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Case Report

Triple Primary Malignant Neoplasms: Uterus, Caecum and Stomach

Piero Tosi, Marcella Cintorino, Pietro Luzi, and Umberto Pavia

Institute of Pathological Anatomy of the University of Siena
Civil Hospital St. Andrea, Massa Marittima

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Summary. A case of triple primary malignant neoplasms is reported: adenocarcinoma of the uterus at age 56 (histerectomy; no radiotherapy); mucinous adenocarcinoma of the caecum and anaplastic carcinoma of the stomach at age 70. The Authors have classified this case as one of multiple primary malignant neoplasms originating in uncorrelated organs. The patient's family history is considered: her mother, a brother, a sister and two daughters died of malignant neoplasms of the digestive system.

Clinical Abstract. M. C., born in Massa Marittima, 1901. The patient's mother, a brother, a sister and two daughters died of malignancies of the digestive system (stomach, colon). Menarche at age 14. Had four normal pregnancies. Menopause at age 53. Was in good health till age 56, when repeated uterine bleeding lead to her admission to a surgical Hospital, where she underwent diagnostic curettage. The histopathological diagnosis was "adenocarcinoma of the uterus". The patient therefore underwent a hysterectomy according to Hertz. Since at the time of the operation the uterus and Fallopian tubes were free of adherences, no radiotherapy was given. In 1969 the patient presented worsening anemia, anorexia and adynamy, for which she was hospitalized the 24th of August, 1971. Anemia, diffuse edema, no chest abnormalities. An irregular firm tumor mass was found in the right lower quadrant of the abdomen. The patient had a right partial colectomy and ileotransversostomy. Careful examination of the abdominal viscera during the operation revealed a tumor mass in the prepiloric gastric wall and gastric lymphoadenopathy. Therefore, subsequently, partial gastrectomy and gastrojejunostomy according to Ofmeister-Finsterer were performed. The resected caecum presented a cauliflower-shaped polypoid mass, whereas the resected gastric wall presented a raised plaque with an ulcerous crater in the middle. The edge of the crater was hardened and folded out, and its base was necrotic and irregular. Three days after the operation, the patient developed bronchopneumonia and died.

Histological Findings

1. Material from Uterine Curettage (M. C. aged 56. Biopsy no. 2406, Inst. of Path. Anat. Univ. of Siena). The many areas that were examined microscopically were entirely occupied by a disorderly glandular proliferation. Small islands and a slander branching connective tissue framework separate and support the glandular formations, many of which, however, are free-floating, suggesting that they come from the surrounding glandular masses (Fig. 1). Some of the glandular formations appear to be isolated, whereas others are attached to a slender axis of edematous connective tissue, into which they sometimes invaginate. Many layers of elongated, highly eosinophilic cells line the glandular formations. Their elongated nuclei, which are often located at one of the cell poles, have a coarse, dense chromatic network. Sometimes there are so many layers of these cells that they appear as solid masses partially blocking the lumen and giving it a very tortuous outline (Fig. 2). Many of the cells lining the glands are misshapen and have a large hyperchromatic nucleus, sometimes in atypical mitosis.

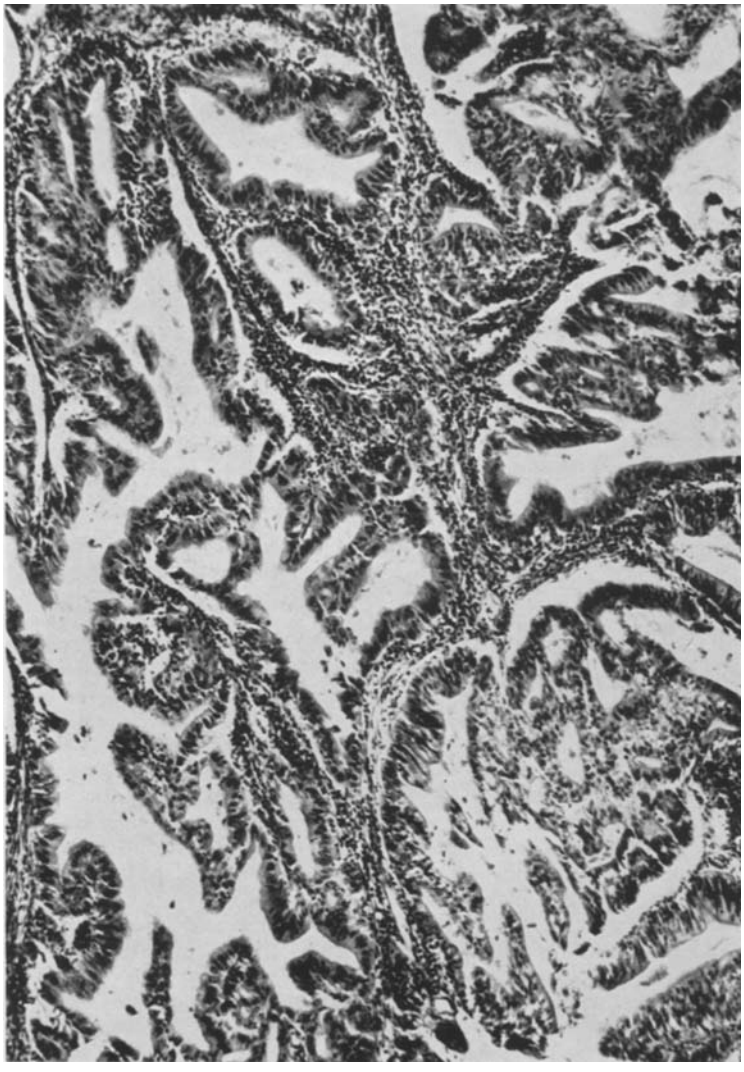

Fig. 1. Endometrium (Biopsy no.2406, Inst. of Path. Anat. Univ. of Siena). Disorderly glandular proliferation. Emat. eos. 160:1

Histopathological Diagnosis. Differenciated adenocarcinoma of the endometrium.

2. Caecum (M. C. aged 70. Biopsy no. 18053, Inst. of Path. Anat. Univ. of Siena). Normal mucosal areas gradually merge into an area where there has been a substantial loss of matter. Here there are disorderly glandular agglomerates of various shapes and sizes sometimes tubular, sometimes cystic, sometimes branching around a solid axis of connective or epithelial tissue (Fig. 3). As one moves towards the muscolature, the lumen of the glandular formations becomes more and more dilated, and there appears an amorphous, colourless or pink material full of cellular debris and sloughed cells. This material, first occupies only the center of the glandular lumen, but then fills it entirely, leading to the formation of large mucinous pools in the muscolature. At higher magnification, numerous atypical and monstruous cells can be seen among layers lining the glandular formations, as well as many tri- and tetrapolar mitoses.

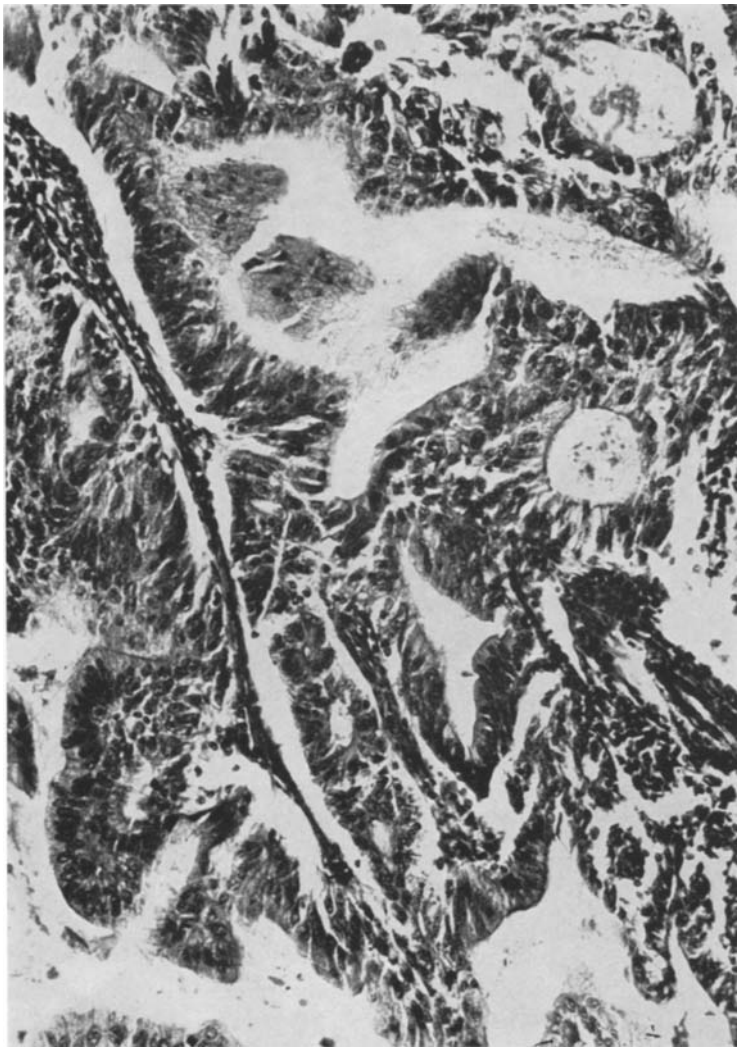

Fig. 2. Idem. Numerous layers of cells, many in mitosis, line the glandular formations. Emat. eos. 360:1

Histopathological Diagnosis. Mucinous adenocarcinoma of the caecum.

3. Stomach (M. C. aged 70. Biopsy no. 18052, Inst. of Path. Anat. Univ. of Siena). At the rim of an area of coagulative necrosis there is a proliferation of small and polymorphic cells sometimes markedly atypical, and often in mitoses. These cells are arranged first in a sort of loose network and then in cords that become more and more densely packed until they occupy most of the wall (Fig. 4). Scattered among these cells are numerous amorphous, dishomogeneous, eosinophilic areas dotted with small hyperchromatic cells and cellular debris. When the actively proliferating cells are not aligned in cords, they are arranged in gland-like structures. However in most of them the lumen is full of the same proliferating cells.

Histopathological Diagnosis. Anaplastic gastric carcinoma.

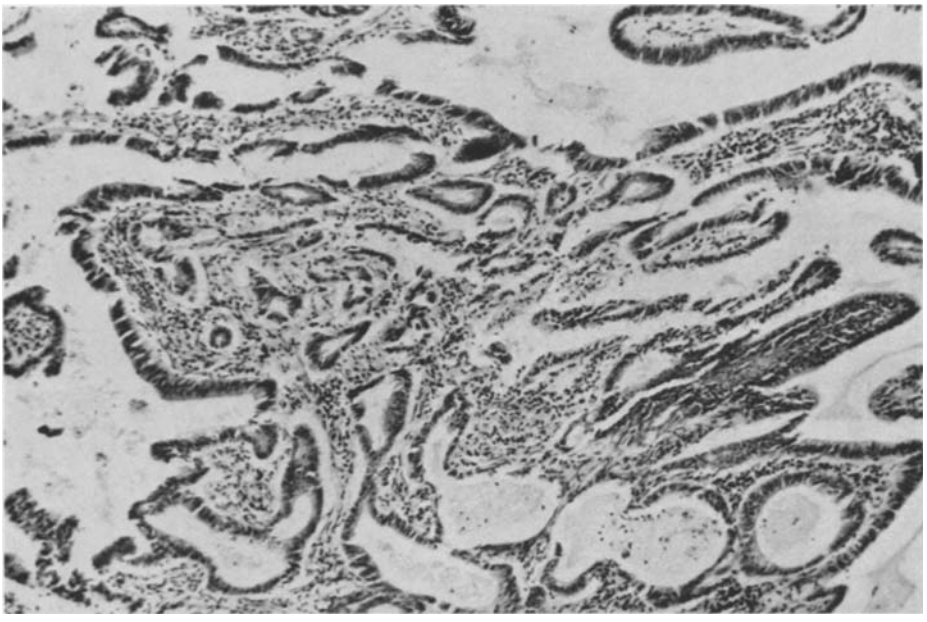

Fig. 3. Caecum (Biopsy no. 18053, Inst. of Path. Anat. Univ. of Siena). Glandular agglomerates, often misshapen; towards the musculature, their lumina dilate and appear full of an amorphous material with slowghed cells and cellular debris. Emat. eos. ×72

In one of the *Lymphnodes* of the lesser gastric curvature the structure is entirely lost and the histopathological picture described for the gastric neoplasm is repeated (glands, clumps of epithelial cells, areas of coagulative necrosis). Only small islets of lymphoreticular tissue remain adjacent to the thickened capsule of the lymphnode.

Histopathological Diagnosis. Cancerous invasion of the lymphnode.

Discussion

One of the most frequently used systems for classification of multiple primary malignancies is Lund's (1933): 1) multiple primary malignant neoplasms with multicentric origins: a) in the same organ and tissue; b) in a common contiguous tissue involving different organs; 2) multiple primary malignant neoplasms in different organs or tissues, and 3) types 1 and 2 combined. Though with reservation, due to the difficulty of distinguishing a metastasis from a second or third primary neoplasm (Moertel, 1966), we have classified our case as one of multiple primary malignant neoplasms originating in different organs. It is a case of malignant tumors with clearly distinct histopathological pictures (according to Warren and Gates's, 1932, criteria): differenciated adenocarcinoma of the endometrium, mucinous adenocarcinoma of the colon, and highly anaplastic carcinoma of the stomach.

The adenocarcinoma of the endometrium preceded the simultaneous development of the carcinoma of the colon and stomach by 14 years (lesions are considered to be simultaneous when they are diagnosed within six months of each other). A similarly long period between the appearance of neoplasms is present

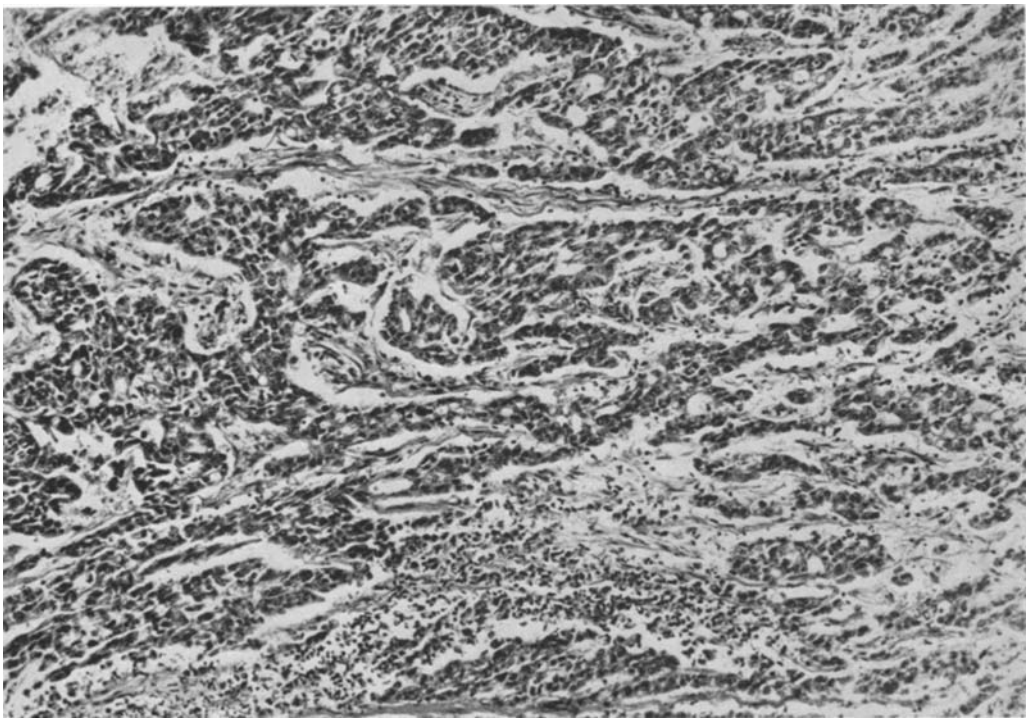

Fig. 4. Stomach (Biopsy no. 18052, Inst. of Path. Anat. Univ. of Siena). Proliferating epithelial cells, which here and there appear to be arranged in gland-like structures, infiltrate the gastric wall sometimes aligned in cords. Emat. eos. 360:1

in only 85 of the 1663 patients with multiple primary malignant neoplasms in Moertel's review (1966), the others being cases of "simultaneous" or "consecutive" tumors (the latter are separated by a mean interval of 6.4 years for the men and 7.7 years for the women).

Some multiple primary malignant neoplasms can be correlated either because they appear in the same system of organs or related systems (cancer of the breast and female sex organs; carcinoma of the bladder and adenocarcinoma of the prostate), or as a result of treatment of an initial malignant neoplasm (ionizing radiations, the Stewart-Treves syndrome, carcinoma of the breast as a result of treatment of carcinoma of the prostate with estrogens). In the case we are examining there appears to be no correlation. The diseased organs do not belong to the same or related systems, even though, according to Bailar (1963), Lynch (1967), Savage (1956), the association of a carcinoma of the uterus with one of the colon is statistically more frequent than other associations.

On the other hand, associations of malignancies of the colon and stomach, or stomach and uterus, are not among the most frequent combinations in the field of multiple primary malignant neoplasms. And, lastly, to the best of our knowledge, the association of adenocarcinoma of the uterus, carcinoma of the colon, and gastric carcinoma has never before been recorded.

Our patient's family history (her mother, a brother, a sister and two daughters died of malignancies of the digestive system—stomach or colon) is relevant to the theory of a constitutional predisposition to cancer. Warren and Ehrenreich (1944) maintain that there is a greater chance that a primary malignant neoplasm will develop in an individual who has already had one that in a normal person because of constitutional predisposition. However Watson (1953) has objected that this assertion was not been proved statistically because all too often the diagnosis of multiple neoplasms lacks a histological confirmation. And Peller's (1941) assertion that a cured malignancy leaves the organism protected against further tumors offers an opposing theory. It seems to us that in the case of our patient, both the number of close relatives tumors and her own triple neoplasms are strong evidence of a constitutional predisposition. Much has been written about the greater frequency of multiple primary malignant neoplasms in individuals belonging to certain blood groups (group A in particular, according to Fadhly and Dominguez, 1963). However, Tsukada *et al.* (1964) and Moertel (1966) did not find a significantly greater incidence of multiple primary malignant neoplasms in individuals of group A when compared with those of group 0 (our patient belongs to the latter group).

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P. Tosi, MD
Assistant Prof. of Pathological Anatomy
University of Siena
Via Laterino 8
I-53100 Siena/Italy