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The importance of family study in the patients with familial adenomatous polyposis.

Jose Antonio Perdomo* Hiromi Iwagaki† Akio Hizuta‡

Noriaki Tanaka** Kunzo Orita††

*Okayama University,
†Okayama University,
‡Okayama Univeristy,
**Okayama University,
††Okayama University,

The importance of family study in the patients with familial adenomatous polyposis.*

Jose Antonio Perdomo, Hiromi Iwagaki, Akio Hizuta, Noriaki Tanaka, and Kunzo Orita

Abstract

Familial adenomatous polyposis (FAP) is a well-known autosomal dominant disorder characterized by the formation of multiple adenomatous polyps of the colon. Gardner's syndrome is a variant of familial polyposis coli, and both can be associated with colonic or extracolonic benign and/or malignant tumors. It has been widely recognized that an adenocarcinoma of the colon develops in virtually all cases, usually at an earlier age, if polyps are left untreated. Families of four individuals diagnosed of FAP were surveyed and 56 relatives of the families were examined. Of these 56, 21 had multiple colon polyps, 3 of whom had early-stage adenocarcinomas. We consider that familial survey of FAP individuals can be of considerable benefit for this high-risk population due to the autosomal nature of the disease, allowing diagnosis of an associated cancer at an earlier stage.

KEYWORDS: familial adenomatous polyposis, colorectal carcinoma, Gardner's syndrome

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— Brief Note —

The Importance of Family Study in The Patients with Familial Adenomatous Polyposis

JOSE ANTONIO PERDOMO*, HIROMI IWAGAKI, AKIO HIZUTA, NORIAKI TANAKA AND KUNZO ORITA

First Department of Surgery, Okayama University Medical School, Okayama 700, Japan

Familial adenomatous polyposis (FAP) is a well-known autosomal dominant disorder characterized by the formation of multiple adenomatous polyps of the colon. Gardner's syndrome is a variant of familial polyposis coli, and both can be associated with colonic or extracolonic benign and/or malignant tumors. It has been widely recognized that an adenocarcinoma of the colon develops in virtually all cases, usually at an earlier age, if polyps are left untreated. Families of four individuals diagnosed of FAP were surveyed and 56 relatives of the families were examined. Of these 56, 21 had multiple colon polyps, 3 of whom had early-stage adenocarcinomas. We consider that familial survey of FAP individuals can be of considerable benefit for this high-risk population due to the autosomal nature of the disease, allowing diagnosis of an associated cancer at an earlier stage.

Key words: familial adenomatous polyposis, colorectal carcinoma, Gardner's syndrome

Familial adenomatous polyposis (FAP) is an autosomal dominant disease which is well known for a long time, although the responsible gene was not identified until 1987 (1). FAP is characterized by the presence of multiple adenomatous polyps in the colon. FAP has a variation, Gardner's syndrome (GS)(2, 3), which is associated with colonic and extracolonic manifestations described by Gardner and Stephens in 1950. This syndrome may include specially osteomas, soft tissue tumors as well as hair and dental anomalies. Since then, attention has been focused on the association between FAP/GS and other benign or malignant tumors. Recently, it has been described in connection with neoplasms of the thyroid (4), liver (5, 6) and adrenal gland (7). Moreover, it is well known that untreated polyps have a high risk for malignant transformation (8). The purpose of this work was to report the findings of a familial study and to discuss the need for careful search for colon polyps and/or associated lesions in the relatives of FAP patients. This approach is of great benefit to provide early diagnosis and early treatment in this high-risk population.

Between January 1980 and January 1990, 4 patients from separate families were initially diagnosed and treated for multiple polyposis of the colon. Then a systematic investigation in 56 relatives of these 4 patients was performed. The investigation consisted of radiographic examination including double contrast enema, colonoscopy and biopsies. Tumor classification and staging were done according to the criteria of the Japanese Research Society for Cancer of the Colon and Rectum (9). The grade of lymph-vascular infiltration was classified as previously published (9). The follow-up examinations were done every 6 months in all patients with a mean of 5 years, ranging from 1 to 10 years. Of the 56 individuals examined, 21 presented with colonic polyps, 3 of whom had an associated cancer. These 3 cases are presented and discussed.

Case Presentation

Case 1. A 54-year-old Japanese man at examination presented with multiple colonic polyps affecting the entire colon, the rectum and the stomach (5 polyps). These polyps had an average diameter of 5 mm. Histopathologically, a pedunculated polyp, 25 mm in diameter located in the posterior wall of the middle rectum 7 cm

* To whom correspondence should be addressed.

from the anal verge was found to be a papillotubular adenocarcinoma. The laboratory and radiographic examinations were normal except for the presence of 3 osteomas in the frontal region.

Case 2. A 45-year-old Japanese man demonstrated on examination multiple polyps involving the rectum, sigmoid colon, descending colon, and 3 gastric polyps. The colonic polyps had a mean size of 6mm. The histology of a polyp measuring 20mm revealed an adenocarcinoma. A dental evaluation showed supranumeric teeth and the remaining examinations were normal.

Case 3. A 42-year-old Japanese woman showed multiple polyps throughout the colon with a 25-mm polyp at the rectosigmoid junction which was histologically confirmed to be a papillotubular adenocarcinoma. No clinical, laboratory or radiological abnormalities were found. Gastroscopy revealed 3 gastric polyps.

At the time of diagnosis, these three patients were asymptomatic. Diagnosis was done by double contrast enema, gastroscopy and colonoscopy. The biopsy revealed villoadenomatous polyps accompanied with focal cancer located in the rectum, descending colon and rectosigmoid junction, respectively. Neither lymph nodes, distant metastasis, nor other associated tumors were detected with the exception of the cranial osteomas. Total colectomy and ileoanal anastomosis with a J-pouch reservoir were performed in all three cases. Histological examination of the surgical specimens revealed adenomatous polyps and colon cancer predominantly confined to the mucosal layer (cases 1 and 2). Although there was a slight invasion into the submucosal layer in case 3, no vascular or lymphatic invasion was noted. All the surgically resected lymph nodes were free of invasion. Two patients (cases 1 and 2) presented with cranial osteomas and supranumeric teeth consistent with GS. The gastric polyps were treated by endoscopic polypectomy. The patients were discharged within 1 month after the operation without any complication.

Discussion

FAP has been defined as an autosomal dominant disease in which the colon contains more than 100 adenomas. In the majority of the patients, the colonic mucosa is covered with hundreds of small polyps extending throughout the colon (10). The GS is a variant of the FAP, and if the polyps are left untreated, adenocarcinoma will develop in virtually all cases. FAP or GS can be associated with extra-colonic lesions originated from embryonic tissues and with malignant tumors (11). The possibility of malignant transformation of the polyps has been a subject of great discussion. An association between FAP/GS with ampullary and thyroid tumors has been reported as well as with gastric and duodenal polyps (12–14).

A total of 56 relatives of 4 initial FAP patients were investigated. Of these, 21 (37.5%) presented with multiple colonic polyps, 3 of whom (5.3%) had colorectal cancers. Bullow (15) in 1984 reported similar findings in Danish families (3%) demonstrating the benefit of prophylactic examination of family members at risk. Since the cancers were diagnosed in an early stage, this assessment has allowed a curative treatment in all those 3 patients.

In conclusion, the relatives of FAP patients should be routinely investigated, thus providing detection and treatment for early staged cancers with the consequent improvement on prognosis (16).

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