IRRADIATION IN THE TREATMENT OF CANCER OF THE BREAST

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There are a few ancient writings which discuss medical subjects including cancer of the breast, the earliest dating back to about 2000 years before Christ. After printing processes were developed, considerably more was written about methods of treatment and it is apparent that cancer of the breast has been treated by caustics, cautery, and excision through many centuries. When Halsted wrote his classical report and described his radical operation he reviewed the literature prior to 1897 and came to the conclusion that up to that time no woman with cancer of the breast had been cured. Following his report and that of Willy Meyer, all other methods of treatment were discarded and radical operations were generally employed.

These radical operations have become quite standardized by skilled and experienced surgeons. In them, the mammary gland, fascia, muscles, and axillary contents are removed "en masse." These are the anatomical limits of the most radical operative procedure recognized as justifiable, but cancer of the breast unfortunately is not always confined within these limitations. It extends beyond the anatomical boundaries of the most radical surgical procedure in a majority of cases as is evidenced by the fact that the general average of surgical curability of cancer of the breast, on the basis of the five year survival rate, is approximately thirty per cent. This average was compiled from reports which eminent surgeons have published since 1900. This means that in seventy per cent of the cases the disease had extended beyond the possibility of removal by the time operations were performed. It may also be concluded that with the modern radical technic, surgeons have reached the limit of the possibility of curing a higher proportion of cases on the basis of the extent of operation alone. This is indicated by their reports in the literature which show that the average five year survival rate has been the same during the past twenty years as it was during the twenty years preceding and immediately following the advent of the radical technic.

It is also interesting to note from reports in the literature that the five year survival rate has varied from fifteen to fifty per cent. These reports were made by skilled and experienced surgeons who operated under the best of conditions and employed a technic which is now quite standardized. If this assumption is justifiable, then a logical explanation of the wide variation in results is due to differences in the types of cases selected for operation, some surgeons operating upon more advanced cases and therefore obtaining a lower percentage of survivals

than those who do not operate upon women in advanced stages of disease.

If a thirty per cent five year survival rate has been the average result obtained by the standardized radical operative technic by the most skilled surgeons operating under the most favorable conditions, then the medical profession should endeavor to find other methods of treatment to supplement operation. The only modern method known to be effective in the treatment of cancer is irradiation by radium and roentgen rays.

If the literature is studied to determine what may be the efficacy of irradiation in the treatment of cancer of the breast, it will be found that there are differences of opinion among surgeons. Of course, radiologists are almost unanimously convinced of the usefulness of their methods of treatment. But in almost every instance when surgeons have reported that irradiation has been of no benefit and have based their conclusions upon comparisons of series of cases in which irradiation was given before or following operations with series in which there was no irradiation at all, it is obvious that the irradiated series contained a considerably greater proportion of cases in which the disease was advanced. Many surgeons have included in the irradiated series cases in which treatment was given any time subsequent to operation, primarily because of recurrences or metastases and not solely to prevent extension of the disease. This is unjust because the treatment of recurrences or metastases presents a different problem and the prognosis is entirely unlike that for primary or early, localized malignant tumors.

Deductions based upon disproportions between early and advanced cases are not justifiable. The only way that logical conclusions can be reached about the benefits of one method of treatment over another is to compare series containing equal proportions of cases in the same stages of disease.

A number of suggestions have been made for classifying cases of cancer of the breast both from the clinical and histological aspects. The latter method has been found to be uncertain because cancers of the breast are not often histologically homogeneous but most are heterogeneous. Indeed, several types of morphology may be found in almost every tumor. Another objection to classifying tumors on the histological basis is that, although this may indicate what the rate of growth or dissemination may be, it tells nothing about the actual extent of the disease which is the most important consideration from the standpoint of prognosis.

Therefore, it would seem that the best method of classifying cases of cancer of the breast for statistical comparisons would be to take into consideration both the clinical and the pathological evidences of the

extent of the disease. A method of classification or grouping of cases on this basis which we have found to be of value not only for statistical purposes but also to indicate what therapeutic procedures are preferable may be stated as follows:

Group I: Cases in which freely movable tumors are definitely localized in the breast, the skin is not involved, and no metastases are present in the axillary lymph glands.

Group II: Cases in which freely movable tumors are definitely localized in the breast, the skin is not involved, but there are metastases in only a few axillary lymph glands.

Group III: Cases in which there is diffuse involvement of the breast, the skin is involved, edematous or ulcerated or with multiple nodules, and metastases are present in numerous axillary lymph glands or other tissues.

In order to illustrate how this method of grouping may be applied, I selected a series of 405 cases of cancer of the breast operated upon by Dr. George Crile. Of these, there was sufficient information about 373 to classify them according to the plan suggested. It was found that about 30 per cent fell into Group I, 25 per cent into Group II, and 45 per cent into Group III. No doubt the same relative proportions would be found in each group in any large series of cases. It should be noted that in 70 per cent of cases axillary metastases were present (Groups II and III).

When an analysis was made to determine the surgical curability based upon the five year survival rates, it was found that in a series of 170 cases in which operation was the only treatment, none of the patients having had irradiation at any time, almost 100 per cent of patients in Group I lived for five years. This might be expected because in this group the cancers were well localized, not having extended even to the axillary lymph glands and therefore all the neoplastic tissue was excisable.

Of the Group II cases in which operation alone was performed, about 50 per cent of the patients survived five years. This indicates that, in an equal proportion of cases, the entire neoplastic process could not be removed and therefore the patients succumbed. Of the Group III cases no patient survived five years without evidence of cancer. Certain conclusions may be drawn from Group II and Group III cases. First, if only a few lymph glands are involved from a cancer of the breast, the neoplastic disease is removable by operation alone in about one-half of the cases because approximately one-half of the patients in this category survived five years. This may mean either that cancer tissue was left locally or in the axilla or that distant metastases had developed prior to operation. Secondly, it has been stated that almost one-half of

all patients are in advanced stages of disease at the time of operation (Group III) and none are cured. This indicates that radical operations upon patients in this category should not be performed but other methods of treatment should be employed instead.

Some surgeons have been skeptical about the advantages of irradiation given immediately after operation because, in certain instances, those unfamiliar with radiological procedures have drawn erroneous conclusions as a result of incorrect analyses of statistics. A few have stated that irradiation not only was of no benefit but that the proportion of patients who died following such treatment was higher than those who did not receive irradiation. Of course, such conclusions must be based upon disproportions between the advanced and early cases in the series used for comparison. It is obvious that irradiation cannot spontaneously inject neoplastic cells before or after operations for cancer of the breast and that if recurrences or metastases do develop the disease must have been present at the time of treatment which may have been as ineffectual as the operation.

Many radiologists have published statistics about their results but, unfortunately, these usually appear in publications that seldom are read by surgeons. It will be found by studying many of these reports that the average five year survival rate for patients treated immediately after operations for cancer of the breast has been 40 per cent by methods employed some years ago. With new developments in technic, this percentage has increased. This shows a distinct benefit as compared with the average of 30 per cent by operation alone.

However, all these statistics were based upon unclassified cases and the wisdom of grouping cases for comparisons has been discussed. A study of our series of 235 cases in which postoperative roentgenotherapy was given immediately following operation for cancer of the breast shows that 230 could be grouped on the basis of the criteria previously mentioned. Of these, 25.2 per cent fell into Group I, 30.4 per cent in Group II, and 44.4 per cent into Group III. It was found that irradiation in Group I cases was of no benefit. This could be expected because almost 100 per cent of these patients are curable by operation alone. Approximately 70 per cent of the patients whose carcinomas were classified as Group II and who were given roentgenotherapy survived five years which was a distinct improvement over the number of patients in the same group but who had operation alone; only 50 per cent of these patients lived five years. Of the patients in Group III, 10 per cent of those who received irradiation survived five years but none was without evidence of cancer. However, in this group the proportion of patients who survived each yearly period up to five was higher than those having operation alone.

It may justifiably be concluded from a comparison of these two series of cases that there was benefit from roentgenotherapy given postoperatively, not necessarily because a greater proportion of patients were cured of cancer of the breast but because some lived longer due to delay in extension of the disease in some cases. Of course, such a statistical analysis does not take into account the benefits of irradiation for the relief of distress from metastases. There is no mathematical basis by which to estimate palliation.

The results of treatment of the patients in the two series grouped according to the extent of the disease indicate what procedures should be employed in the treatment of cancer of the breast.

A woman with a small localized tumor in the breast should be operated upon immediately. It may be difficult in many cases to distinguish between benign or malignant tumors on the basis of clinical findings alone. The tumor should be excised completely and examined microscopically at once. If the tumor is benign, no further operative procedure is necessary. If the tumor proves to be malignant, a more extensive operation should be performed. A simple mastectomy may suffice occasionally if the tumor is very definitely and conclusively found to be well localized. However, in a majority of cases it will be necessary to perform a radical operation and to explore the axilla by complete dissection in order to disclose the extent of the disease.

After removal, the breast and each axillary node should be examined carefully by a pathologist. If no axillary metastases are found the patient will be in Group I or Stage I, and the prognosis will be good because experience proves that almost 100 per cent of the patients in this category are cured by operation alone. Roentgenotherapy given postoperatively is not indicated because all the malignant tissue has been removed. But when metastases are found in even a few axillary lymph nodes, the chances of the patient surviving for five years will be 50 per cent by operation alone. These are Group II cases. Naturally, the number of axillary nodes involved does make a difference in the prognosis. But patients with axillary metastases should receive roentgenotherapy immediately postoperatively in the hope of destroying or delaying the progress of the disease because some neoplastic tissue will remain in one-half of such cases and there is no conclusive way of determining in any case whether or not cancer remains.

The advanced Group III cases offer quite a different problem. A large proportion of these patients will present clinical evidences that the disease is extensive and incurable by the most radical surgical procedures. It should be noted that there is a difference between "operability" and "curability." Technically, it may not be difficult to perform a radical mastectomy but the question of whether the operation will

benefit or cure the patient should be paramount. It has been shown that no patient with manifestations of incurability has survived free from cancer for five years; indeed, there is good evidence which indicates that the lives of patients with advanced cancer of the breast actually are shortened by radical operations. Since patients with clinical evidences of incurability cannot be cured by the most radical surgical procedures, there is no justifiable reason for operating upon them except in very rare instances where a minor operation is performed for purely esthetic reasons. These patients should be given the benefit of irradiation by roentgen rays or combined with radium according to the individual indications. At least this treatment will not shorten life; on the contrary, in many instances it will cause tumors and axillary or supraclavicular metastases to disappear completely, thus definitely prolonging the lives of many patients although a cure may not be effected. It should be recalled that 45 per cent of all patients on whom operation was performed in our series were in Group III and had extensive disease and were therefore incurable. But this proportion of cases does not include some who were considered to be in too far advanced stages of the disease to justify operations. In all probability more than half of the patients who have come to surgeons in the past were incurable by operation.

Sometimes it will be impossible to determine on the basis of clinical examinations alone which patients are incurable by operation. Some patients may have rather small tumors, the skin may not be involved, there may be no evidence of axillary metastases but after operation numerous lymph nodes may be found with metastases or other evidences of incurability. These patients should receive roentgenotherapy immediately postoperatively. On the other hand there are clinical manifestations which should be sought and patients with any of them should not be operated upon but instead irradiation should be given. These evidences of incurability may be tabulated in the following manner:

The skin: Edema
Browny red, indurative and inflammatory
Multiple nodules
Ulcerative

The breast: Edema
Diffuse infiltration
Multiple tumors
Fixation of breast or tumor to chest wall

Metastases: Axillary nodes, numerous, extremely involved, unfixed
Supraclavicular nodes or edema of arm
Distant metastases (lungs alone or other organs).

Conclusions

1. Series of cases of cancer of the breast to be analyzed for statistical purposes should be grouped according to a suggested plan which is based upon the extent of the disease found to be present in each case.

2. Patients with tumors of the breast but with no clinical evidences of incurable cancer should be operated upon immediately.

3. If cancer of the breast is found on immediate microscopic examination, radical mastectomy should be performed in the majority of cases.

4. If no metastases are found to be present on microscopic examination of all axillary lymph nodes removed, no other treatment is necessary and almost 100 per cent of the patients will survive five years (Group I).

5. If axillary metastases are found in only a few axillary lymph glands, about 50 per cent of the patients will survive five years if operation is the only treatment. Immediate postoperative roentgenotherapy should be given to such patients, in which case about 70 per cent will survive five years (Group II).

6. If numerous axillary lymph nodes show metastases, no patient will survive five years free from cancer if operation is the only treatment. Roentgenotherapy should be given immediately to delay extension of the disease and prolong life.

7. Patients with the clinical evidences of incurability which are enumerated should not be operated upon but treated by irradiation alone.

8. Improved technics offer even better results from irradiation than were possible five or more years ago.