CARCINOMA OF THE CERVIX: ITS DIAGNOSIS AND TREATMENT

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In spite of the numerous articles which have been written on the subject of carcinoma of the cervix as well as the educational campaign which The American Society for the Control of Cancer has sponsored, a recent review of the histories of patients whom I personally have examined and treated shows that the disease was just as far advanced in those seen in 1935 as those seen in 1920.

For many years, women refused operation for cancer of the cervix because they felt that early recurrence usually occurred following operation, so that little was to be gained by this procedure. The extensive and successful use of radium in the past 15 years should have eliminated this objection, but the laity has come to believe that the pain which accompanies the late stages of the disease is due to a radium burn and for this reason many patients refuse radium treatment. Therefore, in spite of an educational campaign to inform women of the danger of carcinoma of the cervix, and in spite of the advances in the use of radium, many patients with this condition still do not present themselves for treatment until the disease has advanced to an incurable stage.

On the other hand, it is frequently found that many of these patients with advanced carcinoma of the cervix have consulted a physician from four to six months previously, only to be assured that they had no cause for worry. Had the true nature of the condition been recognized and proper treatment instituted at that time, some hope of cure might have been given to the patient. When a patient consults her family physician because of some supposed menstrual disorder, he must assume the responsibility and convince himself by a thorough physical examination that there is or is not an existing pathologic condition, and if there is, treatment must be instituted promptly. Consultation without proper examination gives the patient a false sense of security which leads to a delay of several months and often is just the time required for a carcinoma to advance from an operable to an inoperable stage.

The controversy regarding the relative merits of surgical and radiation treatment for cancer of the cervix has been fairly well settled. It is generally agreed that surgery is excellent treatment for early cases, but these are so rarely recognized that they can almost be disregarded. On the other hand, it is quite fair to say that radiation will cure as many of the early cases as will surgery without any mortality or morbidity.

Etiology and Prophylaxis

The etiology of cancer of the cervix or of any other part of the body is not known, and I do not propose to discuss the various theories that have been advanced. We can only analyze as carefully as possible the conditions existing in the area in which cancer has developed. The established relationship between chronic irritation and cancer indicates that better obstetric care and surgical prophylaxis in the treatment of ulcers and tears will reduce the incidence of cancer of the cervix.

The fact that 90 per cent of all carcinomas of the cervix occur in multiparous women cannot be looked upon merely as a coincidence. There must be an etiological relationship, and it is generally believed that the basic origin is parturitional trauma with sequential cell metaplasia. This may be regarded as the most definitely known lesion to precede cervical cancer, and it may be considered as essentially the exciting or secondary cause of the disease. It has also been demonstrated conclusively that only in the most exceptional instances does carcinoma develop in damaged cervices when prompt and adequate treatment is given following childbirth. In the final analysis, cancer of the cervix is largely an expression of incomplete maternity service, and it becomes obvious that the solution of the problem rests almost wholly in the hands of the obstetrician who, in most instances, is the family physician. Therefore, the responsibility for prophylaxis of cervical cancer falls upon him more than upon any other individual. The obstetrical service is not complete unless it includes a thorough examination from six to eight weeks after parturition when, if necessary, repair or linear cauterization of the erosion may be applied to insure complete healing.

Graves studied five thousand cases in which cervical repair had been done and found that malignancy developed later in only four patients. While these figures have not been compared with another series of equal size, they furnish sufficient proof that when proper care is given to the cervix after labor, it constitutes a very effective method of prophylaxis.

Erosions, eversions and leukoplakia may also be considered as precursors of malignancy. Erosions and eversions are best treated by linear cauterization with electric cautery and usually this can be done in the office. Electrocoagulation is also an excellent procedure, and the patient is required to remain in the hospital for only a few days.

Although leukoplakia has been known for many years, it has received far too little attention as a causative factor of cancer of the cervix, and this is probably true because it is difficult to recognize the condition unless you are actually looking for it. Its appearance in the mouth and on the tongue is familiar but often it is not recognized in the vagina. It may occur as bluish, pearly or grayish white plaques

which either are level with the mucosa or slightly raised if the hyperplastic process is excessive. In the diagnosis of leukoplakia, the cervix may be painted with Lugol's solution, and the healthy tissue will take the stain while the diseased tissue will not. However, ordinarily all pathology here is visible to the naked eye if one knows what he is looking for.

Diagnosis

When pain, hemorrhage and an odorous discharge are symptoms of carcinoma of the cervix, they usually indicate that the growth has advanced to an incurable stage; therefore, the condition must be recognized before these symptoms appear. The cause of any deviation from the normal menstrual cycle and of any vaginal discharge must be determined. The fact that any discharge is pathologic and the simplicity of the equipment for pelvic examination, as well as the easy accessibility of the cervix for inspection, all should render the diagnosis of carcinoma of the cervix a very simple matter for every physician. In case of any doubt regarding the diagnosis, biopsy may be done and we feel certain that it does no harm.

Some time ago, many articles appeared in the literature on the dangers of biopsy and the general feeling expressed by them was that distant metastases would result. On the other hand, dilatation and curettage were recommended for diagnostic purposes—what is the difference? Distant metastases from cancer of the cervix rarely occur, and in practically all patients who die from the disease, it is found that carcinoma is confined to the pelvis. The caution regarding biopsy may have discouraged physicians from employing this diagnostic procedure and may account in a large measure for some of the delay in diagnosis. Biopsy is not a major procedure, and it can be done in the office with small biting forceps. Less harm will be done by biopsy than by waiting for three or more months just to see how things will turn out. *Take biopsies freely from any suspicious areas.*

Rationale and Technic of Radium Therapy

The simple idea that radiation is a means of destroying cancer cells without too much injury to the normal cells is a good working hypothesis, but our accumulating knowledge regarding the physics and biologic effects of radiation has led to a better understanding of its action. In brief, radium has a threefold action on malignant tissues. It affects (1) the cancer cells, (2) the connective tissue and (3) the blood and lymph vessels. The action on the cancer cell is shown microscopically by swelling and vacuolization of the protoplasm and by shrinking of the nucleus. This is followed by phagocytosis and absorption and re-

placement by a homogenous connective tissue. This contracts and affects the lymphatic and smaller blood vessels and starves the growth.

Many varieties of technic have been used since radium therapy was instituted and many men have contributed to the advancement of our present knowledge, but there still remain two entirely different schools of thought in regard to the method of treatment. In one, the opinion is that it is best to give large massive doses in a short period of time, preferably in one or at most, two sittings. The other school believes that it is preferable to give very small doses over a long period of time. This difference of opinion undoubtedly will be settled before many years after the results of both methods are compared, but I believe that at the present time, most of the workers in this country favor the former opinion. Standardization of radium dosage for uterine cancer is impractical and dosage and technic must vary with the character and location of the involvement. At the Cleveland Clinic, we have altered our technic very little during the past 10 years, the only change being that since a larger amount of radium has been available, larger doses are given over shorter periods of time. We try to give the complete dose at one sitting, whereas previously the total amount of radiation was given in two doses. The average dose in our earlier cases was 4200 mg. hours distributed evenly in and against the cervix. In our later cases, since we have combined radium with high voltage x-ray, the average dose is about 3600 mg. hours. Our standard screen is made of brass, one and one-half mm. in thickness and this is encased in a rubber tube 3 mm. thick. At the present time, we place a tube in the fundus as well as in the cervix because in our earlier cases, we found that frequently a patient may be free from symptoms for a year or so and then suddenly have bleeding and discharge. Examination would then reveal a large undermined cavity at the upper end of the vagina which was the result of not placing the radium high enough in the cervical canal. Because of this finding, we believe that an anesthetic is necessary in order to estimate the extent of the growth and also to facilitate the accurate placement of the radium in proximity to the growth. It is sometimes impossible, even when the patient is under an anesthetic, to insert a tube of radium high in the cervical canal.

In addition to the radium tubes in the fundus and cervix, two or three tubes are placed against the cervix and these are held in position by packing the vagina tightly with gauze. If the growth is of the cauliflower variety, it is frequently curetted away or radium needles are placed in it. A catheter is then introduced into the bladder to keep it empty and, therefore, as far away as possible from the radium. Care should be taken in transferring the patient from the table to the cart and from the cart to the bed. We believe that bending and twisting the

patient during transfer will dislocate the vaginal tube and may account for bladder and rectal symptoms. The best method is to place the cart beside the table and slide the patient on the cart by means of a sheet and from the cart to the bed in the same manner, so that the position of the patient is unchanged throughout the procedure.

We have not used gold seeds in the treatment of any of these primary growths, but they are of great value in the treatment of recurrences because their action is more or less localized. Large, heavily filtered doses frequently are harmful in the treatment of recurrence. We have not had any experience with placing gold seeds in the broad ligaments by laparotomy.

The majority of the patients are able to leave the hospital the day following treatment unless they live some distance away. They are instructed not to be too active and to take a douche once or twice daily. An appointment is given for return in three or four weeks for high voltage radiation therapy which is administered by Dr. Portmann. The treatment is given in four or five doses over a period of four or five days. After patients have been treated, we make an effort to have them return at monthly intervals for three months and after that every three months during the following year. If local recurrences develop, they are treated with radon seed implantation. If the recurrence is deep, radiation therapy is repeated with marked relief for a time. In cases in which there is no ureteral involvement but pain is referred down the legs, we perform a chordotomy, a bilateral lumbar sympathectomy, just as a gasserian ganglion operation is done for relief of pain in cases of extensive malignant disease of the face.

We believe that surgery following apparent cure by radium therapy is not only unnecessary but is frequently disastrous, and many surgeons who employed this procedure from five to ten years ago have now abandoned it. Neither should radiation be relied upon to offset the disaster of an incomplete operation.

Complications

The chief complications of the treatment of carcinoma of the cervix by radium are the production of symptoms referable to the rectum and bladder and of urinary and fecal fistulae. Symptoms of bladder and rectal disturbances are of two types—early and late, and it is quite important that they should be recognized. It is reasonable to assume that if a sufficient dose of radium is given to cure carcinoma of the cervix, it will also be sufficient to produce an erythema to the rectum or bladder. Very often, this erythema is slight and passes unnoticed unless the patient is questioned. If it is severe, it is evidenced by a

slight burning sensation and a desire to go to stool or to void somewhat more frequently than usual. In the mild cases, the condition usually clears up in from ten days to two weeks, but in the severe cases from four to six weeks may be required. In this latter group of cases, the late rectal and bladder complications usually develop six or eight months after the initial radiation treatment. These late symptoms are often mistaken for recurrence of the carcinoma, and if the patient is treated for recurrence, irreparable damage will result. A clue to the true state of affairs is found in the fact that the symptoms are entirely out of proportion to the findings. There are severe pains and tenesmus, and the stool contains considerable blood and mucus. Digital examination causes greater pain than is produced when recurrence is present. The patient is not cachectic. Proctoscopic examination reveals a puckered-up scar or small ulcer at about the level of the cervix with telangiectasis and considerable redness of the mucosa. The condition may be compared to an overtreated area on the skin which has healed by the formation of scar tissue through which fine vessels may be seen. In the rectum, the scarring is subject to trauma and infection from subsequent ulceration which causes the late symptoms.

When bladder symptoms are present, cystoscopic examination reveals an area of intense redness and sometimes of ulceration. Occasionally, urinary salts are deposited in the slough in the bladder, and stones will be formed.

Treatment of the rectal symptoms consists of rest in bed, cleanliness of the lower bowel and the injection of three or four ounces of warm olive oil into the rectum twice a day. Occasionally, an opium suppository is necessary.

Irrigation of the bladder and the instillation of gomenol are recommended for treatment of the bladder symptoms. From four to six months may be required for the treatment of these bladder and rectal complications, but the cases in which these symptoms occur comprise a very small percentage of the total number.

Another complication is a rather new clinical entity which is called benign stricture of the intestine following radiation therapy. This may develop and surgical intervention may be necessary many months or even years after complete regression of or cure of the cervical cancer. The importance of recognizing this complication is perfectly obvious, because the pain due to the obstruction is easily construed as or confused with that produced by metastatic carcinoma. In a series of 451 cases of cervical carcinoma which have been treated by radiation therapy up to July, 1934, seven known cases of benign stricture of the intestine causing obstruction have been observed. In five of these cases, the stricture was in a movable segment of the sigmoid and in two cases in

the small intestine. All of these were observed in patients who had received irradiation for cancer of the cervix, but the increasing use of the radiation for other conditions necessitating exposure of the intestine may result in similar complications. The time of onset of the obstructive symptoms in these cases varied from eight months to eight years, and in no case was there any evidence of malignancy in the pelvis or in the stricture.

The rate of recurrence of cancer is so high that almost any abdominal or pelvic pain may quite naturally and logically be attributed to malignant extension or malignancy. If the condition is actually benign and is caused by radiation therapy, it is quite obvious that additional radiation treatment would aggravate this condition. Before attributing this disability to metastases, thorough pelvic and sigmoidoscopic examination should be made, and this should be followed by roentgen examination of the gastro-intestinal tract if necessary. We know from experience that carcinoma of the cervix generally remains confined to the pelvis, so that if the pelvis is free from induration and the patient has a pain simulating obstruction, exploratory operation is justifiable before the patient is referred for roentgenotherapy which may prove disastrous. In our series, five patients were restored to normal health by resection or short-circuiting operations.

Summary

The incidence of carcinoma of the cervix is not decreasing in spite of improvement in diagnostic and therapeutic procedures and in spite of the efforts of various organizations to inform the laity of the importance of early diagnosis and treatment.

In addition to conditions resulting from childbirth, erosions, eversions and leukoplakia must be recognized and considered as precursors of malignancy.

Early diagnosis depends upon determining the cause of any deviation from the normal menstrual cycle and of any vaginal discharge. Pain, hemorrhage and an odorous discharge are symptoms of late carcinoma of the cervix. Biopsy is an invaluable aid in diagnosis, and should be used in any case where the slightest doubt of the true nature of the condition exists.

Radium therapy is the treatment of choice and is equally as effective in early carcinoma as in the late inoperable stages.

Symptoms referable to the rectum and bladder, urinary and fecal fistulae and benign stricture of the intestine are the usual complications of radiation treatment.