

Gardner Syndrome: A Phenotypic Variant of Familial Adenomatous Polyposis

Bagrodia A¹, Vaithiyam V^{1*}, Goyal S², Dalal A¹ and Sachdeva S¹

¹Department of Gastroenterology, GB Pant Hospital and associated Maulana Azad Medical College, New Delhi, India

²Department of Pathology, GB Pant Hospital and associated Maulana Azad Medical College, New Delhi, India

Received Date : Apr 02, 2026

Accepted Date : Aug 31, 2026

Published Date : Sep 07, 2026

***Corresponding author:** Venkatesh Vaithiyam, Department of Gastroenterology, GB Pant Hospital and associated Maulana Azad Medical College, New Delhi, 110002, India, Tel: +91-9717039754; E-mail: venkateshvaithiyam172@gmail.com

Citation: Bagrodia A, Vaithiyam V, Goyal S, Dalal A, Sachdeva S. Gardner Syndrome: A Phenotypic Variant of Familial Adenomatous Polyposis. Clin Insight Rep J Glob Med Cases. 2026;1(2):57-60.

Copyright: © 2026 Bagrodia A. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Gardner syndrome is a phenotypic variant of Familial Adenomatous Polyposis (FAP), characterized by gastrointestinal polyposis and various extracolonic features. Gardner syndrome exhibits significant variability in extraintestinal features, often leading to under-diagnosis. Diagnosis involves recognizing the clinical constellation of features, supported by genetic testing. We present a case of a 40-year-old man with a history of abdominal pain, bloody diarrhea, and subcutaneous nodules with a family history of malignancy-related deaths in first- and second-degree relatives. Endoscopic evaluation revealed multiple polyps in the stomach, duodenum, and colon, with a large rectal polyp. Genetic testing identified a pathogenic variant in the APC gene, consistent with Gardner syndrome, and the patient underwent total proctocolectomy. The management of Gardner syndrome focuses on cancer prevention, surveillance, and treatment of extracolonic manifestations, with prophylactic colectomy considered when the polyp burden becomes unmanageable, high-grade dysplasia is detected, or colorectal cancer is suspected.

Keywords: Colonic polyps; Epidermoid cyst; Familial adenomatous polyposis; Dysplasia; Proctocolectomy

Case Summary

A 40-year-old man presented with a history of abdominal pain and bloody diarrhea for the past eight months. The patient also complained of urgency, tenesmus, and a sensation of incomplete evacuation. There was no history of weight loss, anorexia, joint pain, rashes, or oral ulceration. He also reported painless, gradually enlarging nodular swelling on both arms for the past two years. The family history included deaths due to malignancy in both first- and second-degree relatives of the patient. Physical examination revealed multiple subcutaneous nodules that were firm, non-tender, non-fluctuant, and fixed to the overlying dermis, with the largest measuring 1 cm to 1.5 cm on the right shoulder (Figure 1A). On per rectal examination, a mass with mucous staining was noted. Laboratory evaluation showed a hemoglobin level of 10.2 g/dL and a platelet count of $5 \times 10^5/\mu\text{L}$, with normal hepatic and renal function tests. Peripheral smear showed microcytic hypochromic red blood cells with anisopoikilocytosis, and low serum iron and ferritin levels, suggestive of iron deficiency anemia. Based on the per rectal findings, lower gastrointestinal endoscopy was performed, which revealed a large rectal polyp (Figure 1C, 1D) and multiple diminutive colonic

polyps. Upper gastrointestinal endoscopy revealed numerous diminutive polyps in the stomach and duodenum (Figure 1B). Contrast-enhanced computed tomography revealed a large sessile polyp in the rectum and no polyps in the small intestine (Figure 1E). Fine-needle aspiration of the right shoulder lesion suggested an epidermoid cyst (Figure 1G). Histopathological examination of the rectal polyp revealed a tubulovillous adenoma with high-grade dysplasia (Figure 1H) and low-grade dysplasia in the gastric polyps. A detailed three-generation family history revealed a significant history of malignancy on the maternal side. The patient is the only child of his parents; his father is alive and has no known history of malignancy, whereas his mother had a brain tumor and died at the age of 45 years. A maternal uncle was diagnosed with colorectal cancer at the age of 38 years and died at the age of 40 years. The maternal grandfather also reportedly died from a brain tumor, while the maternal grandmother had no known history of malignancy. The patient has two daughters, aged 13 and 15 years, who have not yet undergone genetic or endoscopic screening and have been advised to undergo evaluation and appropriate screening at our hospital in view of the patient's newly diagnosed APC-associated

polyposis syndrome. The family history is illustrated in a three-generation pedigree (Figure 2). Based on these findings, we suspected a familial adenomatous polyposis variant. Whole-exome sequencing identified a heterozygous single-base-pair deletion in exon 16 of the APC gene (transcript NM_000038.6), designated c.3479del, resulting in a frameshift and premature termination of the protein (p.(Thr1160LysfsTer5)). The variant is likely pathogenic and associated with an autosomal dominant predisposition to Gardner syndrome. These findings were consistent with the pathogenic variants associated with Gardner syndrome. He underwent total proctocolectomy for rectal high-grade dysplastic polyps (Figure 1F) with symptomatic improvement and regular follow-up.

In view of extensive colorectal polyposis with a large rectal lesion demonstrating high-grade dysplasia and radiological suspicion of malignancy, the patient underwent staging laparoscopy followed by open total proctocolectomy with ileal Pouch-Anal Anastomosis (IPAA) as a single-stage procedure. Intraoperatively, no hepatic, peritoneal, omental, or pelvic metastatic deposits were identified. Multiple sessile and pedunculated polyps were diffusely distributed throughout the colon and rectum, with the largest rectal lesion measuring approximately 8 cm × 5 cm. A 15-cm J-pouch was constructed from the terminal ileum, and IPAA was performed using a 31-mm circular stapler; intraoperative methylene-blue leak testing was negative.

Final histopathological examination of the total proctocolectomy specimen demonstrated more than 100 adenomatous polyps throughout the colon and a large 8 cm × 6 cm × 3 cm rectal ulceroproliferative lesion. The lesion was predominantly villous in architecture and showed areas of high-grade dysplasia with invasion into the muscularis propria. It was classified as a well-differentiated adenocarcinoma (G1), pT2N0 according to AJCC 8th edition. All margins of the main specimen were free of invasive tumor, with no lymphovascular or perineural invasion identified and no regional lymph-node involvement. Additional sampled polyps showed villous/tubular adenomas with focal high- or low-grade dysplasia.

Following definitive colorectal surgery, the patient was enrolled in a regular gastroenterology follow-up for the surveillance of gastrointestinal and extracolonic manifestations of APC-associated polyposis. Given the presence of gastric and duodenal polyps at the initial evaluation, continued upper gastrointestinal endoscopic surveillance was planned. Surveillance also targets clinically relevant extracolonic manifestations of Gardner syndrome, with further evaluation guided by clinical findings. The importance of lifelong surveillance was discussed with the patient, given the hereditary nature of this condition.

In view of the autosomal dominant inheritance of APC-associated polyposis and the identification of a heterozygous likely pathogenic APC variant in the proband, genetic counselling and cascade testing were recommended for the patient's first-degree relatives. The patient's two daughters, aged 13 and 15 years, had not undergone genetic or endoscopic screening and were called for evaluation at our institution. Their genetic status remains undetermined pending appropriate testing.

Discussion

Gardner syndrome is a phenotypic variation of the Familial Adenomatous Polyposis (FAP) spectrum, characterized by gastrointestinal polyposis, osteomas, epidermoid cysts, soft tissue tumors, and various extracolonic features [1]. The onset of colorectal adenomatous polyposis usually occurs during adolescence, with 95% of individuals developing polyps by the age of 35 years.

If left untreated, classic FAP generally progresses to colorectal cancer by the age of 39 years [2]. Significant variability in extraintestinal features often leads to underdiagnosis, especially in patients who initially present with dermatological or maxillofacial symptoms before the onset of intestinal polyposis. Mandibular osteomas are characteristic features that may serve as early markers for extra-gastrointestinal manifestations of FAP. Cutaneous manifestations may include epidermoid cysts, fibromas, lipomas, and pilomatricomas, with epidermoid cysts being the most common dermatological feature [3]. Dental anomalies, including supernumerary teeth, odontomas, and

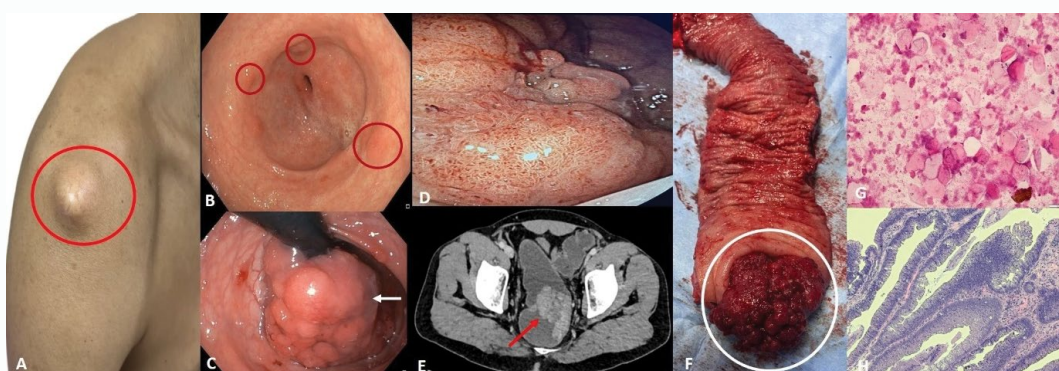
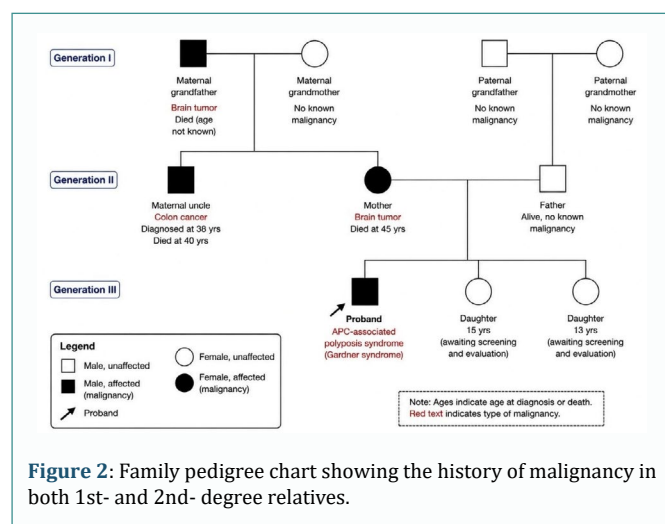


Figure 1: (A): Clinical photograph showing a firm, non-tender, non-fluctuant swelling measuring 1.5 cm, fixed to the overlying dermis on the right shoulder; (B): Upper gastrointestinal endoscopy revealing multiple nodules in the antrum of the stomach (red circle); (C and D): Lower gastrointestinal endoscopy showing a large rectal polyp (white arrow in C); (E): Contrast-enhanced computed tomography demonstrating a large endoluminal sessile polypoid lesion arising from the anterior and posterior walls of the rectum (red arrow); (F): Gross resected specimen of total proctocolectomy with a large rectal polyp (white circle); (G): Cytology smears from the shoulder swelling are cellular and show sheets of anucleated squamous cells suggestive of an epidermal inclusion cyst (20x); (H): Histopathological examination of rectal polyps reveals a tubulovillous adenoma with features of high-grade dysplasia, including loss of mucin, loss of nuclear polarity, nuclear stratification, and hyperchromasia, without any invasion.



impacted teeth, are common. The neoplastic spectrum associated with Gardner syndrome includes desmoid tumors, thyroid carcinoma, hepatoblastoma, adrenal adenomas, Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE), and central nervous system tumors, particularly medulloblastoma [4]. Diagnosis involves recognition of the clinical constellation of gastrointestinal and extracolonic features, supported by genetic testing. The identification of a heterozygous pathogenic APC variant remains the cornerstone of FAP diagnosis. Endoscopic evaluation is essential for characterizing the burden of colorectal and upper gastrointestinal polyps and assessing dysplasia, thereby guiding management. Detailed dermatological, dental, ophthalmological, and soft tissue assessments are critical for identifying extraintestinal markers. Management focuses on cancer prevention, surveillance, and treatment of extracolonic manifestations. Prophylactic colectomy is considered when the polyp burden becomes unmanageable, high-grade dysplasia is detected, or colorectal cancer is suspected [5].

The identified APC variant, NM_000038.6:c.3479del; p.(Thr1160LysfsTer5), is a heterozygous frameshift variant in exon 16 that results in premature truncation of the APC. The variant lies within the APC 15-residue motif region, which contributes to β -catenin binding and regulation of the Wnt/ β -catenin signaling pathway. The predicted loss of normal APC function provides a molecular basis for the development of adenomatous polyposis in this patient.

The present case also has important diagnostic and therapeutic implications. Although Gardner syndrome is well established within the APC-associated familial adenomatous polyposis spectrum, its extracolonic manifestations are variable and may precede or accompany gastrointestinal disease. In our patient, the presence of multiple gastrointestinal polyps, an epidermoid cyst, and a significant maternal history of malignancy provided important clinical clues to an inherited polyposis syndrome. Subsequent identification of a likely pathogenic heterozygous APC variant confirmed the molecular basis of the suspected APC-associated polyposis phenotype. This emphasizes the importance of integrating dermatological findings and detailed family history with endoscopic and histopathological findings, rather than considering these manifestations in isolation.

The colorectal phenotype in this patient was clinically significant, with a large rectal tubulovillous adenoma exhibiting high-grade dysplasia. High-grade dysplasia is an important indication for definitive colorectal surgery in patients with FAP, particularly when associated with extensive or difficult-to-control polyposis. Current guidelines recommend individualized surgical management based on polyp burden, distribution, rectal involvement, symptoms, and histological risk. Thus, the decision to perform total proctocolectomy in this patient was driven by a combination of extensive colorectal disease and high-grade dysplasia rather than by the genetic diagnosis alone.

The diagnosis also has implications beyond the index patient because APC-associated polyposis is inherited in an autosomal dominant manner. Therefore, first-degree relatives require genetic counselling and appropriate cascade testing. Current recommendations support early colorectal surveillance in individuals with confirmed APC-associated FAP, generally beginning during early adolescence, with the exact timing and interval individualized according to genotype and phenotype. This is particularly relevant for our patient, whose two daughters, aged 13 and 15 years, are awaiting evaluation.

The principal clinical lesson from this case is that Gardner syndrome should be considered when extensive gastrointestinal adenomatous polyposis is associated with extracolonic manifestations and a suggestive family history. Importantly, genotype-phenotype correlations in APC-associated polyposis are not absolute, and considerable inter- and intrafamilial variability in extracolonic manifestations has been reported. Therefore, this case illustrates the clinical expression of an APC-truncating variant rather than establishing a specific causal relationship between this variant and each extracolonic manifestation. Recognizing the syndrome enables appropriate definitive management of the index patient while also providing an opportunity for genetic counseling, cascade testing, and early surveillance of at-risk family members.

Authors' Contributions

Amit Bagrodia, Venkatesh Vaithiyam and Sanjeev Sachdeva - Patient management and care.

Venkatesh Vaithiyam, Ashok Dalal and Amit Bagrodia - Original manuscript writing and Conceptualization

Venkatesh Vaithiyam, Surbhi Goyal and Sanjeev Sachdeva - Supervision and review of the manuscript

Statement and Declarations

Informed written consent was obtained from the patient for publication.

Data Availability Statement

All data related to this article in the Department of Gastroenterology, GIPMER will be shared upon reasonable request from the corresponding author.

References

1. Groen EJ, Roos A, Muntinghe FL, Enting RH, De Vries J, Kleibeuker JH, et al. Extra-intestinal manifestations of familial adenomatous polyposis. *Ann Surg Oncol*. 2008;15(9):2439-50.

2. Half E, Bercovich D, Rozen P. Familial adenomatous polyposis. *Orphanet J Rare Dis.* 2009;4(1):22.
3. Juhn E, Khachemoune A. Gardner syndrome: Skin manifestations, differential diagnosis and management. *Am J Clin Dermatol.* 2010;11(2):117-22.
4. Butler J, Healy C, Toner M, Flint S. Gardner syndrome-review and report of a case. *Oral Oncol Extra.* 2005;41(5):89-92.
5. Sinha A, Karstensen JG, Liska D. Surgical management of the colorectum in FAP: Tailored approaches for optimal outcomes. *Fam Cancer.* 2025;24(4):69.