A Two Generation of Familial Adenomatous Polyposis

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ABSTRACT

Familial adenomatous polyposis (FAP) is a part of genetic polyposis syndrome which is caused by germline mutation in the adenomatous polyposis coli (APC) gene located in chromosome 5q21. The pathognomonic features is formation of hundreds to thousands of colorectal adenoma in late childhood and increase in size and number during adolescence. If left untreated, almost 100% patients will develop colorectal cancer by the age 50 years. We present a case of 26 year old male who complain of rectal bleeding, diarrhea, abdominal bloating, and has multiple polyps on colonoscopic finding. Two years ago, his father was diagnosed with polyposis coli and transverse colon adenocarcinoma. The patient was planned for preventive total colectomy. In conclusion, surgery remains the cornerstone treatment of FAP and surveillance program for early detection of cancer for all family member is very important to reduce colorectal cancer-related mortality.

Keywords: familial adenomatous polyposis (FAP), adenomatous polyposis coli (APC) gene, colorectal cancer.

ABSTRAK

Familial adenomatous polyposis (FAP) merupakan salah satu bagian dari sindroma poliposis genetik yang disebabkan oleh mutasi gen adenomatous polyposis coli (APC) yang terletak pada kromosom 5q21. Gambaran klinis FAP yang khas adalah terbentuknya ratusan hingga ribuan adenoma pada usia akhir anak-anak dan adenoma ini cenderung bertambah besar dan banyak pada kelompok usia dewasa muda. Jika tidak mendapatkan penanganan, hampir 100% kasus berkembang menjadi karsinoma kolorektal pada usia 50 tahun. Berikut disajikan sebuah kasus, laki-laki, 26 tahun, dengan keluhan perdarahan rektum, diare, perut terasa kembung, dan dari gambaran kolonoskopi ditemukan adanya polip multipel di sepanjang kolon. Dua tahun yang lalu, ayah pasien didiagnosis poliposis coli dan adenokarsinoma kolon transversum. Pada pasien ini direncanakan untuk menjalani kolektomi total. Sebagai kesimpulan, pembedahan merupakan satu-satunya terapi FAP dan program surveilans untuk deteksi dini FAP pada seluruh anggota keluarga sangatlah penting untuk menurunkan mortalitas terkait karsinoma kolorektal.

Kata kunci: familial adenomatous polyposis (FAP), adenomatous polyposis coli (APC) gene, kanker kolorektal
INTRODUCTION

Familial adenomatous polyposis (FAP) is a part of genetic polyposis syndrome which is caused by germline mutation in the adenomatous polyposis coli (APC) gene located in chromosome 5q21. The incidence is estimated at one in every 8,000-10,000 live births and accounts for less than 1% of cases of colon cancer.2,3 The frequency is constant throughout the world, with men and women equally affected.4

The clinical manifestation of FAP consists of intestinal dan extraintestinal manifestation. Colonic adenoma represents the first intestinal manifestation, meanwhile the extraintestinal manifestation include congenital hyperthrophy of retinal epithelium, epidermoid cyst, desmoid tumor, and pancreatic cancer.1,3 Patients tend to develop hundreds to thousand adenomatous polyp between the second and third decades of life. If left untreated, almost 100% patients will develop colorectal cancer by the age 50 years.3

Colorectal carcinoma (CRC) is the main cause of death among FAP patients, therefore early diagnosis and surveillance is imperative to reduce cancer related mortality.3 Surgery remains to be the definitive treatment of FAP, but the timing and type of surgery performed are still a controversy.1,5

CASE ILLUSTRATION

A 26 year old Balinese man presented with rectal bleeding, diarrhea, and abdominal bloating since 1 year. Two months ago he underwent rectal polypectomy in other private hospital. His father had similar complaints and was diagnosed with polyposis coli and adenocarcinoma of the transverse colon in 2016. On digital rectal examination, no palpable mass was found. His blood investigation were within normal limits. On colonoscopy there were multiple polyps less than 1 cm in entire colon from rectum to caecum, which is very suggestive of polyposis syndrome (Figure 1). Histopathological finding revealed adenomatous polyp with mild to moderate dysplasia (Figure 2). The patient was investigated for FAP-associated lesions and no other significant finding was noted. He was planned for preventive total colectomy with ileorectal anastomosis and his sister had been advised to do a colonoscopy screening.

DISCUSSION

FAP, also known as adenomatous polyposis coli and familial polyposis coli, is the most common genetic polyposis syndrome. It comprises less than 1% of colorectal cancer and typically caused by an autosomal dominant germline mutation in APC gene located on chromosome 5q21. Approximately up to one third of cases appear to be caused by de novo mutation, without any clinical or genetic evidence of FAP in family members. The incidence is estimated at one in every 8,000-10,000 live births, with men and women equally affected.3,4,6

The clinical feature of FAP can be divided into intestinal and extraintestinal manifestation. Colonic adenoma represents the first gastrointestinal manifestation and usually developed in second or third decade of life with average of age 15.9 years.3,7 Classic FAP is characterized by hundreds to thousand colorectal adenomatous polyps, while attenuated FAP developing fewer polyps, usually less than 100 and tend to occur later in life. Over time, the adenomas increase in size and number, so does the risk of cancer. Benign extraintestinal manifestation include congenital hyperthrophy of retinal epithelium, epidermoid cyst, desmoid tumor, supernumery teeth, osteoma, and adrenal adenoma. Other cancer risks are central nervous system, pancreatic, thyroid, and liver cancer.3,8

Herein two generation cases of FAP is presented in which a son and his father had clinical presentation of FAP. Like most cases of the FAP, these two cases showed inherited pattern, which affects father and son in the family. Both of these cases had intestinal manifestation only without any extraintestinal sign. Diagnosis of polyposis syndrome was based on clinical finding with greater than 20 adenomas on colonoscopy and positive family history.9,10 Over time the risk of cancer is increasing and if left untreated, almost 100% of cases will develop colorectal cancer by the aged of 50 years.3 This is in line with his father case who had colorectal adenocarcinoma at 50 (Figure 3). When patients are clinically diagnosed with FAP, they should undergo genetic testing in order to counsel their first degree relatives regarding screening and treatment.9 Unfortunately the genetic testing mutation in this
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The case cannot be done because of limited facility in our hospital. Delay of diagnosis in our case maybe due to his father’s long asymptomatic period. FAP has been a rare diagnosis in Indonesia and probably this above case was the first case documented in Indonesia, especially in Bali. FAP diagnosis is still become a challenge in our setting because of no national guidelines and surveillance has been established yet.

Number, and the present of symptoms. Surgical options are colectomy with ileorectal anastomosis (IRA), proctocolectomy with ileal pouch anal anastomosis (IPAA), and proctocolectomy with ileostomy.3,12,13 Our case was planned for total colectomy with IRA. This approach was considered because of the low rectal polyp burden, has lower complication rate and better quality of life compared to IPAA.

CRC is the main cause of death among patients with FAP and surveillance leads to a reduction in CRC-related mortality. Colonoscopy screening should be performed in individual with clinical or genetic diagnosis of FAP. In those where no mutation can be found, all at risk relatives must undergo endoscopic screening. Colonoscopy should be begin at puberty or whenever the suggestive symptoms appeared. Colon screening guidelines for children with classic FAP is every 1-2 year sigmoidoscopy beginning at 10 to 12 years of age. For those who initially screening at older age should have colonoscopy for the first examination.3,14 His sister was also advised for colonoscopy screening.

Prophylaxis colectomy remains the definitive therapy of FAP. Surveillance program for early detection of cancer for all at risk relatives is very important to reduce colorectal cancer-related mortality. Data concerning FAP in our country is scarce, compromising a better understanding about clinical aspects and treatment outcome. We hope in the future, the national registry could ameliorate this problem and improve medical care of FAP patients.

REFERENCES


