Ulcerative Colitis Patients with a Family History of Colorectal Cancer Should be Subjected to Close and Careful Surveillance

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We report two cases affected by neoplasia after colectomy with ileo-rectal anastomosis (IRA) with a positive family history of colon cancer. Case 1, a 41-year-old ulcerative colitis (UC) patient, underwent IRA in 1977. In 1986, biopsies showed high-grade dysplasia. She underwent resection of the rectal stump in 1986. Submucosal invasive carcinoma was found in the surgical specimen. The immunohistological study demonstrated p53 protein overexpression in the neoplastic lesion. Her family history fulfilled the Amsterdam criteria of hereditary non-polyposis colorectal cancer (HNPPC). Case 2, a 47-year-old UC patient, underwent ascending colostomy in 1975 and the following year IRA. Endoscopic mucosal resection (EMR) for a sessile adenoma was performed in 1995 and subsequently polypectomy was performed for the residual tumor. Recurrent adenoma and dysplasia in another area were detected. The immunohistological study demonstrated p53 protein overexpression only in dysplasia. Renal cancer in the right kidney was detected. Resection of the rectal stump with ileal pouch–anal anastomosis (IAA), loop ileostomy and right nephrectomy were performed in 1998. Her mother and her mother’s sister had been diagnosed with colon cancer. Only in the dysplastic lesion did we detect microsatellite instability at DSS644. Both cases with neoplasia had two relatives with colorectal carcinoma. In 33 cases with UC who had been followed up, 30 cases (96.8%) without neoplasia had no family history of colorectal carcinoma. These findings suggest that UC patients with a family history of colon cancer should be put under close surveillance. It should also be emphasized that IAA is the procedure of choice for UC patients with this particular condition.

Key words: ulcerative colitis – family history – cancer – dysplasia – adenoma

INTRODUCTION

A family history of colon cancer is associated with a 2–3-fold greater risk of colon cancer in individuals with sporadic, non-colitic colorectal carcinoma (1). Little attention has been given, however, to the issue of whether a family history of colon cancer might also be a risk factor in ulcerative colitis (UC) patients. Here we report two cases affected by neoplasia after colectomy with ileo-rectal anastomosis (IRA) with a positive family history of colon cancer.
carcinoma and low-grade dysplasia was observed in the broad area around the invasive carcinoma and high-grade dysplasia (Fig. 1). We studied p53 protein expression in this specimen by the SAB method (2,3). Immunohistological study demonstrated p53 protein overexpression in the neoplastic lesion (Fig. 2). Her family history revealed that both her father and her brother had rectal cancer. This family history fulfills the Amsterdam criteria of hereditary non-polyposis colorectal cancer (HNPCC) (Fig. 3). She has been well for 13 years since her operation.

CASE 2

A 47-year-old woman presented with occasional bloody stools and diarrhea since 1972. She was diagnosed as having UC in 1972. She was treated with systemic steroids, but her condition showed no improvement. She suffered from osteoporosis due to long-term high-dose steroids. She underwent ascending colostomy in 1975 with subsequent withdrawal of steroids and the following year total colectomy with IRA. She had been followed up by annual surveillance colonoscopy since 1981. Since a sessile adenoma 1 cm across was detected by colonoscopy in 1995, endoscopic mucosal resection (EMR) was performed, followed by polypectomy for the residual tumor (Fig. 4). Recurrent adenoma after EMR and dysplasia in another area were detected in the rectal stump. Immunohistological study demonstrated p53 protein overexpression only in the area of dysplasia, and not in the recurrent adenoma (Figs 5 and 6). Furthermore, renal cancer was detected in the right kidney by computed tomography. Resection of the rectal stump with ileo-rectal anastomosis (IRA), ileostomy and right nephrectomy were performed in 1998. The surgical specimen of the rectal stump demonstrated two neoplastic lesions. One lesion was a tubulovillous adenoma with moderate atypia, protuberant sessile type, 1.1 cm in size, and the other was considered to be high- and low-grade dysplasia, flat type, 5 cm in size. Renal cell carcinoma of the right kidney was common type, clear cell subtype, 2 cm in size. Four months after pouch operation (IRA), ileostomy closure was performed. The postoperative course was uneventful. Family history revealed that her mother and her mother’s sister had been diagnosed as having colon cancer. For biopsy samples, we analyzed genetic instability at four selected microsatellite loci: D2S123, D3S1067, D5S644 and TP53. Primer sets for these loci were used as described elsewhere (4-7). Polymerase chain reaction (PCR) was described previously (8). We detected microsatellite instability at D5S644 only in the dysplastic lesion, and not in other lesions at any locus.

DISCUSSION

It is known that a positive family history of colon cancer is associated with a 2–3-fold greater risk of colon cancer in individuals with sporadic, non-colitic colorectal carcinoma (1). Little attention has been given, however, to the issue of whether a family history of colon cancer might also be a risk factor in UC patients. Nuako et al. (9) reported that a family history of colon cancer was twice as common in UC patients with colon cancer than in UC controls matched for extent and duration of colitis, but no papers have been published about a positive family history of colon cancer in UC. Thirty-six patients who had received IRA for intractable colitis have been followed up by surveillance colonoscopy in our department. The average duration since disease onset
was 14 years. It has been reported that 1.3–6.0% of patients develop cancer of the rectal stump after IRA (10–12). In our experience, one patient (2.8%) developed a cancer and another one (2.8%) developed both a dysplasia and an adenoma.

We examined the family history of 33 UC patients receiving IRA (Table 1). All cases in which neoplasia was detected had two relatives with colorectal carcinoma. One (case 1) fulfilled the Amsterdam criteria (13), the other (case 2) fulfilled the Japanese criteria for HNPCC (14) and case 2 showed microsatellite instability in one microsatellite marker. On the other hand, among the 31 cases without neoplasia, 30 (96.8%) had no family history and in the remaining one (3.2%), the patient’s father had suffered from colon cancer and thus a marked difference in a family history of colorectal carcinoma was confirmed between the two groups.
Surveillance for dysplasia and cancer in UC patients has been advocated by most investigators (15–19). Two retrospective studies indicate that mortality is reduced by a surveillance program (15,16). In our department, five cancers were detected during the surveillance program and all patients were alive after a median follow-up period of 7 years. In contrast, out of five patients who had never received surveillance colonoscopy, three (60%) died within 2.5 years after operation for advanced carcinoma with peritoneal dissemination. Presumably, surveillance colonoscopy is useful for the early detection of UC-associated neoplasms. One key issue, that is, the cost-effectiveness of surveillance colonoscopy, however, remains to be clarified.

It has been suggested that annual colonoscopy might be better than biennial examinations so as not to miss interval cancers (17). However, Lynch et al. (20) cast doubts on the value of annual colonoscopy when considering its cost-effectiveness and the definition of a workable program. To improve the cost-effectiveness, a high-risk group of DC-associated colon cancers should be put under close surveillance. It should also be emphasized that IAA is the best surgical procedure that leaves no mucosa positive family history of colon cancer should be put under close surveillance. It should also be emphasized that IAA is the best surgical procedure that leaves no mucosa.

Table 1. Family history of UC cases subjected to surveillance after ileo-rectal anastomosis

<table>
<thead>
<tr>
<th>Family history</th>
<th>UC after IRA with neoplasia group (n = 2)</th>
<th>Without neoplasia group (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal carcinoma (n &gt; 2)</td>
<td>2 cases (100%): Father and brother</td>
<td>0 cases</td>
</tr>
<tr>
<td></td>
<td>Mother and aunt</td>
<td></td>
</tr>
<tr>
<td>Colorectal carcinoma (n = 1)</td>
<td>0 cases</td>
<td>1 case (3.2%): Father</td>
</tr>
<tr>
<td>Non-CRC tumor</td>
<td>0 cases</td>
<td>5 cases (16.1%): Father: gastric cancer</td>
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<tr>
<td></td>
<td></td>
<td>Mother: uterus cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grandfather: gastric cancer</td>
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<tr>
<td></td>
<td></td>
<td>Grandfather: lung cancer</td>
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<tr>
<td></td>
<td></td>
<td>Sister: brain tumor</td>
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<tr>
<td>No tumor</td>
<td>0 cases</td>
<td>25 cases (80.7%)</td>
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References