A COMPARISON OF RESULTS OF SURGERY AND RADIOTHERAPY IN CARCINOMA OF THE CERVIX UTERI

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This series of 179 cases of carcinoma of the cervix shows the five-year results obtained in all patients suffering from this disease who were seen at the Middlesex Hospital during the years 1931-4 and who had received no previous treatment. They afford material for comparing the various methods of treatment adopted. These patients have been treated surgically by several members of the surgical staff, and by radiotherapy by the radiotherapy staff of the Meyerstein Institute of the Middlesex Hospital. We are indebted to them for permission to study and report their results.

The importance of the series is that it gives the results obtained from the total number of cases of carcinoma of the cervix undergoing treatment at a single hospital when both surgical and radiotherapeutic methods have been available. Each patient was seen in the first instance by a surgeon with a view to the performance of Wertheim's hysterectomy, and only those cases which were inoperable by reason of the extent of the growth, of age, or of general condition were referred for radiotherapy. In two cases radiotherapy was given because operation was refused. Sixty-four were treated by surgery, 104 by radiotherapy, and 11 received no treatment.

The surgical cases consisted of 59 patients treated by surgery alone and 5 to whom post-operative x-radiation was given in addition. The radiotherapy cases were made up of 87 patients treated by a combination of radium and x rays, 14 treated by radium alone, and 3 treated by x rays alone. The 11 cases untreated consisted of 1 patient who refused treatment and 10 who, either on account of widespread dissemination of the growth or because of their hopeless general condition, were considered to be too advanced even for palliative measures.

The surgical operability rate was 64 out of 179 cases—i.e., 35.7%. The radiotherapy treatment rate was 104 out of 115 cases—i.e., 90.4%. Eleven cases (6.1%) were untreated. The average age of the patients was 53.5 years, the youngest being 31 and the oldest 80. There were 9 nulliparous women in the series (5%), and one of these was clinically a virgin. Histological confirmation of the diagnosis was obtained in 159 out of the total of 179 cases, but such confirmation was obtained in every patient but one of those who survived five years. There were 152 cases of squamous-celled carcinoma and 7 of adenocarcinoma. All the patients treated have been kept under continuous observation for more than five years, with the exception of two who could not be traced.

Classification of Cases

The series of patients treated by radiotherapy has been divided into the four stages of the League of Nations classification, which is as follows:

Stage 1.—The growth is strictly limited to the cervix uteri. Uterus mobile.

Stage 2.—Lesion spreading into one or more fornices with or without infiltration of the parametrium adjacent to the uterus, the uterus retaining some degree of mobility.

Stage 3.—(a) Nodular infiltration of the parametria on one or both sides extending to the wall of the pelvis, with limited mobility of the uterus or massive infiltration of one parametrium with fixation of the uterus. (b) More or less superficial infiltration of a large part of the vagina with a mobile uterus. (c) Isolated metastases in the pelvic glands, with a relatively small primary growth. (d) Isolated metastases in the lower part of the vagina. [Generally speaking, all cases not falling into Stage 2 or 4 will be placed under Stage 3.]

Stage 4.—(a) Cases with massive infiltration of both parametria extending to the walls of the pelvis. (b) Carcinoma involving the bladder or rectum. (c) The whole vagina infiltrated (rigid vaginal passage), or one vaginal wall infiltrated along its whole length with fixation of the primary growth. (d) Remote metastases.

The League of Nations classification has not been used for the surgical series, which has been divided into two groups according to the results of histological examination of the glands removed at operation: (1) glands free from carcinoma; (2) glands invaded by carcinoma. It was often found at operation that patients clinically belonging to Stages 1 and 2 of the League of Nations classification had invasion of the glands and, conversely, that patients having extensive local growth had no invasion of the glands.

Results

Results have been assessed in terms of five-year survival rather than of cure. This has been done in order to avoid any difficulty in the interpretation of the significance of residual pelvic thickening following treatment. In fact, all the 26 survivors in the radiotherapy group remained free from signs or symptoms of disease during the five years following the completion of their single course of treatment. During the sixth year one patient developed lumbar pain without definite evidence of recurrence. She received a course of x-ray treatment, and now remains well, two years later. Of the 23 patients who survived five years following surgical treatment 2 had signs of recurrence of the growth during the fifth year and have since died.

TABLE I.—Wertheim's Hysterectomy

	No. Treated	Died of Operation	Died of		Un-traced	Five-year Survival
			Cancer	Other Causes		
Glands not invaded	46	6	16	3	2	19 (41.3%)
Glands invaded ..	18	5	8	1	0	4 (22.2%)
Total	64	11 (17.2%)	24	4	2	23 (36%)

Five of the patients in Table I were given post-operative x-ray treatment. We can find no indication for the selection of these patients, as 3 had no glandular involvement and in 2 the glands were involved. They all died before the end of the five-year period.

TABLE II.—Radiotherapy

	No. Treated	Treatment Mortality	Died of		Un-traced	Five-year Survival
			Cancer	Other Causes		
Stage 1	12	0	5	0	0	7 (58%)
" 2	13	1	7	1	0	4 (31%)
" 3	43	2	27	1	0	13 (30%)
" 4	36	2	32	0	0	2 (5.5%)
Total	104	5 (4.8%)	71	2	0	26 (25%)

44% } 35.3%

The routine method of radiotherapy used has been the combination of the insertion of radium to the uterus and vagina by the Paris technique, and the application of *x* rays to the parametria. Eighty-seven patients were treated by this method. Before the adoption of this routine 14 cases were treated by radium alone. At this time a modification of the Stockholm technique was employed. Only one of these patients survived the five-year period. Three were treated by *x* rays alone as a palliative measure because their condition was so bad that radium could not be applied. Two of them died during the course of treatment, and the third shortly after it had finished.

Combined Results of Surgery and Radiotherapy.—Out of the 179 who applied for treatment 49 survived five years—i.e., an absolute survival rate of 27%. If from the 179 patients deductions are made of those untreated (11), those untraced (2), and those who died of other causes while free from disease (6), the relative survival rate is 49 out of 160 cases—i.e., 30.6%.

Discussion

With the two methods of classification employed it is difficult to compare accurately the results obtained by surgery with those obtained by radiotherapy, but such comparison is still of value. Even though cases treated by radiotherapy which are clinically Stages 1 and 2 may have glandular invasion, a comparison of these groups with the surgical gland-free cases shows 44% five-year survivals treated by radiotherapy as against 41.3% of the surgical cases.

The surgical cases with glands may be compared with the Stage 3 (c) radiotherapy cases—i.e., “isolated metastases in the pelvic glands with a relatively small primary growth.” Almost all the remainder of the Stage 3 radiotherapy cases must be regarded as inoperable, as can be seen from the relatively large number considered unsuitable for surgery and referred for radiotherapy. Nevertheless, comparison of the results of all the Stage 3 radiotherapy cases of every category with the “gland-invaded” surgical cases shows 30% of five-year survivals from radiotherapy and 22.2% of five-year survivals from surgery.

If the cases in Stages 1, 2, and 3 treated by radiotherapy are compared with all the surgical cases, both “gland-free” and “gland-invaded,” then the figures show 35.3% five-year survivals from radiotherapy and 36% of five-year survivals from surgery—an approximately equal figure; but there were 63% of Stage 3 cases in the radiotherapy figures and only 28% in the surgical figures.

These results were obtained with an operative mortality of 17.2% in the patients treated by surgery and with a treatment mortality of 4.4% in the patients receiving radiotherapy. In this series, moreover, consideration must be given to the fact that the results of radiotherapy were obtained in patients who had previously been rejected by a surgeon as unsuitable for surgery either on account of extent of growth or of poor general condition. The material for radiotherapy was therefore much inferior to that treated surgically, and allowance must be made for this in any comparison of these two methods of treatment based on this series.

Conclusions

In technically operable cases of carcinoma of the cervix a higher percentage of five-year survivals has been produced by radiotherapy than by surgery.

This result has been obtained with a much lower treatment mortality.

In technically inoperable cases of carcinoma of the cervix a small percentage of five-year survivals has been obtained by radiotherapy.

Clinical Memoranda

Friedländer Pneumonia successfully treated with Sulphapyridine

The following case is an example of a rare type of acute lobar pneumonia which is not widely recognized in this country and is therefore probably often overlooked. Its signs and symptoms have been well described in two series of cases in America (Bullowa *et al.*, 1937; Solomon, 1937), and there can be no doubt that it is a distinct clinical entity. It is characterized by profuse slimy brightly blood-stained sputum containing a pure culture of Friedländer's pneumobacillus, pronounced toxæmia, and a very high mortality (83% in the first series mentioned and 97% in the second). If the patients survive long enough septic complications such as lung abscess or empyema usually develop.

CASE HISTORY

The patient, a man aged 43, was admitted to the Western General Hospital, Edinburgh, in March, 1939. He had been ill for five days with a cough, and during the past three days had been bringing up large quantities of slimy sputum which was heavily blood-stained. On examination he was very collapsed. There were typical signs of consolidation of the right lower lobe; this was confirmed by radiograph. His temperature was 100° F., and the white blood count was 8,000 per c.mm. His sputum, which was quite unlike the usual rusty sputum seen in acute lobar pneumonia, contained many Friedländer pneumobacilli but no other organisms. Blood culture was negative, and remained so.

He was immediately given four 0.5-gramme tablets of sulphapyridine, and four more two hours later, and then two tablets four-hourly. His temperature fell to normal in forty-eight hours, with marked clinical improvement, but rose again after a further twenty-four hours, and two days later he developed a right-sided empyema. The pus contained a pure growth of Friedländer's pneumobacillus. He was treated by rib resection and drainage, and made an uninterrupted recovery. Sulphapyridine was stopped six days after admission, a total dosage of 32 grammes having been given.

DISCUSSION

In a disease with such a mortality the mere survival of a patient following use of sulphapyridine suggests that the drug is potent against the bacillus. This was supported by the rapid clinical improvement in the early stages of treatment. The development of an empyema does not indicate that the drug was without value, as such a development is common in acute pneumococcal lobar pneumonia, in which the value of the drug is of course undoubted.

I have been unable to trace any other detailed report of treatment of a similar case, but Long and Bliss (1939) have had good results in experimental infections in mice, and they recommend the use of the drug in any Friedländer infection in man. Meyer and Antman (1939) report the successful treatment of a case of septicaemia due to the bacillus, the source of infection being unknown.

It is obviously impossible to generalize from one case, but it is hoped that mention of it may help to draw attention to the existence of this interesting condition and to the possibility of its successful treatment.

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REFERENCES

- Bullowa, J. G. M., Chess, J., and Friedman, N. (1937). *Arch. intern. med.*, **60**, 735.
- Long, P. H., and Bliss, E. A. (1939). *Clinical and Experimental Use of Sulphanilamide, Sulphapyridine, and Allied Compounds*, p. 236, Macmillan, New York.
- Meyer, K., and Antman, L. (1939). *J. Amer. med. Ass.*, **113**, 1641.
- Solomon, S. (1937). *Ibid.*, **108**, 937.