidneys were not involved. No tumor was found in the brain.

The histology of the tumor was similar in all affected areas, made up of fibrous tissue, fibroblasts, large and small areas of necrosis, giant cells, both polymorphonuclear and polynuclear, lymphocytes and eosinophils. The para-aortic lymph nodes showed complete destruction of structure crowded with the same type of cells already enumerated. Histologically this case must be accepted as one of Hodgkin's disease since the morphologic picture is fairly typical of the disease. Grossly large masses of tumors in the thorax and soft tissues of the abdominal wall are distinctly invasive in character. It might, therefore, be justifiable in this instance to refer to the disease as Hodgkin's sarcoma.

Comment

The patient had Hodgkin's disease for more than 9 years. A review of her original biopsy specimen shows it to be typical Hodgkin's granuloma. For several years the disease was not particularly malignant and apparently reasonably radiosensitive. It may be assumed that at some time, perhaps in the last year of her life, the Hodgkin's granuloma underwent transition to the sarcoma type. Such transition has been observed and reported by others.

Case 2. A married nurse was admitted to the Cleveland Clinic Hospital on April 30, 1943, complaining of fatigue, pronounced weakness, dyspnea and failure of vision. She believed herself to be about 5 months pregnant, the last menses having occurred on November 15, 1942.

One year previously she had become aware of fatigue and weakness and the presence of two enlarged glands in the neck. The adenopathy subsided without treatment after

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an uncertain interval but weakness persisted. She was able to continue her profession until 2 months before admission when she became totally disabled with asthenia, dyspnea, and failure of vision; concomitantly cervical adenopathy reappeared.

The patient was obviously ill and the mucous membrane and skin were extremely pale, the latter having a faint icteric tint. Enlarged discrete nodes were present in anterior and posterior cervical regions, as well as in the axillary and inguinal regions. The spleen was large and firm with its inferior border at the level of the umbilicus. The pregnant uterus was thought to contain a 5-month fetus and fetal movements could be palpated. A roentgenogram of the chest showed no abnormality. The red blood count was 1,900,000; hemoglobin 4.7 Gm. or 30 per cent; color index 0.79; volume index 0.87; white blood count 7100; reticulocyte count 1 per cent; icteric index was 25 per cent. No abnormal white cells were present. Biopsy of a cervical gland showed Hodgkin's granuloma.

During her stay in the hospital she had a slight daily rise in temperature but never above 101 F. Eight transfusions of 500 cc. of whole blood were given. Extreme asthenia persisted. Irradiation was not attempted because of the continued poor condition of the patient and the generalized disease. At her request she was discharged. Death occurred on May 25, 1943, 1 month after hospital admission and before termination of pregnancy. No autopsy was performed.

Comment

A review of this patient's history indicates that from the onset of the disease to its termination there had been a continuous progression. Pregnancy may have hastened the outcome. It is unfortunate that a diagnosis was not made at an earlier date as the patient had not had the benefit of irradiation.

Case 3. A 24-year-old housewife was first seen at the Cleveland Clinic on May 25, 1943, complaining of swollen nodes in the neck associated with pain in the shoulders and neck. The discomfort had appeared about 4 months previously following delivery of her first baby; and adenopathy had been present for 1 month.

There was a single hard fixed mass in the left supraclavicular region but no definite adenopathy otherwise, and the spleen was not palpable. Red blood count was 3,980,000; hemoglobin 71 per cent; white blood count 9150; differential blood count normal. Roentgenogram of the chest disclosed large mediastinal nodes.

The patient had had a biopsy of a cervical node which disclosed Hodgkin's disease. She had been given roentgen therapy with satisfactory results.

The patient evidenced no further complaints until September 1946. At this time she was 5 months pregnant and a severe generalized pruritus had developed which continued unabated until the time of delivery December 22, 1946. Four roentgen ray treatments in the nature of a spray had been given without relief.

The patient was seen again in the Department of Dermatology at the Cleveland Clinic on February 11, 1947. Numerous excoriations and scars were present over the entire trunk and extremities as a result of almost continuous scratching. No palpable lymphadenopathy existed although a roentgenogram showed that the mediastinum was noticeably widened both to the right and left, presenting irregular nodular shadows consistent with Hodgkin's disease. She was given roentgen therapy to the anterior and posterior mediastinum and to an epigastric and midlumbar area field, after which the pruritus subsided promptly.

The patient manifested no further discomfort until August, 1947, when one large supraclavicular node was found. This swelling subsided after treatment. However,

pruritus reappeared in March, 1948, following which direct anterior and posterior mediastinal fields were irradiated. The pruritus subsided but a persistent cough remained. At this time no nodes were apparent in roentgenogram of the chest although infiltration was present, extending into left upper lobe.

The troublesome cough continued and in March 1948 infiltration of the left upper lung field had increased but no mediastinal adenopathy was apparent. A roentgenogram in May 1948 revealed a decrease in degree of infiltration in both lung fields, but also evidence of enlarged hilar nodes. As pruritus reappeared in October 1948, she was given roentgen therapy to the abdominal and lumbar areas.

Relief from pruritus was obtained, but when last seen on November 12, 1948, her general condition was obviously poor and the patient was considered in the terminal phase of the disease.

Comment

The patient survived for a 5 year period with Hodgkin's granuloma, the onset of which coincided with her initial pregnancy. A definite exacerbation of the disease occurred during her second pregnancy. Her children, however, are healthy.

Case 4. A woman, aged 23, was first seen at the Clinic on July 13, 1949. About 1 year previously, during her first pregnancy, she experienced difficulty in swallowing and occasional choking spells. Shortly thereafter she developed swelling of the lymph nodes of the neck followed by severe substernal pain. Fluoroscopic examination of the chest was made and a mediastinal mass was noted. The patient was given roentgen therapy to the chest and neck.

After delivery of a normal child, now 10 months old, a biopsy was made of a supra-clavicular node which proved to be Hodgkin's disease of the granuloma type.

She returned to the Clinic because of progressive loss of strength and energy and return of respiratory distress. On examination moderately enlarged cervical lymph nodes were palpable. Roentgenograms of the chest showed some enlargement of the hilar nodes. Blood counts were normal as were other routine laboratory examinations.

The patient was advised to return for further roentgen therapy.

Comment

This patient developed the first manifestations of Hodgkin's disease when pregnant. Sufficient time has not elapsed for a prognosis.

Discussion

Inasmuch as Hodgkin's disease is unpredictable, one cannot assume that pregnancy will have either a deleterious effect on the course of the disease or a favorable influence on the outcome. Instances are reported wherein women undergo pregnancy without exacerbation of the disease.⁵ Only 2 of Gilbert's 5 patients had any manifestations of the disease while pregnant.

From published reports one cannot conclude that pregnancy has any effects on the ultimate result. The general average survival of patients with Hodgkin's disease is about 2½ years; however, in our experience about 20 per cent live for 5 years. Epstein's⁶ report of 500 collected cases in both sexes indicates that

the outlook for women is somewhat better than for men by about 1 year. Three of Perrier's group of 5 were living at least 4 years after their respective pregnancies.

The future condition of the offspring of the mother afflicted with Hodgkin's disease cannot be predicted. Adair⁵ refers to the death of a 3½ month old infant born of a mother with Hodgkin's disease. The autopsy revealed a lymphoma of typical Hodgkin's type. There were 7 children in Gilbert's group without manifestations of the disease, the oldest 12 years of age, the youngest 3. One of our patients (Case 3) has 2 healthy children born during exacerbations of the mother's disease. The infant referred to in Case 1 cannot be traced while the 6 month fetus in Case 2 died with the mother.

Although marriage and pregnancy for women with Hodgkin's disease are inadvisable, as Gilbert says, "These events occur in spite of us." Inasmuch as a justifiable course is difficult to decide upon when pregnancy exists, individualization of cases is necessary. Abortion has been performed, followed by irradiation with favorable effect. Cesarean section followed by heavy irradiation failed to save another patient.

The patient, case 1, although having had Hodgkin's disease for 7 years prior to pregnancy, had no exacerbations during that time. However, soon afterwards her condition became progressively worse until death resulted. The original diagnosis was Hodgkin's granuloma and, at autopsy, Hodgkin's sarcoma.

The patient, case 2, was reasonably well for the first 5 months of pregnancy then became rapidly and progressively worse until death. The duration of disease apparently was less than 2 years.

The patient, case 3, first observed manifestations of Hodgkin's disease soon after delivery of her first child and there was probable exacerbation during her second pregnancy. She has survived 5 years and is still under treatment.

The patient, case 4, developed Hodgkin's disease early in pregnancy. It is questionable whether pregnancy influenced the disease.

Conclusions

Although a limited number of cases are presented they nevertheless call attention to the fact that pregnancy may result in exacerbations of Hodgkin's disease.

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