Relapsed Colon Cancer Patient Presenting With Hematuria 13 Years After Primary Tumor Resection: A Case Report

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We report a rare case of postoperative colon cancer recurrence who presented with hematuria 13 years after resection of the primary colonic cancer. The patient was 72 years of age and underwent surgical resection of sigmoid colon cancer at another regional hospital in 1994. Since June 2007, this patient has complained of hematuria and bloody stool. On physical examination, tenderness and a hard, indurated mass was palpable in the lower mid-abdomen. Abdominal computed tomography showed a metastatic tumor at the lower midline peritoneum with invasion of the adjacent abdominal wall. Her serum carcinoembryonic antigen level was elevated to 32 ng/dL. Histopathology revealed metastatic colonic adenocarcinoma in the jejunum and abdominal wall.

Key Words: colon cancer, hematuria, recurrent interval
(*Kaohsiung J Med Sci* 2010;26:211–6)

Colorectal cancer (CRC) is the most common cancer and the third leading cause of cancer death in Taiwan. It was estimated that more than 10,000 patients were diagnosed with CRC and more than 4,100 patients died of this disease in 2006 in Taiwan [1]. This disease has one of the highest rates of increased incidence in Taiwan, and has gradually approached the incidence in Western countries. Even with recent advances in diagnostic modalities, anti-cancer drugs, and surgical techniques, the outcome of advanced CRC remains poor, and the 5-year survival rate has not improved significantly [2–4]. Despite complete surgical resection, about half of the patients die due to recurrence or metastasis of this disease [4–6] and recurrence or metastasis occurs within 3 years after resection in 70–80% of patients [7,8]. It has been reported that 93–95% of patients experience relapse within 5 years of primary tumor resection [9], and very few patients remain disease-free survival for more than 10 years. Here we report a very rare case of postoperative recurrence with an initial presentation of hematuria, 13 years after primary colonic cancer resection.

Case Presentation

A 72-year-old male patient underwent surgical resection of sigmoid colonic cancer [International Union Against Cancer (UICC) stage II] at another regional hospital in 1994. He was free of clinical recurrence or metastasis during a 5-year follow-up program at the same hospital. However, since June 2007, this patient has complained of hematuria and he visited a

Received: Mar 13, 2009 Accepted: Aug 19, 2009
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urological clinic, but no significant improvement was obtained. Therefore, he was referred to the Division of Urology at Kaohsiung Hospital for further management. The laboratory tests, including routine urine analysis, revealed a red blood cell level of more than 100 cells/high-power field. Cystoscopic examination revealed that the domed part of the bladder was slightly hyperemic, but there were no other obvious gross lesions. At the same time, the patient also complained of bloody stool, and colonoscopy showed a benign colonic polyp and mixed hemorrhoids. Colonoscopic polypectomy revealed an adenomatous polyp in this patient.

Three months after the patient's first visit to our hospital, he experienced lower abdominal pain and distension, and visited our outpatient department again. On physical examination, tenderness and a hard, indurated mass was palpable in the lower mid-abdomen. Laboratory tests revealed a decreased hemoglobin level of 10.4 g/dL. His serum carcinoembryonic antigen level was elevated to 32 ng/mL. Abdominal computed tomography showed a metastatic tumor at the lower midline peritoneum with invasion of the adjacent abdominal wall (Figure 1A), and the recurrent tumor adhering to the urinary bladder (Figure 1B). Under the suspicion of recurrent colon cancer, an exploratory laparotomy was performed. During the operation, we found a tumor mass (5 × 4 cm in size) that was adhered to the jejunum and the wall of the bladder. Therefore, a segmental resection of the small intestine and partial cystectomy was performed.

Histopathology demonstrated that the mucosa of the jejunum was eroded, but there was no significant pathologic change. Diffusely neoplastic glands infiltrating the submucosa, muscularis propria, and serosa of the jejunum were present. The neoplastic glands were lined by tall columnar epithelial cells with pleomorphic hyperchromatic nuclei (Figure 2A). In addition to the presence of a desmoplastic reaction and tumor cell necrosis (Figure 2A), vascular invasion (Figure 2B), lymphatic invasion (Figure 2C), and perineural invasion (Figure 2D) were observed. Immunohistochemistry showed that the neoplastic cells were positive for cytokeratin 20 (Figure 3A), which was consistent with metastatic adenocarcinoma from the colonic origin (Figure 3B). Thus, the diagnosis of recurrent sigmoid tumor invasion of the distal jejunum and abdominal wall was made.

Postoperatively, the patient recovered well and was discharged uneventfully. He received the chemotherapy regimen of oxaliplatin/5-fluorouracil/folinic acid (FOLFOX-4) to treat of his relapsed colonic cancer.

Discussion

According to the standard guidelines for postoperative follow-up for CRC, published by the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology™ in 2008 [10], a 5-year follow-up program should be undertaken postoperatively,

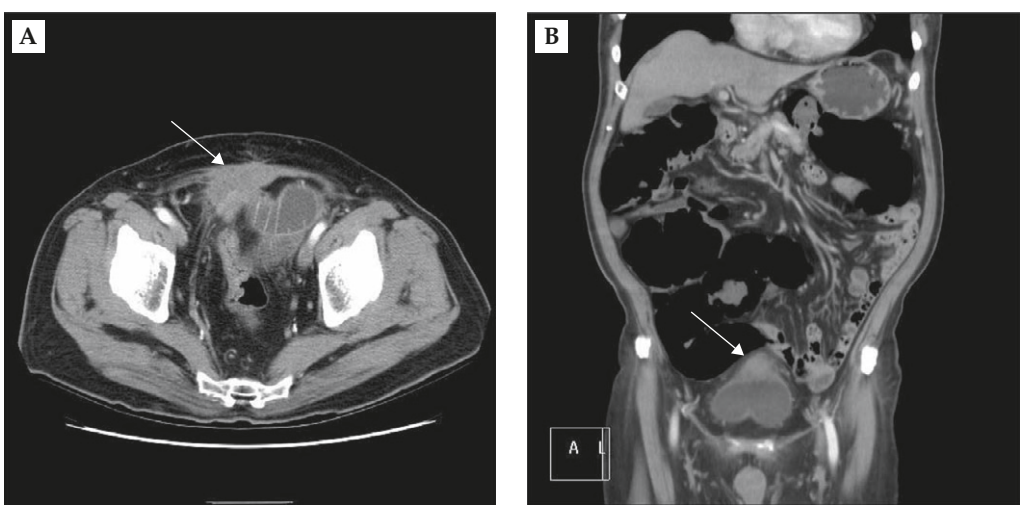

Figure 1. *(A) Metastatic tumor at the lower midline of the peritoneum and invasion of the adjacent abdominal wall (arrow). (B) The recurrent tumor has adhered to the urinary bladder (arrow).*

and should include documentation of the patient's medical history, physical examination, measurement of carcinoembryonic antigen, colonoscopic examination, and computed tomography every year, because of the high risk of recurrence. It has been reported that 93–95% of patients with CRC experience relapse within 5 years of primary tumor resection and the incidence of postoperative recurrence or metastasis

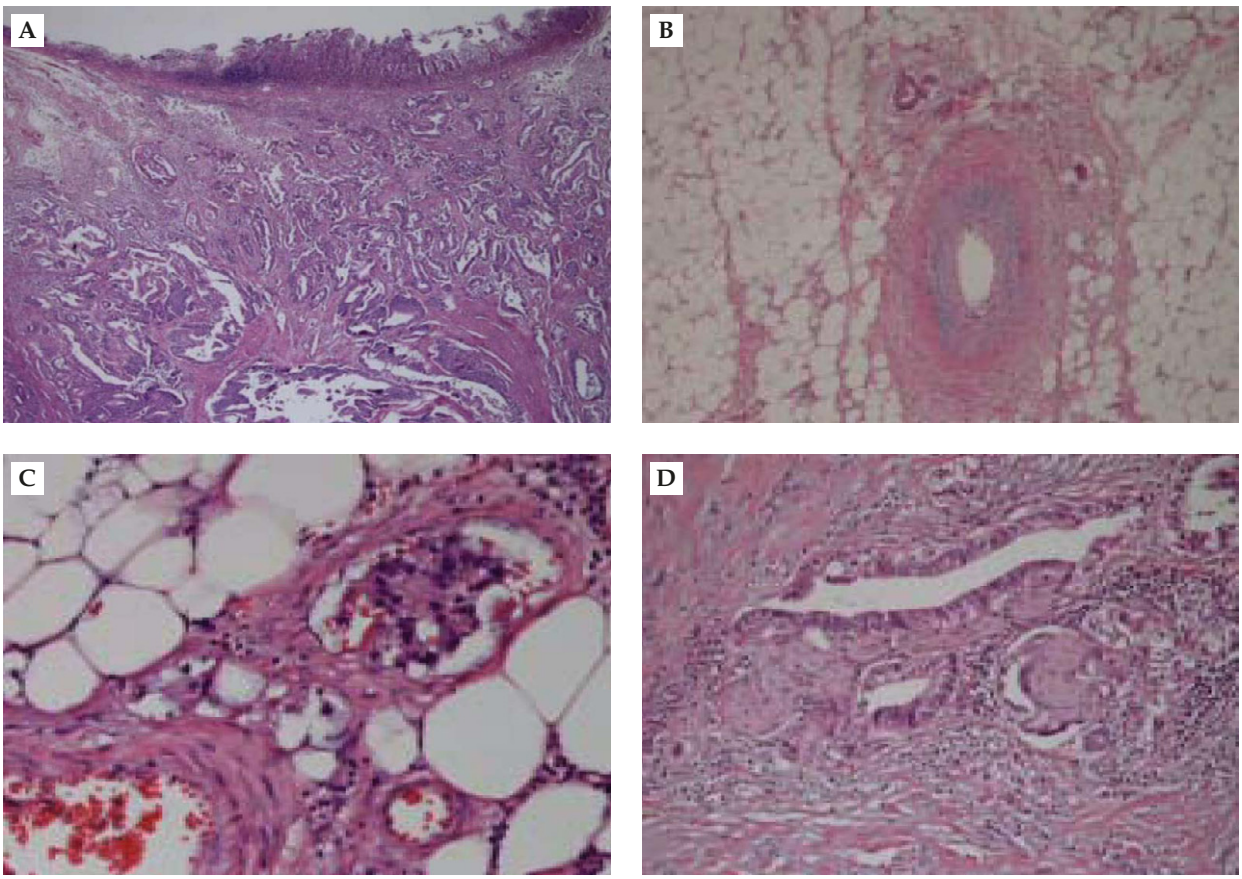

Figure 2. *(A) Diffusely neoplastic glands infiltrating the submucosa and muscularis propria of the jejunum [hematoxylin and eosin (H&E) stain; original magnification, 10×]. (B) Vascular invasion of adenocarcinoma cells (H&E stain, 40×). (C) Lymphatic invasion of adenocarcinoma cells (H&E stain, 100×). (D) Perineural invasion of adenocarcinoma cells (H&E stain, 100×).*

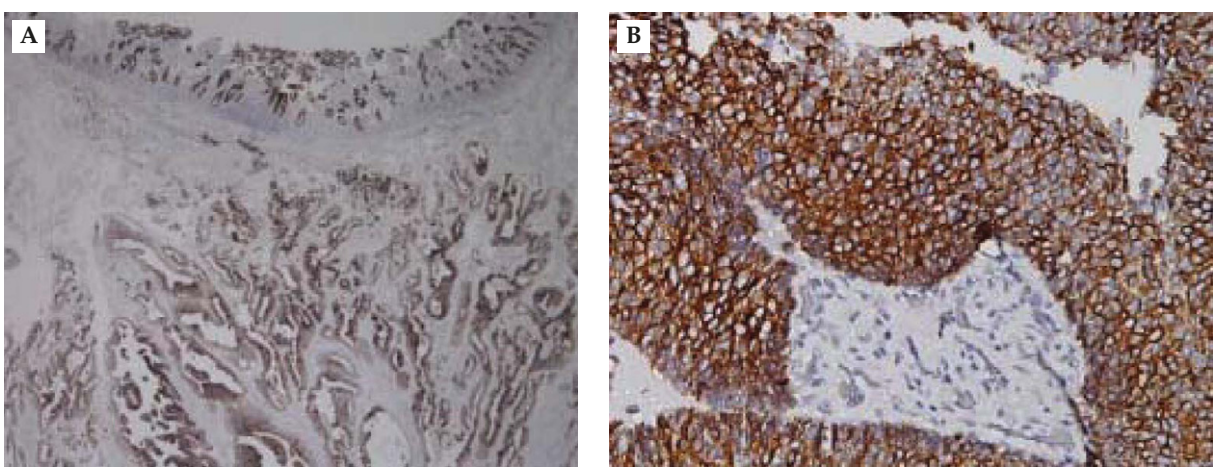

Figure 3. *(A) Neoplastic cells positive for cytokeratin 20 (original magunification, 40×); (B) Neoplastic cells positive for cytokeratin 20 (original magnification, 200×).*

of CRC after 10 years is extremely rare [9]. In another study of patients with CRC who were followed-up for a minimum of 10 years after curative resection, the cumulative recurrence rate of CRC was 100% at 4 years and, for rectal cancer, the 5-, 7-, and 10-year rates were 89%, 98%, and 100%, respectively [10]. Accordingly, postoperative relapse 13 years after resection of the primary tumor is exceedingly rare [11]. Therefore, tumor recurrence or metastasis may be overlooked by physicians and patients. The current patient in whom postoperative recurrent colonic cancer was diagnosed 13 years after resection as a result of hematuria and lower abdominal pain, should remind physicians and patients of the importance of appropriate management of patients with history of cancer if they show any clinical symptoms or signs.

Based on a MEDLINE literature search spanning the period between January 1966 and December 2008, very few cases of colon cancer relapse have been reported in which the patient initially presented with hematuria after the primary tumor resection. Hobdy et al [12] reported a 75-year-old man with sigmoid cancer (UICC stage III, T3N1M0) who was found to have transitional cell carcinoma of the retroperitoneal lymph nodes 10 years after sigmoid colectomy. At that time, he received chemotherapy for this retroperitoneal nodal neoplasm. Eighteen months later, metastatic sigmoid cancer involving the bladder was found with the presentation of hematuria. It seems likely that the occult metastatic colon cancer cells were able to develop as a result of immunosuppression caused by the chemotherapy. Recent studies have shown that complicated biochemical and humoral interactions between the microvasculature of tumors and other cells within the neoplastic microenvironment may play an important role in the dissemination of CRC cells [13,14]. However, our case was originally classified as UICC stage II without nodal involvement, but he still experienced recurrent metastasis 13 years after curative resection. Progressive age-related occult cancer cell reactivation is the only proposed explanation for this recurrence.

Kaiser et al reported that the mean time between the primary and the recurrent tumor was 25 months (range, 1–252 months) with 82% of the recurrences within 3 years after surgery [8]. The recurrence interval was inversely correlated with the initial tumor stage. Poor survival was associated with a short recurrence interval (< 12 months) and a distant recurrence site. The exact mechanism of postoperative colon cancer recurrence after 13 years in our case remains largely unknown. In fact, stage II tumors (negative nodal status), as in our case at initial resection, have a significantly longer recurrence time than stage III tumors. Moreover, there may be some occult metastatic cancer cells that are suppressed by humoral immune cells that are activated when the host's immune function is suppressed for some reason. However, this hypothesis needs to be evaluated in further studies.

The symptoms of hematuria and bloody stool in our patient are probably due to irritation or erosion of the bladder and bowel tract by the metastatic cancer cells based on the intraoperative and pathologic observations. The pathologic findings showed the presence of metastatic cancer cells in the serosa, muscularis propria and submucosal layer, but not the mucosal layer. The mucosal layer only showed erosive changes, but no signs of neoplastic invasion. These findings support the clinical presentation of our patient.

In conclusion, we have described this rare case to remind clinicians that a postoperative relapse can occur as late as 13 years after primary tumor resection, despite its low incidence rate. A comprehensive evaluation of the clinical symptoms and signs in patients after curative resection for CRC might reveal a recurring tumor at a resectable stage and improve the outcome for that recurrence. Further studies are needed to determine whether a more intensive follow-up or increasing the duration of the follow-up period would affect the outcomes for such patients.

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大腸癌手術後十三年復發以血尿為臨床表徵：病例報告

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大腸癌手術後十三年發生復發是非常罕見的病例，通常大腸癌手術後會在三年內復發，而於手術五年後再復發的機率只有 5–7%，手術後超過十年再發的機率更是少數。在此我們報告一名 72 歲男性大腸癌病患，在切除手術十三年後復發，因血尿到診所就診，後有血便情形。理學檢查時發現下腹部正中央處有一個壓痛的硬塊，經由電腦斷層檢查發現一腫瘤附著於遠端空腸壁與膀胱壁外，血清胚胎抗原指數高達 32 ng/dL。經由手術切除病灶後病理組織報告證實為再發性大腸癌侵犯空腸與前腹壁。

關鍵詞：大腸癌，血尿，復發間隔時間

（高雄醫誌 2010;26:211–6）

收文日期：98 年 3 月 13 日

接受刊載：98 年 8 月 19 日

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