Human Chorionic Gonadotrophin Expression in Colorectal Adenocarcinoma

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The presence of human chorionic gonadotrophin (HCG) in colorectal adenocarcinoma was studied histologically in 45 tumors using immunoperoxidase technique. Ten neoplasms (22.2 percent) contained HCG-positive tumor cells. These cells were present mostly at the periphery of the tumors. Many formed parts of glands, while some were arranged in syncytial clumps or columns, or singularly. Thus, these tumor cells resembled trophoblastic tissue not only in being HCG-positive but also in their peripheral distribution and occasionally in morphologic appearance. HCG-positive tumors were seen more commonly in the rectosigmoid region (90 percent) and were more aggressive than HCG-negative tumors. In this study, lymph node or liver metastases were present in 70 percent of HCG-positive tumors compared with 29 percent of negative tumors—a difference which is statistically significant. [Key words: Colorectal carcinoma; Human chorionic gonadotrophin]

UP TO 41 PERCENT OF PATIENTS with colorectal carcinoma have detectable serum levels of human chorionic gonadotrophin (HCG),1-4 and 43 percent have been reported to have HCG-positive stained tumor cells in their neoplasms as demonstrated by immunoperoxidase technique.5 Microscopically obvious choriocarcinomatous elements however, have been described in a few case reports of colonic adenocarcinoma.6-10 This investigation studies the morphology and distribution of HCG-positive cells in colorectal carcinoma, especially with regard to the presence of any similarities to normal or neoplastic trophoblastic tissue. The clinical correlations and histologic differences between HCG positive and negative tumors also are reported.

Materials and Methods

Forty-five patients with colorectal adenocarcinoma treated by colectomy during the period from 1977 to 1983 were selected on the basis of availability of full clinical data and follow-up information. Colectomy specimens were retrieved from the files and a representative section of the tumor was selected. When the tumor had more than one morphologic pattern, e.g., mucinous and nonmucinous, a representative section of each pattern was chosen. Also included in the study were eight sections of normal mucosa from resection margins, and three benign polyps, one tubulovillous and two tubular adenomas detected in the specimens. Five-micron sections were cut from the corresponding formalin-fixed, paraffin-embedded blocks of tissue of all the selected sections.

HCG was demonstrated in the deparaffinized tissue sections by the unlabeled antibody peroxidase-antiperoxidase (PAP) technique.11 HCG antiserum was obtained from DaKo Limited (High Wycombe, UK), and was used at a dilution of 1/1600 and incubated overnight at 4°C. Positive and negative controls were included with each batch of staining. Positive controls included sections of placental tissue, and negative controls were sections of colorectal adenocarcinoma treated in the same way as the test sections except that the step in which HCG antiserum was used was omitted.

The statistical significance of the results was assessed by the fourfold tables of the chi-square test (probabilities were calculated with 1 degree of freedom).

Results

HCG-positive tumor cells were present in 10 of the 45 adenocarcinomas examined (22.2 percent). No HCG-positive cells were seen in sections of normal mucosa or in any of the three adenomas tested. The number of positive cells varied from one case to another; in two cases several scattered positive cells were seen, while in the remaining eight cases, large areas with positively stained tumor cells were present. Most of these cells were concentrated at the periphery of the tumor in its superficial, lateral, or deep parts, or in all three places.

Many positive tumor cells were columnar or cuboidal and formed part of neoplastic glands (Fig. 1). Other cells

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FIG. 1. A neoplastic gland lined in parts by HCG-positive cuboidal and columnar cells (arrows). Note the presence of a clump of neoplastic cells within the same gland (arrow head) that is not stained (immunoperoxidase; X 250).

FIG. 2. Two syncytial groups of tumor cells, one seen continuous with a gland containing positive (darkly stained) areas (immunoperoxidase; X 250).

were arranged in syncytial clumps (Fig. 2), partly solid and partly glandular groups (Fig. 3), columns (Fig. 4), or scattered individually (Fig. 5). Hematoxylin and eosin staining showed that some of these cells had ground glass or vacuolated cytoplasm and some were markedly large and had bizarre shapes and pleomorphic nuclei. In general, parts of the tumor with HCG-positive cells either were infiltrated heavily with neutrophils or showed extensive fibrosis. Occasionally, neutrophils were seen within vacuoles in HCG-positive cells (Fig. 6).

All ten HCG-positive tumors were moderately differentiated, although the areas with HCG-positive tumor cells were usually less differentiated than the rest of the tumor. None of the HCG-positive tumors were mucinous or contained mucinous areas, in contrast to HCG-negative tumors, which included seven (20 percent) mucinous or partly mucinous tumors. Of the remaining 28 HCG-negative tumors, one was well differentiated, 25 were moderately differentiated, and two were poorly differentiated.

In the ten HCG-positive tumors, one (10 percent) was Dukes' Stage A, two (20 percent) were Stage B, six (60 percent) were Stage C, and one (10 percent) was Stage D, in which case metastases were present in the liver. Of the 35 HCG-negative tumors, five (14 percent) were Stage A, 20 (57 percent) were Stage B, and ten tumors (29 percent) were Stage C. The combined incidence of Stages A and B, tumors without metastases, was 30 percent in HCG-positive carcinomas compared with 71 percent HCG-negative carcinomas. Stages C and D, metastatic tumors, were more common in HCG-positive than in HCG-negative tumors (70 vs. 29 percent). All of these differences were statistically significant (P < 0.05).

Nine (90 percent) HCG-positive tumors were present in the rectosigmoid region and one in the transverse colon. None were present in the ascending colon or cecum. In contrast, 22 (63 percent) HCG-negative tumors were present in the rectosigmoid region, two in the descending colon, three in the transverse colon, five in the ascending colon, and three in the cecum.

There were no differences in patient characteristics between the two groups with regards to age and sex distribution. Neither was there a difference between the two groups of patients in the incidence of preoperative elevated levels of serum carcinoembryonic antigen (CEA). Four patients (40 percent) with HCG-positive tumors had CEA serum levels that were higher than 10 ng/ml, compared with nine of 31 (29 percent) patients with HCG-negative tumors, in which serum CEA was determined.

Two patients (20 percent) with HCG-positive tumors have died. These included the patient with a Stage D tumor, who died six months after the operation; and a patient with a Stage C tumor who developed liver metastases and died 27 months after the initial diagnosis. Five patients (14 percent) with HCG-negative tumors have died. These included a patient with Stage C tumor who