

CASE REPORT

AN UNUSUALLY LATE PRESENTATION OF MALIGNANCY IN A PATIENT WITH GARDNER SYNDROME

S. Sopan¹, E.K.D.M. Wickramaratne², H.M.S.R.B. Kotakadeniya³, S. Wijetunge²

¹Teaching Hospital, Peradeniya, Sri Lanka

²Department of Pathology, Faculty of Medicine, University of Peradeniya, Sri Lanka

³Department of Surgery, Faculty of Medicine, University of Peradeniya, Sri Lanka

Corresponding Author: Dr. S. Sopan; Email: siva.sopan@gmail.com

Abstract

A 64-year-old male who presented with bleeding per rectum and altered bowel habits for 6 months was found to have numerous polyps in the colon during colonoscopy. He also had two osteomas on the forehead and several epidermal cysts in the scrotal skin. His brother had a history suggestive of a similar disease. The patient underwent total proctocolectomy and ileal pouch – anal anastomosis. Pathological examination of the resected specimen revealed an adenocarcinoma in addition to numerous adenomata. The patient was diagnosed to have colonic adenocarcinoma complicating Gardner syndrome.

Key words: Osteomas, Epidermal cysts, Adenomatous polyposis syndromes, Gardner syndrome.

Introduction

Gardner syndrome (GS) is a rare autosomal dominant inherited disorder¹ with a high degree of penetrance. It is characterized by the presence of numerous intestinal polyps (more than 100) with extra-intestinal manifestations of bone and soft-tissue such as desmoid fibromatosis, lipomas, osteomas and epidermal cysts. This is regarded as a clinical subgroup of familial adenomatous polyposis (FAP) and may present at any age from 2 months to 70 years with colonic and extra colonic symptoms². Patients with FAP and its variants have an invariable life time risk of one or more intestinal polyps transforming into invasive malignancy at a relatively younger age. GS cannot be separated from FAP when considering studies that describe its overall prevalence. Estimates for the prevalence of the combined syndromes vary

from 1 in 6,850 to 1 in 31,250 (2.29 to 3.2 cases per 100,000 persons)³⁻⁵. Prevalence appears fairly constant throughout the world with men and women affected equally. Twenty to 30 percent of newly diagnosed cases, i.e. those who do not belong to previously identified families, appear to represent new mutations. New cases may also arise from mosaic inheritance, which implies that a mutation has occurred in parents' sperm or ova, but not in other cells of the body, so the parent did not have clinical disease⁶. Data for prevalence in Sri Lanka is not available. We present here a case of Gardner syndrome presenting with malignancy at an unusually advanced age.

Case Report

A 64-year-old male presented with bleeding per rectum and altered bowel habits with a

sense of incomplete evacuation and loss of appetite for the last 6 months. His brother had a similar disease and had undergone a bowel surgery in his fifties. He had hypertension and was an ex-smoker and has consumed alcohol in the past. On examination, he was emaciated. There were two bony lumps over the forehead. His blood pressure was 180/120 mmHg. Abdominal and rectal examination were normal. The scrotum showed several epidermal cysts.

He was anaemic with a haemoglobin level of 8.1 g/dl. Abdominal ultrasound scan did not reveal any intra-abdominal masses. X-ray of the skull showed osteomas over the frontal bone (**Figure 1**).



Figure 1. The skull X ray showing osteomas over the frontal bone (Arrows)

Colonoscopy showed multiple (more than 100) polyps of varying sizes throughout the colon. No malignant appearing masses were observed. Based on these findings a working diagnosis of a variant of familial adenomatous polyposis - Gardner syndrome was made.

Total proctocolectomy and ileal pouch – anal anastomosis with de-functioning ileostomy was performed. Gross pathological examination of the colectomy specimen revealed numerous polyps of varying sizes (**Figure 2**).



Figure 2. Colon with polyps of varying sizes. The arrow indicates the area where the malignant tumour was found.

The largest polyp was pedunculated and was 25 mm in diameter. The rest of the polyps were both pedunculated and sessile and the sizes ranged from 25 mm to less than 1 mm in diameter. A firm tumour was noted as a thickening of the wall in the sigmoid colon. The mucosa over the tumour was flattened (**Figure 2**).

Microscopic examination through the tumour showed a moderately differentiated adenocarcinoma, infiltrating the entire thickness of the colonic wall but not extending into the subserosal adipose tissue. The tumour did not appear to be arising from a polyp. Two pericolic lymph nodes showed tumour deposits. The TNM stage was T2N1M0. The polyps were villous, tubulo-villous (**Figure 3**) and tubular adenomata with low grade dysplasia. There were oligocryptal and flat adenomata as well.

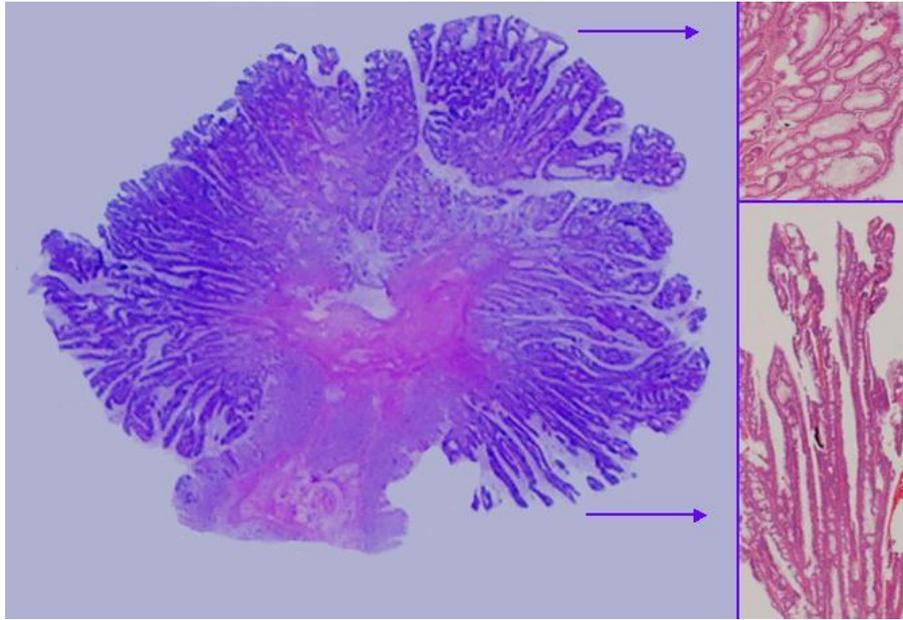


Figure 3. A tubulovillous adenoma (H & E whole mount view). Insets: the lower box shows villous structures and the upper box shows tubular structures (H & E X4).

The patient was referred to an oncologist and the reversal of the ileostomy was planned after 6-8 weeks. The family members are also going to be screened.

Discussion

Patients with FAP and its variants have a 100% lifetime risk of one or more of the polyps developing in to an adenocarcinoma through adenoma – carcinoma sequence and they develop carcinoma earlier than in sporadic cases, usually at around 40 years¹⁰. Therefore, the late presentation with malignancy in this patient is somewhat unusual. Furthermore, the malignancy in this patient did not appear to be arising from a polyp and the luminal surface of the malignancy was flattened. The entire spectrum of adenoma from microscopic monocryptal and oligocryptal to polypoid adenomata and flat adenomata can be demonstrated in patients with FAP. Usually high grade dysplasia and subsequent invasive

malignancy is associated with larger polypoid adenomata. Infrequently flat adenomata show malignant transformation. Therefore, it is possible that this malignancy developed in a flat adenoma. Furthermore, the tumour had predominantly outward growth with only subtle mucosal changes which may have led to unrecognition with colonoscopy.

It was reported that Gardner syndrome is caused by truncating mutations of the APC gene (codons 1403 and 1578) differing from classic FAP (codons 169-1600) and attenuated FAP (amino terminal to codon 157)². However, there is evidence that patients with identical mutations may have different phenotypic expressions because of unclear reasons¹¹. The unusual features observed in this patient could be due to a variation from the typical genetic mutation. We were unable to perform the genetic testing for APC mutation in this patient.

The majority of patients with FAP and its variants have a family history, however, about 25% can present without a family history due to a new dominant mutation. In the present case, presence of an affected brother indicates inheritance of a germ line mutation. In FAP, screening of the family members and prophylactic colectomy for those who are affected are indicated. However, extracolonic manifestations such as desmoid tumors of the mesenteric and abdominal wall can develop even after colectomy¹.

The total proctocolectomy in combination with ileal pouch – anal anastomosis is the best surgical procedure for patients with FAP and its variants. This procedure has the advantage of removal of the entire large intestine mucosa, thus preventing the possible carcinogenesis and avoiding a permanent stoma¹².

There were four cases on variants (Cribriform morular and columnar variant) of Papillary Thyroid cancer and a study on Congenital hypertrophy of retinal pigment epithelium (CHRPE) in patients with FAP reported from Sri Lanka⁷⁻⁹. A study on uses of familial adenomatous polyposis registry also had been published¹⁴.

Though our patient had a positive family history (His brother had colectomy at another hospital, details were not available) he did not undergo screening. A national Polyposis Registry with a system to screen (Genetic study and Colonoscopy) the family is needed in Sri Lanka. It will allow the family members of the patients to have prophylactic colectomy before cancer sets in.

Conclusion

FAP or its variants may present at older age with late development of cancer. A polyposis registry and a family screening system is needed to improve the outcome of patients with FAP and its variants.

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