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CASE REPORT
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A Rare Co-occurence of Acromegaly and Attenuated Familial Adenomatous Polyposis in a Young Patient: A Case Report and Review of Colonoscopy Screening Recommendations in Acromegaly

ABSTRACT

Acromegaly raises the incidence of colorectal polyps, leading to recommendations for colonoscopy screening in these patients. Here, we present a case of a patient diagnosed with both acromegaly and multiple colon polyps. A 29-year-old male patient was referred to our clinic due to typical symptoms of acromegaly. A macroadenoma was detected on pituitary magnetic resonance imaging. Comprehensive complication screening was performed after confirming the diagnosis of acromegaly. A colonoscopy revealed numerous polyps. Several polyps were removed, and a subsequent colonoscopy was recommended to remove the remaining polyps. The patient underwent successful transsphenoidal surgery for acromegaly. Postoperatively, he underwent a repeat colonoscopy, during which multiple polypectomies were performed. Genetic testing was performed because of a family history of multiple polyps; no clinically significant pathogenic variants were detected. Following a gastroenterological evaluation, the patient with fewer than 100 polyps and a family history was clinically diagnosed with attenuated familial adenomatous polyposis (aFAP). Attenuated familial adenomatous polyposis represents a milder phenotype of familial adenomatous polyposis characterized by 10-100 colon polyps. Genetic mutations are rare and typically manifest with a familial predisposition. Regular colonoscopic surveillance and polypectomy are recommended. The polyps were excised in this case, and ongoing follow-up colonoscopies were planned.

Keywords: Acromegaly, attenuated familial adenomatous polyposis, co-occurrence

Introduction

In acromegaly, excess growth hormone (GH) and insulin-like growth factor 1 (IGF-1) lead to various comorbidities, including cardiovascular, respiratory, metabolic, musculoskeletal, and neoplastic conditions.[1] Current guidelines recommend various screenings to detect these comorbidities.[2-4] Despite the controversial results of many studies, colorectal screening recommendations for colon cancer in patients with acromegaly are more definitive.

Herein, we present a rare co-occurrence in a young acromegaly patient clinically diagnosed with attenuated familial adenomatous polyposis (aFAP).

Case Presentation

A 29-year-old male patient was referred to Ankara Etlik City Hospital Endocrinology Clinic due to clinical features of acromegaly, including snoring, sweating, and growth in the hands and feet. Physical examination revealed acral enlargement, widening of dental gaps, and malocclusion. In the family history, his father had colon polyps but no malignancy. Biochemical tests showed no notable pathology except for dyslipidemia. The patient's IGF-1 level was measured at 1095 ng/mL (reference range: 120-257) and the GH level at 13.3 ng/mL (reference range: 0.03-2.47). The values of other anterior pituitary hormones were as follows: prolactin 34 ng/mL (reference range: 4-20), follicle-stimulating hormone (FSH) 1.81 IU/L (reference range: 1.5-12.4), luteinizing hormone (LH) 1.38 IU/L (reference range: 1.7-8.6), and total testosterone 270 ng/dL (reference range: 249-836). Other hormonal values were within normal limits. An oral glucose-GH suppression test showed no suppression of GH. The pituitary magnetic resonance imaging (MRI) detected a 15 × 14 mm macroadenoma (Figure 1). Visual fields were regular.

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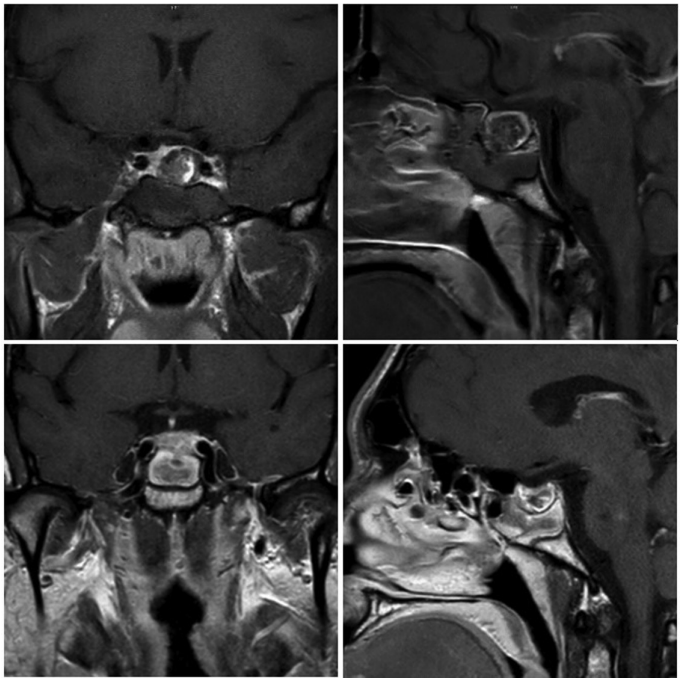


Figure 1. Pre-operative (top) and postoperative (bottom) MRI images.

Comprehensive screenings were performed for the patient diagnosed with acromegaly. Echocardiography and thyroid ultrasonography were routine. A benign liver lesion was detected in abdominal ultrasonography. Colonoscopy revealed numerous polyps, some more significant than 10 mm in size, primarily pedunculated, and a few sessile polyps were detected in the region starting from the rectum and extending to the hepatic flexure (Figure 2). Some of the polyps were excised. Due to the risk of post-polypectomy syndrome, a second session for additional polypectomy was planned. Pathology results of polyps excised from the sigmoid colon showed hyperplastic features, while those from the descending colon, splenic flexure, and rectum were reported as tubular adenomas. The second colonoscopy was postponed after pituitary surgery.

The patient underwent successful transnasal transsphenoidal pituitary surgery for pituitary macroadenoma. The pathology results were consistent with a pituitary adenoma. Immunohistochemical analysis showed positive staining for GH and PIT-1, alongside positive staining for FSH and LH, which were clinically irrelevant. No normal pituitary tissue was observed, and other immunohistochemical stains were negative. In the third postoperative month, IGF-1: 302 (120-257) ng/mL and GH: 0.22 (0.03-2.47) ng/mL were measured. Pituitary MRI at postoperative 6 months showed slight irregularities with an area reaching 8.9 × 7.9 mm, compatible with topical hemostatic agent (Figure 1). Due to the mildly elevated serum IGF-1 levels, it was considered that residual tissue of millimeter size might be present. According to guideline recommendations, low-dose cabergoline therapy was initiated for the patient as the first-line medical treatment for mild elevation in serum IGF-1 levels.[3]

During follow-up, the patient underwent a control colonoscopy and polypectomies. Pathological findings were consistent with hyperplastic polyps and tubular adenomas, and multiple polyps were excised. Due to numerous polyps and a family history of colon polyps, a genetic consultation was requested for genetic analysis. Evaluation of 247 genes associated with acromegaly, including aryl hydrocarbon receptor-interacting protein (AIP) and adenomatous polyposis coli (APC), did not reveal clinically significant pathogenic variants. With the current findings, the patient was clinically evaluated as aFAP by gastroenterology, and all polyps that could be seen with repeated colonoscopies were planned to be removed.

Informed consent was obtained from the patient. As no directly patient-identifying information is presented, no specific further consent was required. Verbal informed consent has been obtained from the patient.

MAIN POINTS

- Colonoscopy screening is recommended in patients with acromegaly due to the increased incidence of colon polyps and the potential increased risk of colorectal cancer.
- In patients with acromegaly, the recommended age for initiating colonoscopy screening, the preparation process, and the procedure's outcomes may differ from those suggested for the general population.
- The presence of numerous polyps on colonoscopy, along with family history and genetic results, should suggest the possibility of attenuated familial adenomatous polyposis.

Discussion

While debates continue regarding the increased risk of colorectal cancer in acromegaly, it is acknowledged that the frequency of colorectal polyps is increased.[5] Polyps in acromegaly patients tend to be larger, multiple, and of higher dysplasia levels compared to the general population.[5] Although high IGF-1 levels, GH levels, and disease activity have been associated with polyp development, no correlation has been found with polyp size.[6]

The first step in the development of colorectal cancer is the inactivation of the APC gene, followed by the activation of the KRAS gene and the inactivation of the tumor suppressor gene p53.[7] While GH receptor expression is low in normal colon, it is increased in colon adenomas or adenocarcinomas.[8] High GH levels are believed to suppress p53, APC, and other DNA repair pathways and apoptosis via GH receptors, thereby promoting carcinogenesis.[5] Insulin-like growth factor 1 increases vascular endothelial growth factor, which is responsible for angiogenesis and contributes to neovascularization.[9]

Therefore, guidelines recommend colonoscopy screening for acromegaly patients at diagnosis and during follow-up. While the American Association of Clinical Endocrinologists, Pituitary Society, Endocrine Society, and Acromegaly Consensus Group guidelines recommend colonoscopy at diagnosis, the British Society of Gastroenterology recommends colonoscopy after age 40.[2-4,10,11] (Figure 3). Türkiye Society of Endocrinology and Metabolism recommends colonoscopy surveillance for acromegaly patients at diagnosis or starting from age 40. Decisions should be made based on the initial colonoscopy and IGF-1 levels for follow-up colonoscopies. However, screenings in high-risk patients like ours should be tailored to the specific disease and appropriately intensified.

The increased colon length and slow intestinal motility in these patients, which are related to acromegaly or the use of somatostatin

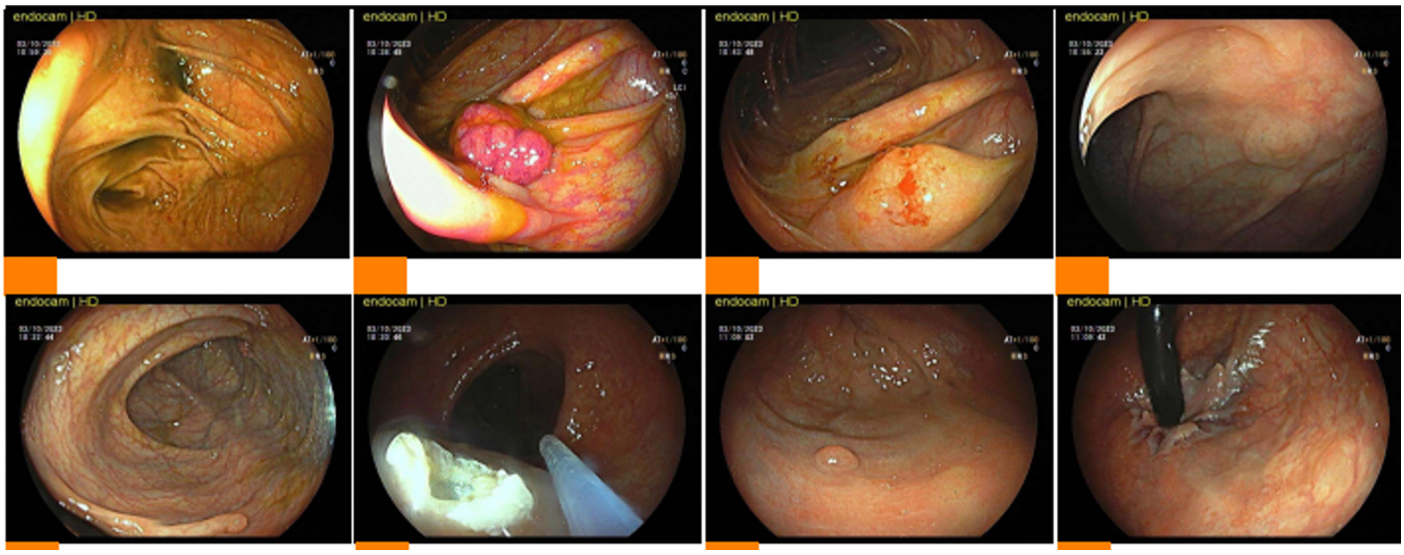
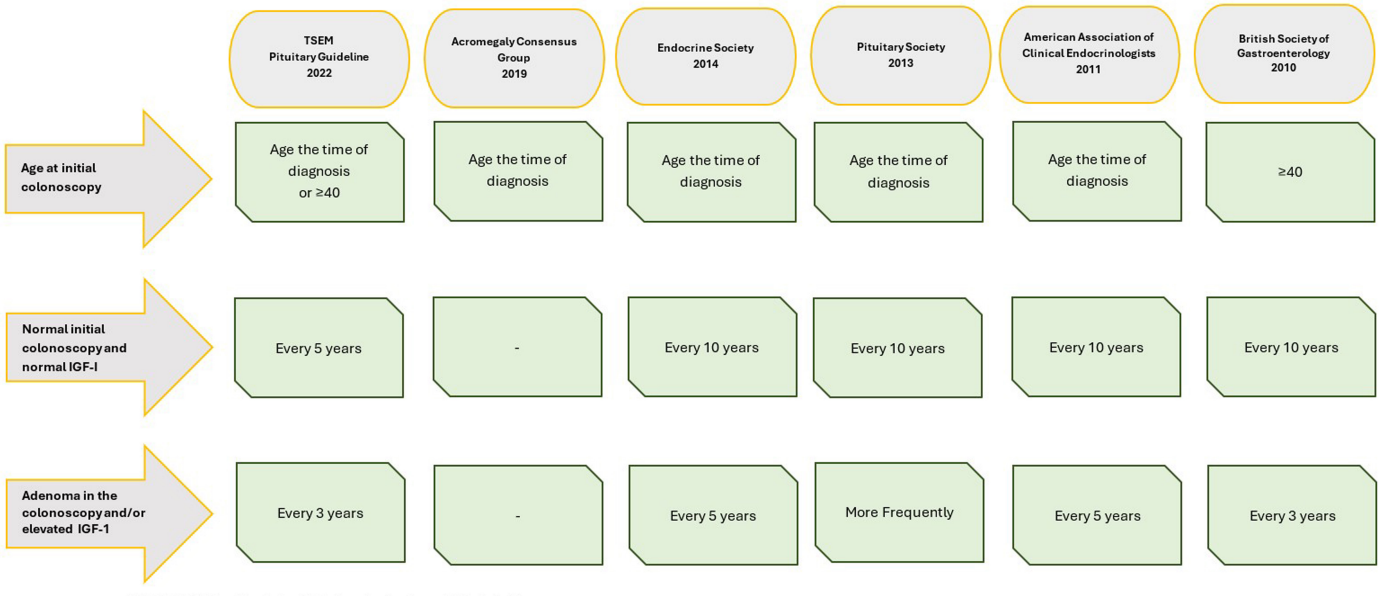


Figure 2. Multiple polyps detected during colonoscopy.

receptor ligands, necessitate careful preparation for colonoscopy.[5] Standard bowel cleansing protocols may not be sufficient. Furthermore, in patients with acromegaly, the use of oral sodium phosphate for bowel cleansing may be associated with the development of phosphate nephropathy, necessitating caution in such cases.[12] For all these reasons, an experienced gastroenterologist is essential to perform colonoscopy screening in acromegaly patients.

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited disease caused by mutations in the APC gene. It is characterized by over a hundred colorectal adenomas at a young age and a family history. If left untreated, the risk of developing colorectal cancer in FAP is nearly 100%. Attenuated familial adenomatous polyposis is a milder phenotype distinguishable from FAP, with fewer than 100 but more than 10 colon polyps.[13] Less than half of cases show mutations in APC, mutY DNA glycosylase (MUTYH), or other genes. Recent studies suggest that combining RNA sequencing with DNA analysis can enhance the identification of pathogenic variants in aFAP/FAP diagnosis.[14] In aFAP, there is usually a family history. Regular colonoscopy surveillance with polyp removal is recommended. If complete polypectomy is not possible or carcinoma is detected, surgical treatment is mandatory.[13] In our case, there was a family history; fewer than 100 polyps were detected in the colon, and most of the polyps were removed in the 2 colonoscopies performed. Regular colonoscopy surveillance was recommended for the patient. There is a case reported in the literature of a patient who was diagnosed with testicular seminoma at a young age, had numerous colon polyps detected in their 50s, and was diagnosed with acromegaly and kidney cancer at the age of 64.[15] As far as we know, this is the first reported case of acromegaly combined with aFAP in the literature.



TSEM: Türkiye Society of Endocrinology and Metabolism

Figure 3. Colonoscopy screening recommendations of current guidelines.

Conclusion

Although the recommended frequency varies across different guidelines, colonoscopy screening is advised due to the increased incidence of colon polyps and the potentially heightened risk of colorectal cancer. By presenting the rare co-occurrence in this case report, we emphasize that performing a colonoscopy at the time of diagnosis, regardless of age, seems more reasonable despite the ongoing debate about the appropriate initial age for colonoscopy in patients with acromegaly.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Informed Consent: Verbal informed consent was obtained from the patient who agreed to take part in the study.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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