Original article

The epidemiological and clinical features of familial adenomatous polyposis in Ribeirão Preto☆

Marley Ribeiro Feitosaa,*, Tais Helena Garcia Fernandes de Oliveirab, Bruno Ravenna Pinheiro Kondob, Haline Gomes de Lira, André Antonio Abissamraa, Rogério Serafim Parraa, Omar Féresa, Jose Joaquim Ribeiro da Rochaa

*Divisão de Coloproctologia, Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (USP), Ribeirão Preto, SP, Brazil
bFaculdade de Medicina de Ribeirão Preto, USP, Ribeirão Preto, SP, Brazil

Article info

Article history:
Received 4 May 2013
Accepted 13 June 2013

Keywords:
Familial adenomatous polyposis
Colorectal cancer
Ileal pouch

Abstract

Purpose: to study 75 familial adenomatous polyposis (FAP) patients treated in a single institution in Ribeirão Preto/SP, from January 1981 to December 2011.
Methods: this is a retrospective study and the following data were collected: gender, age, main symptoms, familial history, coexisting malignancies, surgical treatment, surgical morbidity and mortality, factors related to life quality.
Results: median age was 29 years. Male-to-female ratio was 1.2:1. Bleeding was the most common symptom (62.6%). Colorectal cancer incidence was 25.5% (n = 19). Extracolonic neoplasia incidence was 8%. Colectomy with ileorectal anastomosis (IRA) was performed in 72% of the patients. Eighteen patients (24%) were submitted to proctocolectomy with “J-pouch” ileoanal anastomosis. In three patients (4%) proctocolectomy with terminal ileostomy was performed. Early and late complication rate were similar (22.7% × 24%). Ileal pouch surgery exhibited tendency to a higher morbidity and mortality but no significance could be found. Overall mortality rate was 7.46%. Malignant neoplasia was the main cause of mortality, accounting for 60% of deaths.
Conclusion: FAP is a rare pathology in our country. Genetic counseling and proper screening programs are essential tools to early diagnosis and follow-up. Surgery is the most effective treatment and the best option to prevent malignant neoplasia.
Familial adenomatous polyposis (FAP) is an autosomal dominant genetic syndrome first described in 1721 by Menzelio. It is the result of a germline mutation in the adenomatous polyposis coli (APC) gene located in chromosome 5q21 responsible for cell growth and apoptosis regulation. In its classical phenotype, patients develop hundreds to a thousand adenomatous polyps between the second and third decades of life. There is also a milder form of the disease called attenuated FAP (AFAP) with fewer polyps throughout the colon. Both exhibit precancerous nature and, without proper treatment, degeneration to colorectal carcinoma (CRC) is inexorable by the fifth to sixth decades of life. There are no studies regarding the incidence of FAP in our country but worldwide incidence is considered the same and estimated at one in every 5,000-10,000 live births.

Family history is of great importance for diagnosis because most patients are asymptomatic or present with nonspecific symptoms such as intestinal bleeding, abdominal pain or changes in bowel habit. FAP may also present with other complications such as desmoid tumors, adenocarcinoma of the small bowel, thyroid cancer, medulloblastomas and osteomas.

Surveillance of patients leads to a reduction in CRC-related mortality. Individuals with a positive family history should begin annual colon evaluation (i.e. sigmoidoscopy or colonoscopy) by 10-12 years of age. Genetic tests are useful to confirm an APC gene mutation. Once the mutation is discovered in an individual, genetic testing can help identify affected members of the same family.

Surgery is the definitive treatment and options include proctocolectomy with terminal ileostomy (PCI), colectomy with ileoanal anastomosis (IRA) and proctocolectomy with ileal pouch anal anastomosis, also known as restorative proctocolectomy (RCP). Both the patient and the physician have to solve the dilemma of neoplasia control and functional compromise to choose the right procedure. General agreement is that the surgeon must always consider the individual characteristics of each patient.

The aim of this study is to describe the epidemiologic and clinical characteristics, as well as evaluate the outcome of a group of FAP patients treated in our institution.
Results

The present study included 75 patients. Average age was 29 years (8 months-60 years) and men [41 (54.7%)] prevailed over women [34 (45.3%)]. The most common symptoms were intestinal bleeding (62.7%), abdominal pain (40%), change in bowel habits (30%) and weight loss (14.7%). We discovered that sixty patients (80%) had other members of the family affected by FAP. Adenomatous polyps were found by upper gastrointestinal endoscopy in 24 (32%) individuals, most of them in the stomach (75%).

CRC incidence was 25.3% (11 men and 8 women) and the average age of this group was 40.9 years old (22-59 years) [Fig. 1]. The diagnosis was made preoperatively in 73.7%, during the surgery in 10.5% and during the follow-up in 15.8% of the cases.

The incidence of extra-colonic neoplasia was 8% (4 desmoid tumors, 1 duodenal adenocarcinoma and 1 thyroid cancer).

Regarding the treatment, IRA was performed in 54 (72%) patients. Eighteen (24%) patients were submitted to RCP and 3 (4%) undergone PCI. The overall early and late post-operative complication rates were similar [22.7% (17 patients)] × [24% (18 patients), respectively]. We noticed a tendency of higher percentage rates of morbidity and mortality for RCP but no significance was found (Tables 1, 2 and 3).

The incidence of diarrhea and use of antidiarrheal agents after RCP was 33.3%. Reported incidence of fecal incontinence was 5%. The rate of diarrhea requiring pharmacologic treatment after IRA was 11% and no fecal incontinence was reported. Sexual dysfunction was noted only after IPAA in a rate of 11%. Rectal cancer incidence after IRA was 3.7% (2 patients).

The cancer incidence after IPAA was 5.5% (one patient developed cuff adenocarcinoma).

Loss to follow-up rate was 10.7%. The maximum follow-up time was 29 years. Overall mortality rate was 7.46% (5 patients). Advanced malignant neoplasia was the main cause of death [60% (3 patients)] and surgical complications (hypovolemic shock and necrohemorrhagic pancreatitis) accounted for the rest.

Discussion

The development of adenomas in FAP precedes symptoms and the disease remains silent for a long period of time. The Danish Polypsis Register analyzed the course of the disease and found a median age at diagnosis of FAP of 19 years. The present study found a higher mean age at diagnosis (29 years) that could be explained by the lack of compliance of screening programs, difficult access to healthcare and medical or patient's negligence.

The symptoms presented by the patients were intestinal bleeding (62.7%), abdominal pain (40%), change in bowel habits (30%) and weight loss (14.7). We found that 42.7% of the patients were asymptomatic and FAP was diagnosed during screening of relatives.

Esophagogastroduodenoscopy helps the detection of gastric, duodenal and periampullary adenomas. Upper gastrointestinal cancer incidence in FAP is higher than general population but rare before the age of 30 years. General consensus recommends endoscopic surveillance starting from 25-30 years of age, at intervals of 1-5 years depending on the severity of the disease. The incidence of gastric and duodenal polyps in our study was 24% and 12% respectively. Adenocarcinoma of duodenum was diagnosed in one (1.3%) patient.

Colonrectal carcinoma is the main cause of death among patients with FAP. Most patients develop cancer by the age of...
CRC was found in 19 (25.3%) patients in the present study (Fig. 2). The diagnosis was made pre-operatively in 73.7% of the cases during colonoscopy. Desmoid tumor is a benign neoplasia and the most important extracolonic manifestation of FAP. It has an infiltrative growth pattern and a high recurrence rate after resection. Such aggressive behavior makes this neoplasia the second most common cause of death in FAP. Leal et al. found an incidence of 13.2% in a series of 68 patients with no recurrence in a mean follow-up time of 63.1 months after treatment.

Other national registry reported an incidence of 11.9% in 55 patients with 28.5% death rate. An English series of 88 patients reported a cure rate of only 14% and deaths in 13% of the cases. The incidence of desmoid tumors in our study was 5.3% (4 patients). Half of the cases was located in the abdominal wall and the other half inside the abdominal cavity. Curative resection was possible in three patients (75%) and no recurrences were noted. No deaths were attributed to this neoplasia (Fig. 3).

Surgery is the most effective treatment option and controversies regarding the best procedure still exist mainly because the choice depends on several factors such as age of the patient, sphincter function, mutation locus, number and site of the polyps, cancer association, patients’ commitment to long-term follow-up, and experience of the surgeon. There are no guidelines regarding the optimal timing of operation and most patients undergo surgery between 15-25 years of age.

Most patients in our study (54 [72%]) underwent IRA. IRA is technically simpler than RCP with lower morbidity and mortality rates. It also avoids the need for a permanent ileal stoma seen in PCI, with better quality of life. The main advantage of rectal preservation is better functional outcomes. Disadvantages are the need of periodic rectal surveillance for new polyps and the association to metachronous rectal cancer in some cases. It is usually recommended when there are very few polyps in the rectum (less than 20) and in patients with mild genotype. In the present study early and late complication rates were similar (22.2% × 20.4%). The main cause of early morbidity was anastomotic dehiscence (41.7%) and the most common late complication was intestinal obstruction (63.7%). Mortality rate related to the procedure was 1.85%.

Conclusions

FAP is an uncommon disease that affects young people culminating with malignant neoplasia if untreated. Specialized centers are required to treat and follow this condition since it demands a multidisciplinary approach. Surgery is the definitive treatment and data concerning FAP in our country is scarce, compromising a better understanding of the epidemi-
ology, clinical aspects and treatment outcomes. We believe that a national registry should ameliorate the problem and improve medical care.

**Conflicts of interest**

The authors declare no conflicts of interest.

**REFERENCE**