Signet-ring cell carcinoma of the colon radiologically simulating Crohn's colitis

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WCP KWAN, HJ FREEMAN. Signet-ring cell carcinoma of the colon radiologically simulating Crohn's colitis. *Can J Gastroenterol* 1991;5(2):71-74. A 35-year-old male with abdominal pain and weight loss was referred with a diagnosis of Crohn's colitis. Subsequent colonoscopic examination and laparotomy revealed diffuse infiltration of the colonic wall with a primary signet-ring cell carcinoma and widespread metastases. The poor prognosis of this lesion appears to reflect difficulty in early diagnosis as well as the unusual cell biological features of this highly invasive histological variety of colon carcinoma.

Key Words: Colonic carcinoma, Crohn's disease, Inflammatory bowel disease, Linitis plastica of colon, Signet-ring cell carcinoma

Carcinome à cellules en bague à chaton simulant une maladie de Crohn à localisation colique sous radiologie

RESUME: Un patient âgé de 35 ans, souffrant de douleurs abdominales et d'un amaigrissement, s'est présenté avec un diagnostic de maladie de Crohn à localisation colique. Une colonoscopie et une laparotomie subséquentes ont révélé l'infiltration diffuse de la paroi colique par un carcinome à cellules en bague à chaton, et des métastases étendues. Le mauvais pronostic de cette lésion semble refléter la difficulté de poser un diagnostic précoce ainsi que les caractéristiques biologiques cellulaires inhabituelles de cette variété histologique invasive de carcinome du côlon.

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SIGNET-RING CELL CARCINOMA IS most commonly found in the stomach and comprises at least 10% of all gastric carcinomas. It rarely appears in other organs including breast, gallbladder, urinary tract, pancreas and colon. Histologically, it is a mucinous adenocarcinoma with very prominent intracytoplasmic mucin. The authors report a case of signet-ring carcinoma of the descending colon in a 35-year-old man with barium enema findings simulating Crohn's colitis. The clinical, radiological and pathological features are discussed and compared with previous reports.

CASE PRESENTATION

A 35-year-old Caucasian male was referred in September 1990 with left lower quadrant abdominal pain and constipation for five weeks, associated with a weight loss of 5 kg. There was no rectal bleeding. Barium enema revealed diffuse narrowing, rigidity and scattered ulcerations in a 12 cm segment of descending colon; the radiological inter-

Figure 1) Barium radiograph showing 12 to 14 cm stenosed segment of sigmoid colon with mucosal ulceration

pretation was Crohn's colitis (Figure 1). There was no family history of inflammatory bowel disease, colorectal carcinoma, colonic polyps or cancer of the female reproductive organs. Examination revealed a tender left lower quadrant mass. There was no adenopathy and rectal examination was unremarkable. Laboratory studies showed a hypochromic, microcytic anemia with a hemoglobin of 101 g/L and mean cell volume of 68 fL. Erythrocyte sedimentation rate was 32 mm/h and liver enzymes were normal except for a minimally elevated alkaline phosphatase. Colonoscopy showed normal mucosa to 40 cm from the anal verge. At this point, the lumen was severely narrowed, prohibiting passage of the instrument. The mucosa at this level was extremely erythematous and friable, but without ulceration or erosion. There was no intraluminal mass lesion. The endoscopist, however, suspected a malignant stricture, and mucosal biopsies showed a poorly differentiated infiltrating adenocarcinoma. Chest radiographs, abdominal ultrasound and abdominal computed tomography scan revealed no evidence of metastatic disease.

Laparotomy showed a large tumour in the distal descending colon. The stomach was normal. There were numerous small tumour deposits around the tumour, in the posterior perito-

Figure 2) Surgically excised specimen with extensive tumour infiltration

neum, side wall and floor of the pelvis, together with obvious lymph node metastases. A localized palliative resection was done. Examination of the resected specimen revealed an extensive length of infiltrating adenocarcinoma invading through the muscularis propria into the serosal fat (Figure 2). Histologically, the predominant cell type exhibited the classic morphology of signet-ring cell carcinoma, with large intracytoplasmic mucin droplets that displaced nuclei to the cell periphery (Figure 3); five of six lymph

nodes were positive for metastatic adenocarcinoma, as were sections of the omentum and pelvic deposits.

DISCUSSION

Signet-ring cell carcinoma of the colon is an unusual variant of adenocarcinoma of the colon. It was first reported by Laufman and Saphir in 1951 (1). They described a 'linitis plastica type' colon cancer, referring to permeation of the wall by tumour cells, resulting in a rigid, contracted segment of colon.

Figure 3) Photomicrograph showing histological findings of a signet-ring cell carcinoma of the colon with intracellular mucin and displacement of nuclei to the cell periphery (hematoxylin and eosin x360)

The precise incidence of colonic signet-ring cell carcinoma is not known; various reports estimate the ratio of signet-ring cancer to adenocarcinoma of the colon at 0.1 to 1.5 in 100. In a review of 12,000 colorectal carcinomas from the Mayo Clinic published in 1961, only 11 cancers were judged to belong to the signet-ring variety; the incidence was 0.1% of all colon cancers (2). Bonello et al (3) stated in 1980 that a total of 30 cases of signet-ring cell carcinoma of the colon had been reported in the literature since 1951. Giaccherio et al (4) summarized their experience at the National Cancer Institute of Genoa, Italy and found nine cases of primary signet-ring cell carcinoma from a review of 800 cases of colonic adenocarcinoma. In a report from Singapore in 1985, signet-ring cell carcinoma comprised 1.5% of 565 cases of colonic carcinoma (5). Finally, Lui et al (6) reported three cases of signet-ring cell carcinoma in a major general hospital in Hong Kong after reviewing 1531 cases of colorectal adenocarcinoma, ie, an incidence of 0.2%.

A survey of reported cases reveals several interesting features. In most but not all reports, patients with signet-ring cell colon cancer are younger than those with the usual colonic adenocar-

cinomas (4). The initial presentation usually occurs in the fourth or fifth decade of life. Indeed, signet-ring cell carcinoma of the colon has been described in children, with one report in a six-year-old Japanese boy (7). Most reported tumours were found in the left colon, particularly the rectum. Clinical presentation may not be much different from the usual colonic carcinomas, with rectal bleeding and change in bowel habit. However, diagnosis may be delayed because carcinoma is not an expected cause of rectal bleeding in a young person. Furthermore, because of the infiltrative nature of the tumour with relative sparing of the mucosa, symptoms may be minimal early in the clinical course. Negative mucosal biopsies, despite the presence of a large underlying tumour, have been reported (3). Although the tumour in the present patient proved to be very large and extensive, gross rectal bleeding was absent; a microcytic anemia was evident, likely due to chronic occult fecal blood loss. The radiographic findings on barium enema examination seen in the present patient have been previously described but warrant emphasis (8,9). There is usually marked narrowing of the colon over a considerable length, with rigidity and fixation. Be-

cause signet-ring cell carcinoma is so different radiographically from more conventional ulcerating, fungating or annular colonic carcinomas, the neoplastic nature of a signet-ring cell lesion may be obscured. The radiographic appearance could mimic spasm, diverticular disease or ischemic colitis. Inflammatory bowel disease, particularly Crohn's colitis, is an important differential diagnosis. The age of the present patient, together with the extensive length of markedly narrowed colon associated with mucosal ulceration seen on barium enema, led to the initial radiological interpretation of Crohn's colitis. Previous case reports by Jacobi (10) and Nelson (11) have also illustrated this difficulty. Furthermore, radiography of the involved segment in signet-ring cell carcinoma may or may not show more typical features, including filling defects, mucosal destruction and overhanging edges.

Pathology of the resected specimen in the present case revealed typical signet-ring cell carcinoma. Neoplastic cells were filled with intracytoplasmic mucin, pushing nuclei to the periphery of the cell. The cells were arranged in clusters and were also seen infiltrating the submucosa and muscularis propria. The present patient had diffuse tumour spread throughout the pelvis and peritoneal cavity. Although signet-ring cell colon cancer has a very poor prognosis because it is usually discovered at a late stage, it is unclear whether this is due to the biology of the tumour cells per se, with propensity to infiltrate and invade surrounding tissues, or if it is due to difficulty in early detection. Surprisingly, there seems to be a relative paucity of hepatic metastases with this histological variety of colon cancer. Except for the experience from Italy showing similar survival in patients with signet-ring colon cancer compared to the usual colonic adenocarcinoma (4), most reports have indicated a very poor survival. Not infrequently, as in the present case, only palliative resection can be offered. The invasiveness of signet-ring cell carcinoma has been demonstrated in vitro with cultured colon cancer cells. DLD-2, a cell line which resembles signet-ring carcinoma

histologically, was three times more invasive than moderately well differentiated colon cancer cell lines through a basement membrane (12). In addition, enhanced adherence to basement membrane matrix was also observed compared to other colon cancer cell lines (13). These in vitro observations appear to correlate with clinical findings of diffuse intramural spread in signet-ring cell carcinoma; hence the low cure rate by resection alone (14).

Other aspects related to the tumour cell biology of this intriguing carcinoma require clarification. There is no firm evidence to support a polyp-tumour sequence as demonstrated for the typical colonic adenocarcinomas. Nevertheless, there have been occasional case reports of signet-ring cell carcinoma coexisting with adenoma, and in one case the signet-ring cell was actually found in a polyp (7). The relationship between signet-ring cell carcinoma and chronic inflammatory bowel disease is

also unknown. Colon cancers arising in a background of ulcerative colitis are less likely to be well differentiated (15). Indeed, there have been several reports of signet-ring cell carcinoma found in patients with ulcerative colitis (16) and Crohn's disease (17). Of additional interest is the striking histological resemblance between signet-ring carcinoma of the colon and colon cancer induced by the carcinogen azoxymethane in a rat model (18). This resemblance may be a major weakness in the use of this animal model to explore the pathogenesis of more typical colorectal cancers.

Aside from surgical resection, other therapies for locally invasive or metastatic colonic carcinoma have been extensively reviewed (19). In general, adjuvant or palliative chemotherapy has been unequivocally successful in a small number of publications. A recent study from the Mayo Clinic demonstrated significant improvement in sur-

vival of Dukes's stage C colon carcinoma with a combination of levamisole and 5-fluorouracil (20). Whether signet-ring cell carcinoma of the colon will also respond to this form of treatment is unknown, in part because this form of colon cancer is rare. Radiotherapy may have some value in the treatment of rectal cancer (21), but its overall role in the treatment of colon cancer is limited; it is unknown if signet-ring cell carcinoma is radiosensitive.

The clinical behaviour, epidemiology and histological characteristics of signet-ring cell colonic cancer are so different from the usual colonic adenocarcinoma that it is reasonable to consider this malignancy a distinct subgroup with a different pathogenesis. The practical problem with signet-ring cell colonic carcinoma is the difficulty in diagnosis that may arise because of its behaviour, and radiologically it may simulate Crohn's colitis, particularly in a young patient.

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