MULTIPLE PRIMARY MALIGNANT NEOPLASMS

REPORT OF A CASE OF CARCINOMA OF LUNG AND CARCINOMA OF RECTUM EACH PRODUCING METASTASES *

DAVID P. SEECEO

From Division of Laboratories, Montefiore Hospital, New York

The rarity of true multiple primary malignant neoplasms, we believe, justifies the report of the following case:

M. F. Age 55. Illness began in 1917 with obstinate constipation and pain in rectum. One year later she noticed a sanguinous discharge from rectum, and on one occasion lost about 500 cc. of blood. In June, 1921, a left iliac colostomy was made. During three months previous to admission patient had experienced constant severe pain in the right chest. The past history was negative.

Physical examination of the chest revealed flatness, diminished breath sounds and vocal fremitus, and a few moist rales from the angle of the scapula to base on the right side. In the epigastrium and right hypochondrium were felt two separate and freely movable masses. There was a functioning left iliac colostomy. The inguinal glands were enlarged on both sides. In the rectum, an obstructing tumor mass was felt 3 cm. from anus. The X-ray report of chest stated: "The picture is suggestive of neoplasm; the possibility of a small amount of effusion cannot be excluded." The clinical diagnosis was carcinoma of the rectum with metastases.

Necropsy December 24, 1921. The right pleural cavity was practically obliterated by thin sheet-like fibrous adhesions. About three-fifths of the right lung was occupied by a large irregular mass which appeared on the surface only in the interlobar space posteriorly over an area 2 cm. wide and about

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5 cm. long. On section, a single tumor about 15 cm. in diameter, consisting of a granular grayish-white necrotic tissue, was seen replacing almost the entire middle lobe and the adjacent halves of the upper and lower lobes. At the root of the lung the tumor tissue surrounded and almost completely occluded the bronchi to the middle and lower lobes. The lower half of the lower lobe was atelectatic; the remainder of the lung was edematous. Both lobes of the left lung contained several tumor nodules up to 2 cm. in diameter, made up of firm granular grayish hemorrhagic tissue.

The colostomy opening was situated about 50 cm. from the anus. An irregular, roughly globular mass, 10 cm. in diameter, filled the lesser omentum, its inferior border adapted to, but not involving, the lesser curvature of the stomach; posteriorly, this mass invaded the body of the pancreas at about its middle third. On section the tumor, like that in the right lung, consisted of a grayish-white, hemorrhagic, soft tissue containing large areas of necrosis. Both suprarenals were enlarged. On section, each contained several tumor nodules measuring up to 1 cm. in diameter. When the distended urinary bladder was emptied, the pelvis was found to be occupied by a large mass, above which the body of the uterus and both tubes and ovaries were seen uninvolved. Dissection of the pelvic structures revealed an annular, hard, granular, ulcerated tumor growth 3 cm. long obstructing the rectal canal, its lower margin 3 cm. from the anus. The upper portion of the rectum and the sigmoid were normal. The mass in the posterior cul-de-sac, which was continuous with the tumor in the wall of the rectum, anteriorly, invaded the posterior wall of the cervix, but did not involve its mucous membrane.

Microscopically, two types of tumor tissue were found in the various organs. The tumor in the rectum, posterior wall of cervix, and nodules of the left lung, was typically adenocarcinoma of the rectum (see Fig. 1). In the right lung, peribronchial lymph-nodes, adrenals, omental mass, pancreas and pelvis, the growth was made up of compact small round and polygonal epithelial cells, with scant pink staining cytoplasm and large
irregular heavily staining nuclei, growing in an abundant fibrous stroma (see Fig. 2). An occasional syneytial giant cell was seen. Throughout, there were extensive areas of hemorrhage and necrosis. There was one section of the rectum showing the mucous membrane suddenly terminating in a large area of

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**Fig. 1. Metastasis of the Rectal Adenocarcinoma in Left Lung.** × 10

**Fig. 2. Primary Carcinoma of Right Lung Showing Growing Border.** × 160.
characteristic adenocarcinomatous tissue, which, when traced through the muscle layers, can be seen lying adjacent to a metastatic growth of the primary lung tumor (see Figs. 3 and 4).

Fig. 3. Margin of the Rectal Adenocarcinoma Overlying a Metastasis of the Lung Carcinoma in the Muscular Layer of the Rectum. × 8

SUMMARY

The presence of two entirely different tumors suspected from the gross findings was substantiated by the microscopic examination. Sections of lung showed metastatic nodules of the rectal carcinoma, separate and distinct from the large primary carcinoma of the right lung. On the other hand, the primary lung tumor, in addition to growth in the regional lymph-nodes, adrenals and omentum, had metastasized to the pelvis, so that the unusual occurrence of a primary lung tumor metastasis invading a primary rectal tumor can readily be demonstrated.
DISCUSSION

This is the only instance of multiple primary malignant neoplasms in a series of 170 autopsies of cancer cases at Montefiore Hospital. The frequency of "multiple tumors" as given in the literature reports varies greatly. Ewing (1) quotes Hansemann as finding 5 out of 1,000 tumor cases, and Redlich 14 out of 1,225 cases, and adds: "when a minute search is carefully conducted and all forms of tumor growth included, the proportion of multiple tumors is much greater." He then quotes Symmers: "of 250 autopsies, of which 55 had tumors, 22 showed more than one type."

It appears to us that the mere collecting of numbers of cases is not sufficient. The significance of multiple tumor formation is not known, and although some have attempted to attach much importance to the occurrence of multiple primary tumors as shedding some possible light upon the etiology and distribution of malignant tumors, we are inclined to agree with Ewing (1) that "the rather common occurrence of two or more tumors in different or same organs of the same subject suggests nothing more than the accidental coincidence in several organs of the general biological factors in the genesis of tumors."
Nevertheless, if the data on multiple tumors are to add any information to the tumor problem, even from the statistical viewpoint, it will be only by more carefully analyzing and grouping the different types and forms.

We believe that a more satisfactory evaluation of the collected material on multiple tumors would be possible if the factor of malignancy was made of prime importance. Bearing this in mind, cases with multiple tumors may be classified into three groups:

1. Cases with multiple benign tumors.
2. Cases with one malignant and one or more benign tumors.
3. Cases with multiple malignant tumors.

(1) Multiple benign tumors are of very common occurrence, as, for example, multiple lipomata, angiomata, neuromata, lymphomata; in “systens” of anatomically or physiologically related tissues, as polypi of the gastrointestinal tract, benign tumors in the female reproductive organs; and in “paired” organs as the kidneys, adrenals, testes, ovaries. There were 44 cases out of 621 autopsies in which multiple benign tumors alone occurred.

(2) Likewise, the existence of one malignant and one or more benign tumors in the same individual is quite common. Among the 170 malignant tumor cases there were 56 in which one or more additional benign tumors were found. Examples of both these groups are very common in old age. These groups are mentioned to emphasize the infrequent occurrence of multiple malignant tumors.

(3) There is an abundant literature on multiple primary neoplasms. Woolley (2) in 1903, and Major (3) in 1918 have given extensive reviews, though not complete, and many cases have been reported since. But one is struck by the inconstant standards used in recording cases of multiple tumors. As an illustration, reference may be made to the excellent review of “Multiple Primary Malignant Neoplasms” by Major (3). Under his grouping “Different Types of Tumors in Various Organs,” he includes a case with angioma of the liver; angioma
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of the kidney; adenoma of the liver; adenoma of the adrenal; polyp of the uterus; malignant myoma of the broad ligament; fibroma of the ovary; and pigmented naevi, where there was but one malignant and several benign tumors. There are many such instances in the literature where, under various groupings, cases with multiple tumors, consisting of one malignant and one or more benign tumors, are listed among cases with multiple primary malignant tumors. Likewise, in reports of collected cases, some have included, and others have omitted, because of their frequency, cases with multiple carcinomata or sarcomata when found in "systems" as skin, lymph-glands, bone-marrow, or "paired organs" like the ovaries, breasts and adrenals. Instances of the so-called sarcocarcinoma or carcinosarcoma are listed among the multiple primary malignant tumors. These inconsistencies result in different percentages. Evidently Hansemann's 5 out of 1,000 and possibly Redlich's 14 out of 1,225 represent cases of multiple primary malignant tumors, whereas no doubt the 22 multiple tumors of 55 in Symmers' series include multiple benign tumors or one malignant and one or more benign tumors. Because of this rather loose usage of the term "multiple tumors" the number and percentages of cases appear to be of little value.

Billroth suggested three criteria for the diagnosis of multiple carcinomata in the same individual:

1. Different histological appearances;
2. Different locations (points of origin);
3. Each produces its own metastases.

In attempting to apply this standard to all types of malignant tumors, we must consider the following:

1. (a) The presence merely of different histological appearances is of little value because of the possible change of type cell in metastases and regional or local recurrences (especially after biopsy or treatment).

   (b) On the other hand, the absence of different histological appearances may be of little value on the negative side, because in "system" and in "paired organ" instances there may be
multiple foci with the same type cell, e.g., epitheliomata of the skin, multiple carcinoma of the gastrointestinal tract, bilateral hypernephromata.

2. (a) That they are found in different locations may be of little value because of the possible error of misjudging a metastatic focus in an apparently definite case, especially when the change in type cell is marked.

(b) In the absence of different locations a case might well be ruled out were it not for the group of mixed tumors, i.e., the so-called sarcocarcinomata—a much disputed group.

3. (a) When each primary focus produces its own metastases, the case is definitely one of multiple malignant neoplasms. To prove that the second apparently primary focus is not a "changed" metastasis from the first may not be possible in a given case with our present methods.

(b) Multiple primary malignant tumors may exist without demonstrable metastases.

In view of all this, it is not surprising that there is no standard definition of the term "multiple malignant neoplasms," and, although as yet no importance can be attached to such instances, regardless of the criteria used for their recognition, it is possible that there may be some special significance in the occurrence of the rare cases in which one finds multiple primary foci of different histological appearances, each producing its own metastases.

CONCLUSIONS

1. A more accurate working classification of multiple tumors is desirable.

2. A case of multiple primary malignant neoplasms, in which each produced its own metastases, is presented.

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BIBLIOGRAPHY