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The Incidental Diagnosis: Familial Adenomatous Polyposis Unmasked by CT in a Young Male Presenting with Chronic, Refractory Anemia

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ABSTRACT

Background: Familial adenomatous polyposis (FAP) is an autosomal dominant disorder characterized by early-onset colorectal adenomatosis and a near-absolute risk of malignancy. Young patients often present with nonspecific symptoms like chronic anemia, leading to diagnostic delays.

Case Presentation: We report a 32-year-old male with no significant family history who presented with a 12-month history of severe, symptomatic iron-deficiency anemia (Hb nadir 4.9 g/dL), temporarily responsive to intravenous iron. Associated symptoms included fatigue, hematochezia, weight loss, and palpable abdominal masses. A contrast-enhanced computed tomography (CT) scan, obtained during the evaluation of severe anemia, revealed highly suggestive findings of innumerable colonic polyps. Subsequent colonoscopy revealed the classic phenotype of extensive polyposis, and biopsy confirmed tubular adenomas with low-grade dysplasia. Genetic testing identified a pathogenic APC variant (c.4391_4394del). He underwent total prophylactic colectomy with ileal pouch-anal anastomosis (IPAA).

Management and Outcome: Postoperatively, high-output diarrhea was managed with loperamide and cholestyramine. At 6-month follow-up, his anemia had completely resolved (Hb 14.8 g/dL).

Conclusion: This case underscores CT's role in suggesting FAP in cases of refractory anemia, prompting definitive endoscopic and genetic diagnosis and life-saving surgical intervention. Unexplained iron-deficiency anemia in young adults warrants thorough investigation to identify underlying polyposis syndromes.

INTRODUCTION

Familial adenomatous polyposis (FAP) is a hereditary cancer syndrome caused by germline mutations in the adenomatous polyposis coli (APC) gene on chromosome 5q21 [1]. It accounts for less than 1% of all colorectal cancers (CRC) but carries a near 100% lifetime risk of CRC if untreated, typically manifesting by the fourth decade [2,3]. The classic phenotype involves the development of hundreds to thousands of colorectal adenomas. Presenting symptoms are often subtle and nonspecific, including rectal bleeding, unexplained iron-deficiency anemia, abdominal pain, diarrhea, or unintentional weight loss [4,5]. Up to 25% of cases arise from de novo mutations,

presenting without a family history and posing a significant diagnostic challenge [6]. While colonoscopy remains the gold standard for diagnosis and surveillance, cross-sectional imaging such as computed tomography (CT) is increasingly the first investigation to suggest extensive polyposis when evaluating abdominal pain or unexplained anemia [7,8]. We present a case in which CT imaging was instrumental in suggesting the diagnosis of FAP, which was then confirmed by colonoscopy and genetic testing in a young man with profound, chronic anemia refractory to iron supplementation, highlighting a critical diagnostic pathway.

CASE DESCRIPTION

Clinical History and Examination

A 32-year-old male presented to his primary care physician with a 12-month history of progressive fatigue, exertional dyspnea, dizziness, palpitations, and intermittent episodes of bright red blood per rectum. He reported an approximate 8 kg weight loss over this period and had noted gradually enlarging, painless abdominal masses. He denied fever, night sweats, or significant changes in bowel habits aside from the hematochezia. There was no known family history of colon cancer, polyps, or other hereditary cancer syndromes.

The patient had been managed for severe iron-deficiency anemia over the preceding 6-12 months. His lowest recorded hemoglobin was 4.9 g/dL. He received multiple units of packed red blood cells and both oral ferrous sulfate and intravenous iron sucrose, which provided transient symptomatic and hematologic improvement, but anemia invariably recurred.

On presentation, his vital signs were significant for tachycardia (108 bpm) with a blood pressure of 110/70 mmHg. Packed red blood cell transfusions were administered based on institutional protocol for symptomatic anemia (typically for hemoglobin <7-8 g/dL) [13].

Notable clinical signs on examination included:

General: Marked pallor of conjunctivae and palmar creases.

Abdominal: Palpable, firm, non-tender masses in the periumbilical region and right flank. No hepatosplenomegaly or ascites.

Digital Rectal Examination: Bright red blood on the glove; no palpable rectal masses.

Other Systems: No lymphadenopathy, mucocutaneous pigmentation, or thyromegaly.

Diagnostic Workup Rationale

Despite the localizing signs of hematochezia and a positive fecal occult blood test, the initial evaluation prioritized a rapid, non-invasive assessment due to the patient's profound symptomatic anemia and palpable abdominal masses. A contrast-enhanced CT scan was obtained to evaluate for an overt mass, significant bowel pathology, or extra-intestinal sources of bleeding before endoscopy [7, 13].

Laboratory Investigations

Initial laboratory workup confirmed profound microcytic (mean corpuscular volume: 59 fL), hypochromic (mean corpuscular hemoglobin: 15.2 pg) anemia (hemoglobin: 4.9 g/dL) with iron deficiency (serum ferritin: 8 ng/mL) (Supplemental Table 1). Notably, inflammatory markers were not elevated. The fecal occult blood test was strongly positive.

Imaging and Histopathological Findings

A contrast-enhanced CT scan of the abdomen and pelvis (portal venous phase) revealed highly suggestive findings of innumerable intraluminal polypoidal lesions carpeting the entire colon,

with specific larger polyps noted in the descending colon (2.4 cm) and hepatic flexure (6 mm), respectively (Figure 1). No metastatic lesions or desmoid tumors were identified.

Colonoscopic Correlation: A confirmatory colonoscopy revealed innumerable sessile and semi-pedunculated polyps (5-15 mm) carpeting the entire colon, consistent with the CT findings (Figure 2). The bowel preparation was adequate (Boston Bowel Preparation Scale score: 6) [22]. Key endoscopic findings are summarized in Figure 2. Selected polyps were resected for histopathological diagnosis.

Histopathological Correlation: Histopathological examination of the retrieved specimens was diagnostic. The analysis revealed multiple tubular adenomas with low-grade dysplasia across all sampled sites. Critically, no high-grade dysplasia or adenocarcinoma was identified. The detailed findings are presented in Table 2.

Genetic Testing

Based on the suggestive radiological and definitive histopathological findings, a clinical diagnosis of a polyposis syndrome, most likely FAP, was made. The patient was referred for genetic counseling and testing. A next-generation sequencing panel identified a heterozygous pathogenic variant in the APC gene: c.4391_4394del (p.Glu1464Valfs*8) (Supplemental Figure 1), confirming the diagnosis of classic FAP. All other genes on the panel were negative for reportable variants.

Management and Postoperative Course

Given the confirmed diagnosis and high polyp burden, the patient underwent a total prophylactic colectomy with ileal pouch-anal anastomosis (IPAA). His immediate postoperative course was uncomplicated.

Postoperative Course & Diarrhea Management:

By postoperative week 2, he developed high-frequency, watery diarrhea (6-8 episodes/day), consistent with functional high-output diarrhea common after IPAA. Symptomatic management was initiated with a stepwise approach [10,11]:

First-line treatment: Loperamide (4 mg initially, then 2 mg after each loose stool, maximum 16 mg/day) and dietary modification.

Second-line: After one week with a partial response, cholestyramine (4 g once daily, titrated to 4 g twice daily) was added for suspected bile acid malabsorption.

Supportive Care: Adequate fluid and salt intake was emphasized.

Follow-up and Outcomes

The patient was followed consistently for 6 months. His diarrhea was well-controlled on loperamide 2 mg twice daily and cholestyramine 4 g once daily. Repeat laboratory investigations showed complete resolution of his iron-deficiency anemia (Supplemental Table 3), confirming the colon as the source of chronic blood loss.

In accordance with guideline-based management for FAP [5, 21], he was referred for esophagogastroduodenoscopy (EGD) to screen for duodenal/ampullary polyps and to a clinical geneticist for family cascade testing. A structured surveillance plan was established, including annual EGD with side-viewing examination, annual pouchoscopy, and consideration of an annual thyroid ultrasound [5, 21, 24].

DISCUSSION

This case exemplifies a classic yet diagnostically delayed presentation of FAP, where cross-sectional imaging served as a critical

catalyst. The patient's year-long history of severe, transfusion- and iron-dependent anemia is a paramount teaching point. Iron-deficiency anemia in a young male, after excluding common causes, mandates exhaustive investigation for occult gastrointestinal bleeding [13]. The transient response to IV iron should not provide false reassurance but rather intensify the search for a persistent source [14].

The CT finding of "innumerable colonic polyps" is highly suggestive of polyposis syndromes and should immediately redirect the diagnostic workup to definitive colonoscopy and a hereditary cancer evaluation [7,8]. In this case, the colonoscopy (Figure 3) provided both visual confirmation of the polyposis phenotype and the tissue samples necessary for histopathological diagnosis, creating an unambiguous bridge from radiographic suspicion to genetic confirmation. While extra-colonic manifestations were absent here, their presence can further support the diagnosis [15].

Genetic testing with a multi-gene panel is the standard for confirmation and differential diagnosis, ruling out other polyposis syndromes [16,17]. The identified APC variant (c.4391_4394del) is a known pathogenic mutation associated with a classic, severe FAP phenotype [18].

Prophylactic surgery remains the definitive treatment. IPAA is preferred for rectal cancer prevention and quality of life in young patients [19]. Postoperative diarrhea is a common challenge, often due to bile acid malabsorption or functional adaptation. Management follows a stepped approach, starting with antimotility agents and adding bile acid sequestrants as demonstrated, reserving therapies for pouchitis for cases with confirmed endoscopic inflammation [10,11,20].

Conclusion

This report reinforces that unexplained, refractory iron-deficiency anemia in a young adult is a red flag requiring thorough investigation. Contrast-enhanced CT can be a pivotal study suggesting extensive polyposis, prompting definitive endoscopic, genetic, and surgical intervention. A systematic approach to postoperative complications ensures a good quality of life. Early diagnosis of FAP through such "incidental" radiological findings enables curative surgery, mandates family screening, and transforms a near-certain cancer trajectory into a manageable chronic condition with structured surveillance.

ARTICLE INFORMATION

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Table 1. Diagnostics and Management Timeline

Time Point	Event/Intervention	Key Findings/Outcome
Month 0	Symptom onset (fatigue, hematochezia)	
Month 6-11	Outpatient management for anemia	Multiple RBC transfusions, oral/IV iron. Transient response.
Month 12 (Presentation)	Hospital admission	Hb 4.9 g/dL, palpable abdominal masses.
Day 1	Contrast-enhanced CT Abdomen/Pelvis	Innumerable colonic polyps.
Day 3	Colonoscopy with polypectomy & biopsy	>100 polyps; histology: tubular adenomas.
Week 2	Genetic Testing Result	Pathogenic APC variant confirmed.
Week 4	Total Prophylactic Colectomy with IPAA	Uncomplicated surgery.
Post-op Week 2	Complication onset	High-frequency, watery diarrhea.
Month 6 Post-op	Follow-up	Hb normalized (14.8 g/dL). Surveillance plan initiated.

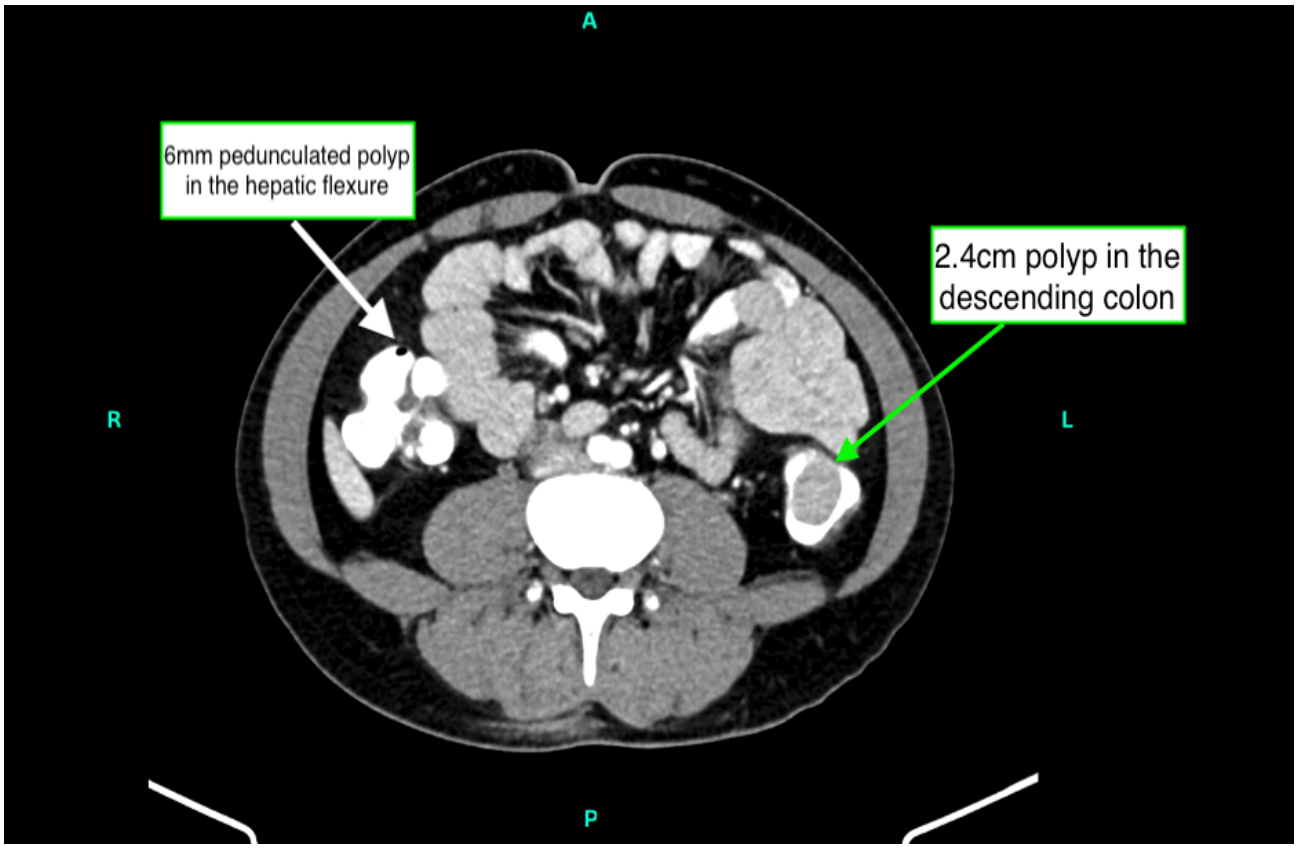

Figure 1. Contrast-enhanced axial CT abdomen demonstrating a large 2.4cm polyp in the descending colon (green arrow) and a 6mm pedunculated polyp in the hepatic flexure (white arrow).

Colon Segment	Findings	Procedure / Management
Rectum	Numerous sessile/semi-pedunculated polyps (5-10 mm). Two adjacent polyps in distal rectum (each 7-8 mm; Paris Isp).	Both polyps resected via endoscopic mucosal resection (EMR) with submucosal injection (ORISE Gel/epinephrine) and hot snare polypectomy. Prophylactic hemostasis with 4 endoclips.
Sigmoid Colon	Innumerable sessile/semi-pedunculated polyps (5-15 mm). One large pedunculated polyp (~2-3 cm; Paris Ip) on a long stalk.	The large pedunculated polyp was resected via EMR. Prophylactic hemostasis with 1 endoclip.
Descending Colon / Splenic Flexure	Numerous sessile/semi-pedunculated polyps (5-15 mm). Multiple sub-centimeter polyps.	Not removed during this diagnostic procedure.
Anal Canal	Engorged and irritated internal	Not treated.
Week 2	Genetic Testing Result	Pathogenic APC variant confirmed.
Week 4	Total Prophylactic Colectomy with IPAA	Uncomplicated surgery.
Post-op Week 2	Complication onset	High-frequency, watery diarrhea.
Month 6 Post-op	Follow-up	Hb normalized (14.8 g/dL). Surveillance plan initiated.

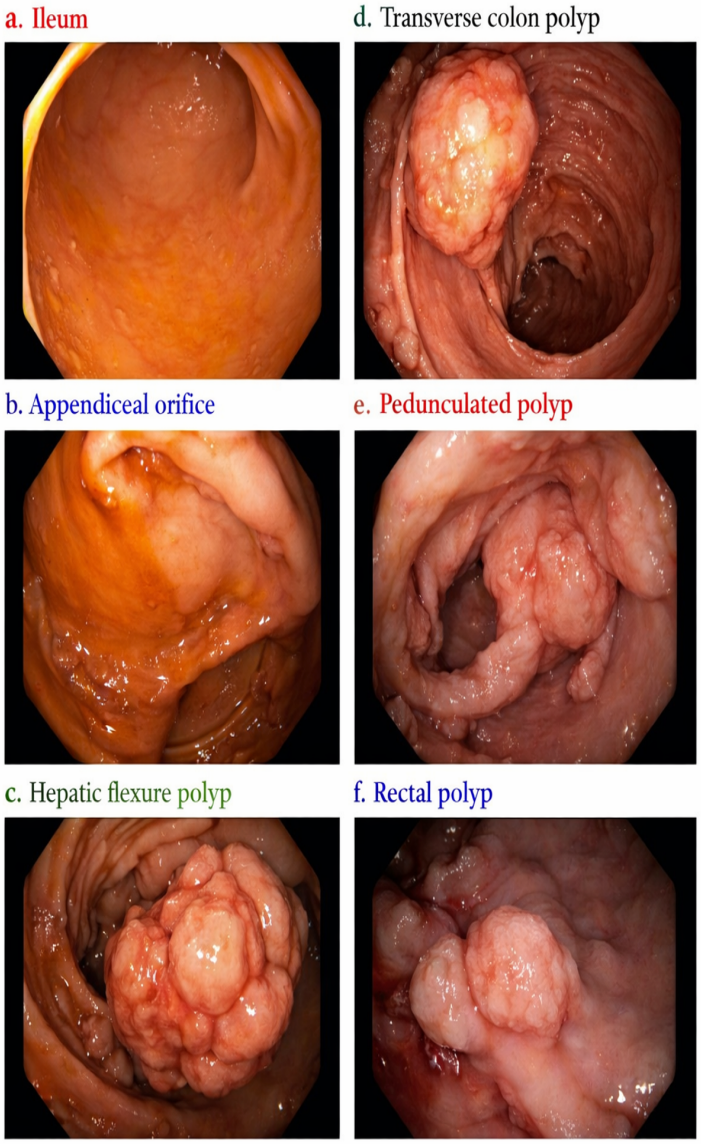

Figure 2. Endoscopic findings on diagnostic colonoscopy demonstrating diffuse colonic polyposis

(a) Terminal ileum with normal-appearing mucosa, intubated briefly for confirmation of cecal landmarks.

(b) Cecum showing the appendiceal orifice with surrounding mucosa; no focal lesion identified at this site.

(c) Hepatic flexure demonstrating a lobulated sessile polyp consistent with adenomatous morphology.

(d) Transverse colon showing a large lobulated polyp with a broad base protruding into the lumen.

(e) Sigmoid colon demonstrating a pedunculated polyp measuring approximately 2–3 cm with a long stalk and smaller attached polyps, consistent with Paris classification Ip (NICE type II); this lesion was resected endoscopically with a hot snare following submucosal injection and prophylactic clip placement.

(f) Rectum showing a sessile to semi-pedunculated polyp (approximately 7–8 mm), corresponding to Paris classification Isp (NICE type II); representative of the numerous small polyps observed in the distal colon.

Table 2. Histopathological Findings from Colonoscopic Polypectomy and Biopsies.

Specimen Location & Procedure	Gross Description	Microscopic Diagnosis	Notes
Hepatic Flexure Mass (Cold Forceps Biopsy)	Fragments from a 5-6 cm multilobulated mass.	Tubular adenoma with low-grade dysplasia.	Limited sampling. No carcinoma.
Hepatic Flexure Polyp (Hot Snare Polypectomy)	Single polypoid fragment, 3.5 cm.	Tubular adenoma with low-grade dysplasia.	Margins free of adenoma.
Proximal Sigmoid Polyp (Hot Snare Polypectomy)	Pedunculated polyp, 2.5 cm, on a long stalk.	Tubular adenoma with low-grade dysplasia.	Stalk uninvolved.
Distal Sigmoid Polyps (Hot Snare Polypectomy)	Two semi-pedunculated polyps (0.7 & 0.8 cm).	Tubular adenomas with low-grade dysplasia.	Margins free of adenoma.
Final Pathologic Impression *: Multiple colorectal tubular adenomas with low-grade dysplasia, consistent with the phenotypic diagnosis of familial adenomatous polyposis (FAP). No high-grade dysplasia or adenocarcinoma was identified.*			