The Influence of Syphilis in Cancer of the Cervix Uteri

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The problem of the influence of syphilis upon the neoplastic process in general has not been solved. Some investigators, on the one hand, have ascribed to syphilis an etiological role. Others deny any relationship between the two diseases. The consensus of opinion (2), however, is that an inter-relation exists between the two in the case of carcinoma of the buccal cavity, though the mode of interaction is not known. In addition to a causative role is the influence that syphilis may exert on the clinical course of a tumor through the personal equation involved or through some alteration in the pathology of the disease. Regardless of the lack of objective data bearing upon this subject there is a widespread impression among radiologists that when cancer appears in a syphilitic patient the prognosis is very much less favorable than in the absence of a spirochetal infection. In a recent article Rosh (5) has summarized the opinion of radiologists as follows: "We may state at this point, that patients who had a previous syphilitic infection show a tendency to earlier recurrence. It is our impression that this applies to the untreated syphilitic as well as to the treated ones, particularly in the younger age groups."

To a lesser degree the opinion is held among pathologists and clinicians that cancer is more highly malignant in the syphilitic patient. Black (1) concluded that "A final possibility is that in leaving syphilis untreated during the treatment of cancer the prognosis may be worsened, but I do not know of any evidence to this effect." Recently Schrader (6) reported 47 cases of cervical cancer occurring in women with positive serology for syphilis, a group representing approximately 4 per cent of his total series. In this group of 47 only 7 had had adequate antiluetic therapy. He concluded that syphilitic women, with or without adequate antisyphilitic therapy, respond poorly to radiation treatment and suggested that radiation morbidity from such causes as bladder and rectal distress and anemia is greater than in those free from syphilis.

The following investigation was undertaken to study this problem, using data obtained at the time a positive diagnosis of cervical uterine cancer was made. The symptoms, physical findings, and histopathology have all been tabulated and considered. No attempt has been made to include the results of treatment as this aspect will be dealt with in full at a later date. The data available do not give reliable information on the treatment given for syphilis in the 7 cases which had been diagnosed prior to the diagnosis of cancer. Three of them had received known efficient treatment for a period of 4 and 5 years. Unfortunately the question of leukoplakia and condylomas preceding the development of carcinoma in this series cannot be answered from our records.

CLINICAL MATERIAL

The data were derived from the records of 227 consecutive cases of epithelioma of the cervix uteri seen at the Los Angeles General Hospital and the Hornsby District Hospital in Sydney, Australia. The only factor of selection operating on the total series consisted of the restriction that the patients be unable to pay for treatment in private hands but this in no way affects the comparison within the group. A histopathologic confirmation of the diagnosis is available in each case, obtained either by biopsy or autopsy. Serologic examination of the blood was made in each patient and a positive complete fixation reaction was accepted as the criterion for the presence of syphilis. By this method 36 patients were considered to be syphilitic and 191 were classed as free from the disease. This gives a percentage incidence of 15.8. The total incidence of syphilis as indicated by routine blood tests in the hospital averages about 5 per cent but it cannot be used here for comparison as it is not corrected for the age and sex factors which obviously operate in a series of patients with cancer of the cervix uteri. The history, evaluation of the stage of involvement, and the pathologic grade of malignancy were made by independent observers and confirmed by the author.

INFLUENCE ON AGE DISTRIBUTION

It has been suggested that syphilis predisposes to the earlier appearance of cancer. The age distribution as regards extremes was the same in both groups varying from cases in the 3rd to the 8th decade. The incidence of the disease before 40 years of age shows a slight weighting on the side of the luetic, though it is not statistically significant. The average age, however, for the series of syphilitic cases was 47 years,
and for the nonsyphilitic 51.1 years. The age distribution in periods of 5-year groups is graphically shown in Fig. 1.

Fig. 1.—Graph showing the age distribution in 5-year periods in percentage of incidence. The dotted line represents the syphilitic cases.

Fig. 2.—Diagram showing the percentage distribution of the pathologic grades of malignancy. The shaded area represents the syphilitic group.

Fig. 3.—Diagram showing the percentage distribution according to stage of involvement when first seen clinically. The shaded area represents the syphilitic group.

INFLUENCE ON GRADE OF MALIGNANCY

The conception of assessing the degree of (malignant) activity present in a tumor is largely credited to Broders who worked out his system of four grades in epitheliomas. Depending upon the degree of anaplasia he classifies tumors in grade 1 when the cells resemble, to a large degree, the cells from which they have originated. If the majority of the cells are poorly differentiated and abnormal in morphology they are considered to indicate a rapidly growing tumor and this is called grade 4. Grades 2 and 3 are the intervening stages. In the case of cervical epithelium the grading as advocated by Martzloff (3, 4) considers only three grades, as the highly differentiated type known as grade 1 in Broders' system is rarely, if ever, seen.

For our purpose we have used the Martzloff grading (3, 4). Grade 1 is composed of cells showing marked differentiation and with the presence of intercellular bridges. These may be termed the spinal cell type. The grade 3 cells are the most rapidly growing cells and are typified as the spindle cell group. The grade 2 tumors are transitional cell growths between grades 1 and 3 in type. The results of grading the carcinomas in this series are shown graphically in Fig. 2. In both classes the highly malignant growths composed 20 per cent of the group. However, the grade 1 carcinomas comprised 35 per cent of the cases in the nonluetic group and only 20 per cent in the luetic group. This difference is not sufficient to be conclusive but does give an indication of a tendency in this series. Further tabulation on a larger series will be undertaken at a later date.

INFLUENCE ON CLINICAL STAGE AT FIRST EXAMINATION

At the time the positive diagnosis of cervical cancer was made each case was classified according to the extent of clinical involvement. The importance of the degree of invasion upon the question of operability or prognosis is so well recognized as to require no further comment. The stages are numbered from 1 to 4, as follows: 1. involvement limited to cervix; 2. limited to cervix and contiguous tissue (no fixation); 3. invasion of parametrium; 4. marked fixation in pelvis or distant metastases.

In Fig. 3 the percentages in each stage of the luetic and nonluetic group are compared. It must be pointed out that 37 per cent of the nonsyphilitic group were found in stages 1 and 2 in contrast to only 22 per cent of the syphilitic group in the same stages. The importance of this difference in the prognosis of the disease is at once obvious. That this difference is not due to the time element is seen from the fact that the period of time elapsing from the appearance of the first symptom to the time of seeking medical attention
was 7.1 months in the syphilitic group and 8.4 months in the other. No significance is attached to this difference as it is probably due to several long-neglected cases in the nonsyphilitic series who entered the hospital in a moribund condition after approximately 4 years of symptoms.

INFLUENCE OF MULTIPLE PREGNANCY

It has been suggested that syphilis may exert an influence upon cancer of the cervix through the repeated injury to the cervix due to the many miscarriages which so often accompany the disease. The present series of cases was studied in this aspect and it was found that the syphilitic patients had had an average of 4.9 pregnancies while the nonsyphilitic group had an average of 4.0. This could not be considered a reliable difference as one woman in the former group had had 38 miscarriages, a number sufficient to make the difference in two averages. Twenty-one nonsyphilitic women of this series had never been pregnant, an incidence of approximately 12 per cent. This fact stresses the importance of adequate local examinations in nulliparous women who complain of bleeding or discharge from the vagina.

SUMMARY

1. Syphilitic women develop carcinoma at an average age of 47 years, as compared to 51 years in nonsyphilitic women in this series.
2. A higher per cent of nonsyphilitic cases is classified as grade I according to Martzloff's classifications.
3. The nonsyphilitic group showed less extensive involvement when first examined than the syphilitic group.
4. No significant difference existed in the delay in obtaining adequate therapy.
5. The influence of multiple pregnancies when the two groups are compared appears negligible.

REFERENCES

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