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Case report

Melena Revealing an Attenuated Familial Adenomatous Polyposis in an Elderly Patient: A Case Report

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Abstract

We describe a patient who was diagnosed with multiple tubulleuvillous adenomas with focus of high-grade tubular dysplasia all over the colonic mucosa, discovered during a colonoscopy performed during an episode of melena. Genetic testing has identified a germline truncating mutation at the codon (5q22.2) of the adenomatous polyposis (APC) gene. This mutation is localized in the alternately spliced region of exon 12, a region which is associated with an attenuated familial adenomatous polyposis (PAFA) phenotype. Our patient had no extracolic manifestations of PAFA and none of her relatives had a history of rectocolic polyposis. Treatment consisted of colectomy with ileorectal anastomosis. PAFA is an ill-defined condition of unknown prevalence and penetrance, requiring individual treatment and lifelong monitoring. It is essential to identify these patients with a view to setting up appropriate endoscopic surveillance at an early age in family members carrying this mutation, due to the marked intra-family phenotypic variance.

Keywords: ***attenuated familial adenomatous polyposis, adenomatous polyposis gene, exon12, colectomy with ileorectal anastomosis, case report, Morocco.***

Introduction

Familial adenomatous polyposis (FAP) is an autosomal dominant disease with high penetrance. There are attenuated forms around 10% in which adenomas appear late and the risk of colorectal cancer is late [1]. We report the case of a patient with no family history of colorectal cancer, in whom the diagnosis of attenuated PAF was made by colonoscopy who showed a number of polyp more than 10 over the entire colonic mucosa and whose genetic study has been carried out. Revealed a mutation in the APC gene whose phenotype was related to an attenuated form.

Patient information

Patiente RZ, 77-year-old, known to be hypertensive for 20 years, on amlodipine 10 mg / day, admitted for an etiological examination of an upper digestive hemorrhage made up of several episodes of melena, the last episode of which dates back to 2 and a half months, associated to a terminal constipation at the rate of a saddle every 3 days, hard with difficulty of exemption.

Clinical findings

The clinical examination was strictly normal, apart from a slight cutaneous-mucous pallor and a deterioration of the general state of asthenia, and marked but not quantified weight loss, on abdominal examination showed diffuse peri-umbilical sensitivity, in the absence of palpable lymphadenopathy. The hemodynamic constants were correct.

Diagnostic assessment

A routine blood count gave the following results: white blood cell count = 6400 / µL, hemoglobin = 10.9 g / dL, platelets were 220,000 / mm3. Tumor markers which are normal; without other biologically notable abnormalities. The colonoscopy performed found multiple polyps, both sessile and pediculate, spread over the entire surface of the colonic mucosa, more than 10 polyps, including a raspberry polylobate and broad base of implantation more than 3cm in the left colon, the rectal mucosa was normal in appearance. Endoscopy showed an appearance of erythematous and atrophic pangatsritis and erosive bulbitis. Histological study of the colonic biopsy showed tubulleuvillous adenomatous

proliferation with focus of high-grade dysplasia. A mutation in the APC gene was subsequently revealed by genetic study using next-generation sequencing technology. In the APC gene (5q22.2), a pathogenic variant concerning exon 12 was identified, leading to a diagnosis of attenuated familial adenomatous polyposis (AFAP). After obtaining these results, the analysis of the single-site variant was carried out on his 3 daughters. In her second and third daughters, the same variant was confirmed.

Therapeutic intervention and follow up

The patient subsequently underwent a total colectomy with an ileorectal anastomosis (figure 1). Screening by colonoscopy was thus offered to all members of her family leading to a diagnosis of Attenuated Familial Adenomatous Polyposis (AFAP).

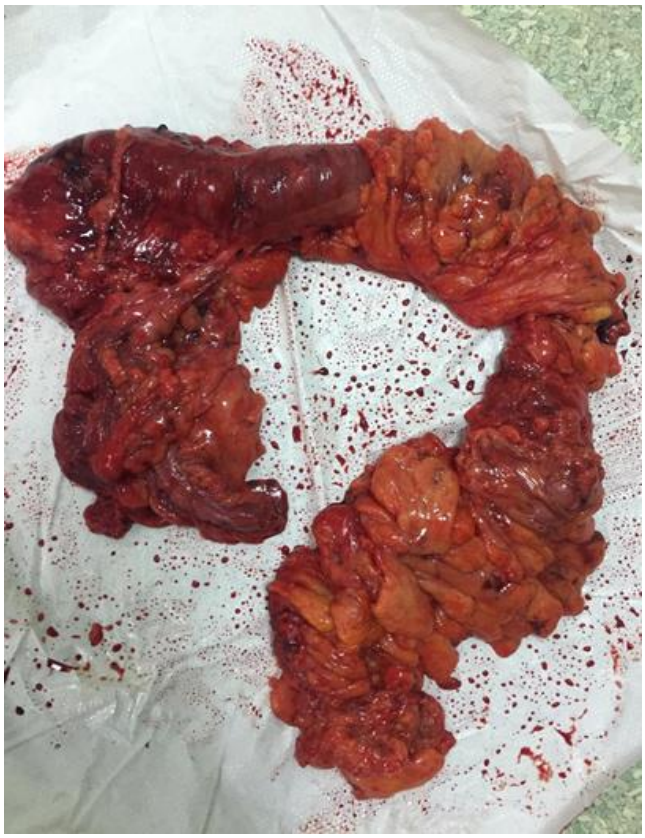

Figure 1: colon showing polyps after total colectomy with colorectal anastomosis

Discussion

Familial adenomatous polyposis (FAP) is an inherited disease with dominant transmission predisposing strongly to colorectal cancer, is due to a constitutional alteration of the APC gene, located in 5q21.It is characterized by the development of hundreds or thousands of colorectal adenomatous polyps that can progress to colorectal cancer (CRC) in the absence of treatment [2,3]. The prevalence of PAF is 2.29-3.2 cases per 100,000 individuals, it affects both men and women equally [4,5]. Germline mutations of the APC gene on chromosome 5q21 which can subsequently lead to colorectal carcinogenesis are found in classic familial adenomatous polyposis, attenuated (AFAP) and polyposis associated with MUTYH. The three syndromes increase the potential for the development of colorectal cancer. APC is a tumor suppressor gene and its inactivation only occurs if the patient has both allele affected by the mutation [6,7]. In patients with attenuated FAP, mutations in the APC gene occur in 3 separate locations: the proximal end (5′) of the gene (first 5 exons), the distal end (3′) of the gene (after codon 1580) [8,9]. Mutations associated with the attenuated phenotype are found predominantly in the 5 'region of the gene or in the last third [10]. Generally, they affect around 8% of individuals carrying an APC mutation located on exons 1-3, 9 or at the end of exon 15 (beyond codon1550) of the APC gene [11].

The number of adenomatous polyps is less than 100 in attenuated FAP, the age of onset later (between 30 and 40 years), the median age at the time of diagnosis of CRC was 55-58 years, with a range from 29 to 81 years [12]. Patients with attenuated FAP, by definition, have fewer adenomas than patients with classical FAP and the majority of adenomas originate from the right colon and the rectum is most often spared according to some reports [13,14] such as the case of our patient. In this "attenuated" form, only between 20 and 100 colorectal adenomas are found, a remarkable variation in the phenotype of the disease among affected members of the same family, as well as a wide variety of other lesions from the upper gastrointestinal tract [15].

The most important problem with AFAP is that many affected people are difficult to distinguish from people with sporadic adenomatous polyps or colon cancer without genetic testing, as indicated by the number of people with few polyps, although they are more numerous, even at an advanced age. However, an accurate diagnosis of AFAP is necessary due to the risk of cancer [16].

Accordingly, Hernegger [17] and colleagues recommend a screening colonoscopy at age 15, with annual repetition, even if other family members have polyposis only at age average adult. While for classic FAP, prophylactic proctocolectomy is offered as standard in early adulthood [17,18].

In patients with AFAP, it is more difficult to design surveillance because there are few data, according to the available guidelines for attenuated FAP, adenomas and cancers occur 10 to 20 years later than in typical FAP [4]. A study by Knudsen et al [19] revealed that the risk of developing CRC in attenuated FAP is probably lower than that in classical FAP.

The incidence of cancers of the upper digestive system was similar to that of typical FAP, that is above all extracolic malignancies, particularly gastric and duodenal, and the expression of upper gastrointestinal polyps. The screening recommendations for the upper gastrointestinal tract of patients with AFAP should therefore be similar to those for typical FAP [19,20].

Patients with FAP may not need a colectomy and can be managed effectively with endoscopic polypectomy for decades [15]. Immediate colorectal surgery for FAP, AFAB is indicated for documented or suspected cancer or significant symptoms [19]. Surgery may be considered if several adenomas larger than 6 mm are detected, if there is a significant increase in the number of adenomas between 2 surveillance endoscopies and if high-grade dysplasia is diagnosed in one of the adenomas resected [19]. In the case of AFAP, total colectomy with ileorectal anastomosis is a preferred surgical technique based on data from various studies suggesting rectal sparing and the rarity of cancer development in the remaining rectum [13].

Conclusion

The attenuated FAP represents a separate entity next to the classic FAP, the management of which is quite complex and not yet clarified. Knowledge of the different phenotypic forms is fundamental in terms of FAP to better understand the therapeutic management. This is based on close endoscopic monitoring low but also high and prophylactic colorectal surgery in a few special cases.

Declarations

Conflicting interest

The authors declare no conflict of interest.

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Contributions from the authors

All authors have contributed to this study since conception, reading and have approved the final version of the manuscript

Reference

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