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LETTERS TO THE EDITOR

Lethal neuroendocrine carcinoma in ulcerative colitis

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Abstract

A 48-year old male with longstanding and extensive pancolitis developed a high grade and rapidly lethal malignant lesion in the ascending colon characterized by a neuroendocrine carcinoma. Prior biopsies obtained from multiple sites in the colon during endoscopic surveillance were reported to show only inflammatory changes without dysplasia. Although operator-dependent, repeated endoscopic studies may have limitations during surveillance programs because the biological behavior of some colonic neoplastic lesions may have a rapid and very aggressive clinical course.

Key words: Colorectal cancer; Neuroendocrine carcinoma; Ulcerative colitis; Surveillance colonoscopy; Dysplasia

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TO THE EDITOR

An article recently published in *World Journal Gastroenterology* concerning two patients, aged 35 and 77 years respectively, with left-sided ulcerative colitis, was of special importance[1]. In spite of colonoscopic and histologic follow-up in the previous year, both developed large neuroendocrine carcinomas in the rectum, and one patient was reported to have died due to multiple liver metastases.

We had a similar experience in a 48-year old male with longstanding extensive pan-ulcerative colitis for 16 years, first diagnosed in 1992. During the clinical course, his symptoms were initially treated and controlled with 5-aminosalicylates and corticosteroids. Endoscopic studies eventually showed virtually complete mucosal healing and biopsies showed only minimal inflammatory changes. No other immunosuppressive drugs or biological agents were used. During the last decade, he continued to use 5-aminosalicylates alone and remained completely asymptomatic. He underwent repeated surveillance colonoscopies with multiple site biopsies throughout the colon, which showed minimal inflammatory changes. Dysplasia was not reported in any colonic biopsy specimen. Approximately ten months after his last endoscopic procedure, he developed right upper quadrant abdominal pain. Blood studies, including liver chemistry tests, were normal, but an ultrasound and a computerized tomographic (CT) scan suggested possible liver metastases. In addition, the CT suggested a focal thickening area in the ascending colon. Colonoscopy confirmed an ulcerated sessile lesion. Histologic examination of the endoscopic biopsies showed an ulcerating tumor with predominant trebecular architecture and vascular stroma. The tumor cells had hyperchromatic nuclei with small nucleoli and scant pale-stained cytoplasm. Mitoses were numerous and there was abundant apoptosis, consistent with a high grade malignancy. Immunohistochemical stain for chromogranin and synaptophysin showed moderately intense staining of a neuroendocrine carcinoma. Tumor cells were positive for CK7 and negative for CK-20. Subsequent studies also showed pulmonary metastases and palliative chemotherapy was provided with FOLFOX B (12 cycles), but the disease remained progressive so FOLFIRI (10 cycles) was given. He died fourteen months after diagnosis.

Neuroendocrine carcinomas of the colon and rectum, accounting for less than 1% of colon and rectal cancers reported over more than a decade from Memorial Sloan-Kettering in New York, United States[2], are very distinct from well-differentiated carcinoid tumors (or neuroendocrine tumors, using the World Health Organization schema discussed elsewhere[3] seen with inflammatory bowel disease but often detected incidentally during surgi-

cal treatment[4,5]. About 70% of those classified as neuroendocrine carcinomas present with metastatic disease and appear to have a dismal prognosis with a reported overall mean survival of about ten months[2]. These carcinomas have been subdivided into small and large cell types based on their histological and immunohistochemical features, similar to those of pulmonary neuroendocrine cancers with most positively stained for neuroendocrine markers, such as chromogranin, synaptophysin and/or neuron-specific enolase[2]. Interestingly, in a report from Taiwan, there were 2 patients with small cell carcinomas that were believed to represent gastrointestinal metastases from a primary pulmonary site, possibly emphasizing the difficulty in defining their origin in some cases[6].

Scattered reports are available on poorly differentiated neuroendocrine carcinoma with inflammatory bowel disease have been notedwith an equally dismal outcome[7-9]. In a recent report by Grassia *et al*[1], however, surveillance studies were completed during the preceding year, and yet, large lesions in the most distal colon were eventually detected later. Although the present case of pancolitis developed a carcinoma in the ascending colon, the surveillance efforts for longstanding extensive colitis failed, in spite of multiple site endoscopic biopsies for dysplasia over many years. While colonoscopic evaluation, especially in surveillance programs, remains operator-dependent, these cases emphasize that repeated and systematic endoscopic and histological evaluations have limits because the underlying biological behavior of some colonic neoplastic lesions may result in a rapidly developing and aggressive clinical course.

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