

Characteristics and potential malignancy of colorectal juvenile polyps in adults: a single-center retrospective study in China

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Abstract

Background

Colorectal juvenile polyps are rare and usually considered benign in adults. Carcinogenesis or neoplastic changes are rarely mentioned in the literature. We aimed to systematically evaluate the characteristics and potential malignancy of colorectal juvenile polyps in adults.

Methods

We retrospectively reviewed the medical records of 103 adults diagnosed with colorectal juvenile polyps from 9/2007 to 5/2020 in our hospital. The characteristics, endoscopic findings, occurrence of intraepithelial neoplasia, carcinogenesis and diagnostic value of chicken skin mucosa (CSM) were analyzed.

Results

The average age of patients with juvenile polyps was 43.2 years (range, 19 to 78). A total of 101 patients (101/103, 98.1%) had a single juvenile polyp, while two had multiple polyps (107 polyps in total). Polyp sizes ranged from 0.5 to 5 cm. One (1/107, 0.9%) juvenile polyp was cancerous, and 7 (7/107, 6.5%) developed low-grade intraepithelial neoplasia. Neoplasia or cancerization was not associated with the number of polyps. A 27-year-old female had a polyp with well-differentiated adenocarcinoma in the mucosa that was 2 cm in the sigmoid colon with erosion on the surface. According to immunohistochemistry, the Ki-67 was approximately 80%. P53 was mutated with diffuse and strongly positive expression. CSM was observed beside 17 polyps, which were all located in the rectum and sigmoid colon; one polyp had low-grade intraepithelial neoplasia.

Conclusions

Colorectal juvenile polyps in adults have neoplastic potential. Neither neoplasia nor carcinogenesis was associated with the number of polyps. CSM was not a tumorigenesis marker in colorectal juvenile polyps in the distant colorectum. Colorectal juvenile polyps in adult may go through a 'low-grade intraepithelial neoplasia to high-grade intraepithelial neoplasia to carcinoma' path and should be treated and regularly followed up as adenomas.

Introduction

Juvenile polyps are a type of hamartoma. Although they are the most common type of polyps in children¹, colorectal juvenile polyps are rare in adults^{2,3}. The occurrence rate of juvenile polyps in children and adolescents is 2%, which accounts for the majority (approximately 80-90%) of polyps in pediatric patients^{1,3,4}. In adults, hyperplastic polyps and adenomas are the two most common types of polyps. Less than 1% of juvenile polyps occur in adults⁵, and there are few studies concerning juvenile polyps in adults. Juvenile polyposis syndrome (JPS) is usually characterized by multiple hamartomatous polyps

throughout the gastrointestinal tract and is considered an autosomal dominant disorder. JPS is usually accompanied by an increased risk of both colorectal and gastric cancers^{6,7}. Unlike JPS, sporadic juvenile polyps in the colon are often solitary and rarely undergo malignant transformation^{1,4,8}. However, sporadic juvenile polyps may also exhibit dysplasia^{5,9,10}. Except for research from Denmark⁵, there have been few studies about adult colorectal juvenile polyps in a large sample population, especially in the Asia-Pacific area.

Herein, a retrospective study was conducted among adult patients diagnosed with colorectal juvenile polyps in a Chinese population in a single center. Demographic characteristics, clinical symptoms, endoscopic manifestations and pathological results were analyzed. This study aimed to summarize the characteristics and evaluate the potential malignancy and carcinogenic factors of colorectal juvenile polyps in adults.

Methods

Study design

A retrospective analysis was performed on the clinical and pathological data of adult patients diagnosed with colorectal juvenile polyps admitted to our clinic from 9/2007 until 5/2020. The inclusion criteria were as follows: (1) older than 18 years; and (2) a diagnosis of colorectal juvenile polyps by pathology. The exclusion criteria were JPS, Cronkhite-Canada syndrome or other types of polyposis. Patient age at initial diagnosis (years), sex, abdominal pain, diarrhea, hematochezia, mucous in the stool and other clinical manifestations, numbers, maximum diameter (cm), position, polymorphic morphology of polyps, endoscopic features such as mucosal changes near polyps and pathological results were collected and analyzed. Chi-square tests were used to compare detection rates between groups. The expressions of MutL homolog 1 (MLH1), MutS homolog 2 (MSH2), MutS homolog 6 (MSH6) and Postmeiotic segregation increased 2 (PMS2) in the samples were tested with immunohistochemical staining with the EnVision two-step procedure. Ethical approval for the study was obtained from the Ethics Committee of Zhejiang Provincial People's Hospital.

Results

Subjects

From 9/2007 to 5/2020, a total of 103 patients with 107 juvenile polyps were included in this study. Patients were divided into two groups according to the number of polyps (1 polyp and 2-4 polyps). A total of 101 patients (98.1%) had a single juvenile polyp, while two had multiple polyps. Sixty-four patients were male, and 39 were female. The median age was 43.2 years (range, 19 to 78 years). None of the patients had a family history of polyposis. Five patients had a history of cancer. One hundred patients were treated with endoscopy. A total of 35.8% (19/53) of patients had positive fecal occult blood test results (Table 1).

Clinical manifestations

Among the 103 patients, 18 (16.8%) complained of abdominal pain, 11 (10.3%) visited doctors for diarrhea, 45 (42.1%) experienced bloody stool and 5 (4.7%) had mucous in their stool. Juvenile polyps were found by colonoscopy in 35 (32.7%) patients upon examination (Table 1).

Endoscopic features

A total of 101 patients (98.1%) had a solitary juvenile polyp, while two had three polyps. Of all 107 polyps found, most were located in the sigmoid (38, 35.5%) and rectum (35, 32.7%), while 1 (0.9%) was in the ileocecum, 10 (9.3%) in the ascending colon, 10 (9.3%) in the transverse colon, 13 (12.1%) in the descending colon, and 35 (32.7%) in the rectum. The size of the polyps ranged from 0.5 to 5.0 cm. The majority (43; 40.2%) were from 1-1.9 cm, while 34 (31.8%) were less than 1 cm, 19 (17.8%) were from 2.0-2.9 cm and 11 (10.3%) were larger than 3 cm. Eighteen (16.8%) were Paris 0-Is polyps, 39 (36.4%) were Paris 0-Isp polyps, and the other 50 (46.7%) were Paris 0-Ip, which accounted for the majority of polyps. Fifty-four (54/107, 50.5%) polyps had reddish surfaces. Chicken skin mucosa (CSM) was observed adjacent to 17 polyps, which were all located in the rectum and sigmoid colon, accounting for 23.2% (17/73) of all rectosigmoid juvenile polyps (Table 1).

Treatment

One hundred patients underwent endoscopic therapy, including thermal biopsies, loop snare techniques or endoscopic mucosal resection (EMR), and 3 underwent surgery. One patient was considered to have colon cancer before the operation based on biopsy, while the postoperative specimen was a juvenile polyp with high levels of stromal edema and focal tubular adenoma with low-grade intraepithelial neoplasia. The polyp was located in the descending colon with a maximum diameter of 5.0 cm. One patient complaining of abdominal pain and diarrhea was diagnosed with colon cancer before surgery and underwent radical surgery. The third patient was found to have three large polyps approximately 5.0 cm in diameter (Table 1).

Pathological results

One colorectal juvenile polyp had focal carcinogenesis and 7 had low-grade intraepithelial neoplasia. They were all single polyps. There were two tubular adenomas with low-grade intraepithelial neoplasia near two juvenile polyps. One was accompanied by colon cancer. The patient with focal carcinogenesis was a 27-year-old female. Her polyp, which was approximately 2.0 cm, was located in the sigmoid colon and had erosion on the surface. The immunohistochemical staining of the polyp showed a Ki-67 of approximately 80%, and p53 was mutated and showed diffuse and strongly positive expression. The expression levels of MLH1, MSH2, MSH6 and PMS2 were positive, which indicated microsatellite stability (Figures 1, 2). The immunohistochemical results of the 7 polyps with low-grade intraepithelial neoplasia showed that the average Ki-67 was approximately 40% (Figure 3). P53 was wild-type and not overexpressed. MLH1, MSH2, MSH6 and PMS2 were expressed. The Ki-67 was approximately 20%

(Figure 4) in other simple juvenile polyps, and p53 was wild-type and not overexpressed. Among the 17 polyps with CSM, 1 (5.9%, 1/17) had low-grade intraepithelial neoplasia. Six polyps with low-grade intraepithelial neoplasia and 1 with carcinogenesis were found in the left 90 polyps without CSM. The chi-square test did not show significance ($P>0.05$) (Table 1).

Discussion

This study is, to the best of our knowledge, the largest single center study on colorectal juvenile polyps in adults in the Asia-Pacific area to date. Colorectal juvenile polyps are rare in adults. The incidence of juvenile polyps in Danish adults ranges from 1:65000 to 1:40000⁵. Based on our study, the average age of onset in adults was 43.2 years. The ratio of males to females was 1.6:1. These findings were in line with those of previous reports that showed that the average age was between 25.5 and 48.9 years^{5,11}, and the male:female ratio was 0.8-1.4:1⁸.

The clinical manifestations of juvenile polyps are similar to those of other types of polyps, including abdominal pain, rectal bleeding, prolapse, and diarrhea. Juvenile polyps can occur in any part of the colon, but most in this study were located in the rectum and sigmoid colon (68.2%), which is similar to the distribution of juvenile polyps in children¹² and in previous studies in adults⁵. A total of 98.1% (101/103) of the patients had a single juvenile polyp, which was similar to the 94.9% reported by other researchers⁵. In children, 42%-75.9% had a single polyp^{12,13}. A total of 83.2% of the polyps were Paris 0-Isp/Ip according to the Paris endoscopic classification^{14,15} in our study, which is similar to previous reports¹⁶.

The size of juvenile polyps ranged from sessile nodules of a few millimeters to pedunculated lesions of up to several centimeters, as determined by endoscopy. Large polyps may be multilobulated, while small polyps are usually round and smooth. Erosion and granulation tissue hyperplasia are often observed on the surface of polyps¹⁷. Sometimes, there are small yellow particles around juvenile polyps, which are referred to as CSM¹⁸.

Histopathology is the gold standard for diagnosing juvenile polyps since the clinical symptoms and endoscopic features are not entirely typical. This condition mainly manifests as mucinous gland hyperplasia and mucous cysts of different sizes in fibrous tissues. Juvenile polyps are composed of differentiated glandular ducts. The glandular cavity is dilated to varying degrees. This is usually accompanied by interstitial hyperplasia and the infiltration of large numbers of inflammatory cells in the stroma, such as lymphocytes, plasma cells, neutrophils and eosinophils. These characteristics distinguish juvenile polyps from juvenile polyposis and Peutz-Jeghers syndrome.

Juvenile polyps are a type of hamartoma. It is generally believed that the risk is minimal^{8,19,20}, while the potential of solitary or sporadic juvenile polyps to develop into cancer is not clear. Only a few cases of carcinogenesis from solitary or sporadic juvenile polyps have been described in the literature. Intramucosal carcinoma arising within a solitary juvenile polyp was regarded as 'a wolf in sheep's clothing'^{16,21}. Other researchers^{10,22,23} have reported three cases of signet ring cell carcinoma in juvenile

polyps. In our study, one juvenile polyp with focal carcinogenesis and 7 with low-grade intraepithelial neoplasia were identified. They were all single polyps. Neither neoplasia nor carcinogenesis was associated with the number of polyps in adults, as reported in children¹³.

The polyp with focal carcinogenesis showed a higher Ki-67 and p53 expression level than the 7 polyps with low-grade intraepithelial neoplasia. These 7 polyps showed a higher Ki-67 than simple polyps. As previously reported, the expression of p53 and Ki-67 may be used as prognostic factors for adenomas. A high cell proliferation suggests more aggressive behavior. Greater expression of p53 and higher expression of Ki-67 were found in adenomas with high-grade dysplasia^{24, 25}. Other studies showed that higher cyclooxygenase-2 (COX-2) indicated a higher potential for carcinogenesis. Colorectal juvenile polyps, hamartomatous polyposis, adenoma and adenocarcinoma groups showed no difference in the expression of COX-2, which was higher than that in the normal mucosa²⁶.

Based on the results of the immunohistochemical markers mentioned above, we hypothesized that juvenile polyps may follow a 'low-grade intraepithelial neoplasia to high-grade intraepithelial neoplasia to carcinoma' pathway. In a study involving 213 pediatric patients, the researchers also found adenomatous changes, suggesting the same progression¹³. Based on these findings, the risk of carcinogenesis and route of cancerization are independent of age and the number of polyps. On the basis of previous studies and our research, we believe that even sporadic juvenile polyps might carry an inherent potential for malignancy.

CSM was first identified in 1998²⁷ and was described as specific mucosal morphologic changes adjacent to colorectal neoplasms. CSM is characterized by a pale yellow-speckled pattern of colorectal mucosa on endoscopy. Histologically, CSM is caused by a large accumulation of lipid-filled macrophages in the lamina propria. The prevalence of CSM was 30.7% (225/733) in patients with adenomas. CSM-related adenoma was mainly found in the distal colon (93.3%). Adenomas with CSM, compared to those without CSM, presented more high-grade dysplasia and carcinoma, higher expression of Ki-67, COX2 protein and survivin, and lower expression of caspase-3, which indicated the carcinogenetic progression of colorectal adenomas^{28, 29}. Hence, CSM is generally considered a tumor marker in colorectal adenomas. In contrast, since the levels of Ki-67 or p53 do not increase in juvenile polyps with CSM in children, CSM was not regarded as a marker for subsequent malignancy^{30, 31}. In our study, there was no difference in the incidence of neoplasia or tumorigenesis between polyps with or without CSM. Hence, CSM was not identified as a tumorigenesis marker of colorectal juvenile polyps as it has been in children.

Endoscopic polypectomy is the main therapy for colorectal juvenile polyps. Thermal biopsies, loop snare techniques, EMR, and even endoscopic submucosal dissection (ESD) have been proven to be safe and effective for sporadic, semipedunculated or sessile large juvenile polyps. However, for multiple or diffuse juvenile polyps, very large polyps, or polyps with suspicious malignant transformation, colectomy may be a beneficial^{32, 33}. Patients with more complete removal of juvenile polyps and improved compliance with follow-up had a reduced risk of carcinogenesis.

Conclusions

This is the largest single center study on the characteristics and potential malignancy of colorectal juvenile polyps in adults ever reported in the Asia-Pacific area. Colorectal juvenile polyps have a low incidence in adults but possess a risk of malignancy. We reported a 0.9% (1/107) incidence of cancer and a 6.5% (7/107) incidence of low-grade intraepithelial neoplasia in colorectal juvenile polyps. Juvenile polyps may follow a 'low-grade intraepithelial neoplasia to high-grade intraepithelial neoplasia to carcinoma' pathway, and neither neoplasia nor carcinogenesis was associated with the number of polyps. Unlike CSM-related adenoma, CSM was not a tumorigenesis marker of colorectal juvenile polyps in the distant colorectum. Colorectal juvenile polyps should be treated and regularly followed up.

Declarations

Ethics approval and consent to participate: Ethical approval for the study was obtained from the Ethics Committee of Zhejiang Provincial People's Hospital.

Declaration of Conflicting Interests: The authors declare that they have no conflicts of interest.

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Author contributions: JD reviewed the literature, designed the study, and drafted the paper. YHX performed the literature review and was responsible for collecting the medical data. PL and JFT reviewed the literature and analyzed the data. TSM and WYC provided the pathological results. YWC designed the study with JD and revised the manuscript. All authors gave final approval for the submission of the final version.

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Tables

Table 1. Summary of patients' condition and medical procedures

	Age, years	
Characteristic	Mean	43.2
	Range	19-78
	Gender, n	
	Male	64
	Female	39
Clinical manifestations, n	abdominal pain	18
	diarrhea	11
	bloody stool	45
	mucous stool	5
Numbers of polyps, n	Single	101
	Multiple	2
Location, n	ileocecum	1
	ascending colon	10
	transverse colon	10
	descending colon	13
	sigmoid	38
	rectum	35
Gross appearance, n	Paris 0-ls	18
	Paris 0-lsp	39
	Paris 0-lp	50
Maximum diameter(cm), n	0-0.9	34
	1-1.9	43
	2-2.9	19
	≥3	11
Chicken skin mucosa, n	with	17
	without	90

Pathological results, n	With low grade intraepithelial neoplasia	7
	With cancerization	1
Therapy, n	Endoscopic therapy	100
	Surgery	3

Figures

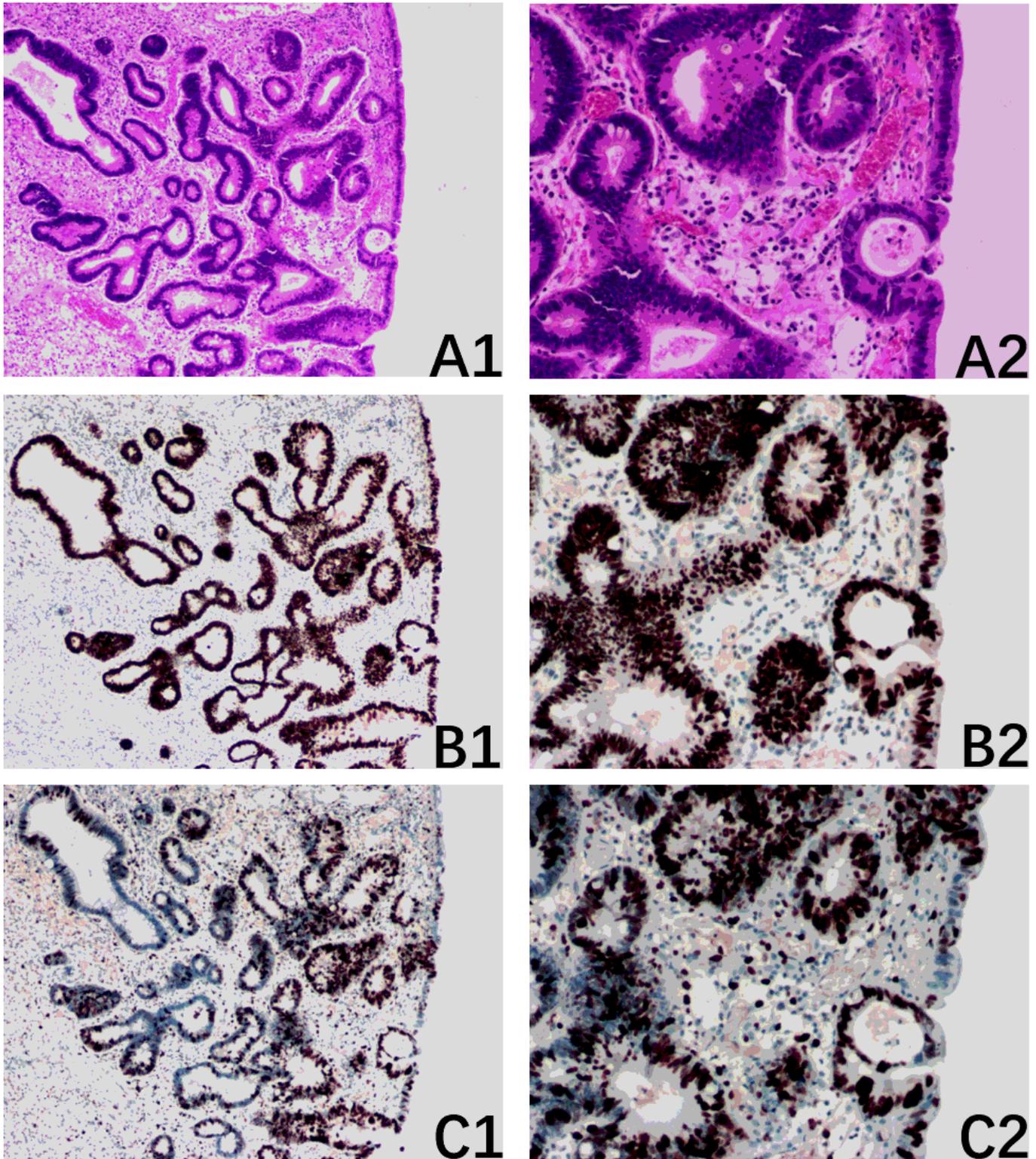


Figure 1

Juvenile polyp with carcinogenesis. A Hematoxylin and eosin staining (A1 $\times 40$; A2 $\times 100$). B Immunohistochemical staining for p53 showed p53 mutation and overexpression (B1 $\times 40$; B2 $\times 100$). C Immunohistochemical staining for Ki-67 was 80% (C1 $\times 40$; C2 $\times 100$).

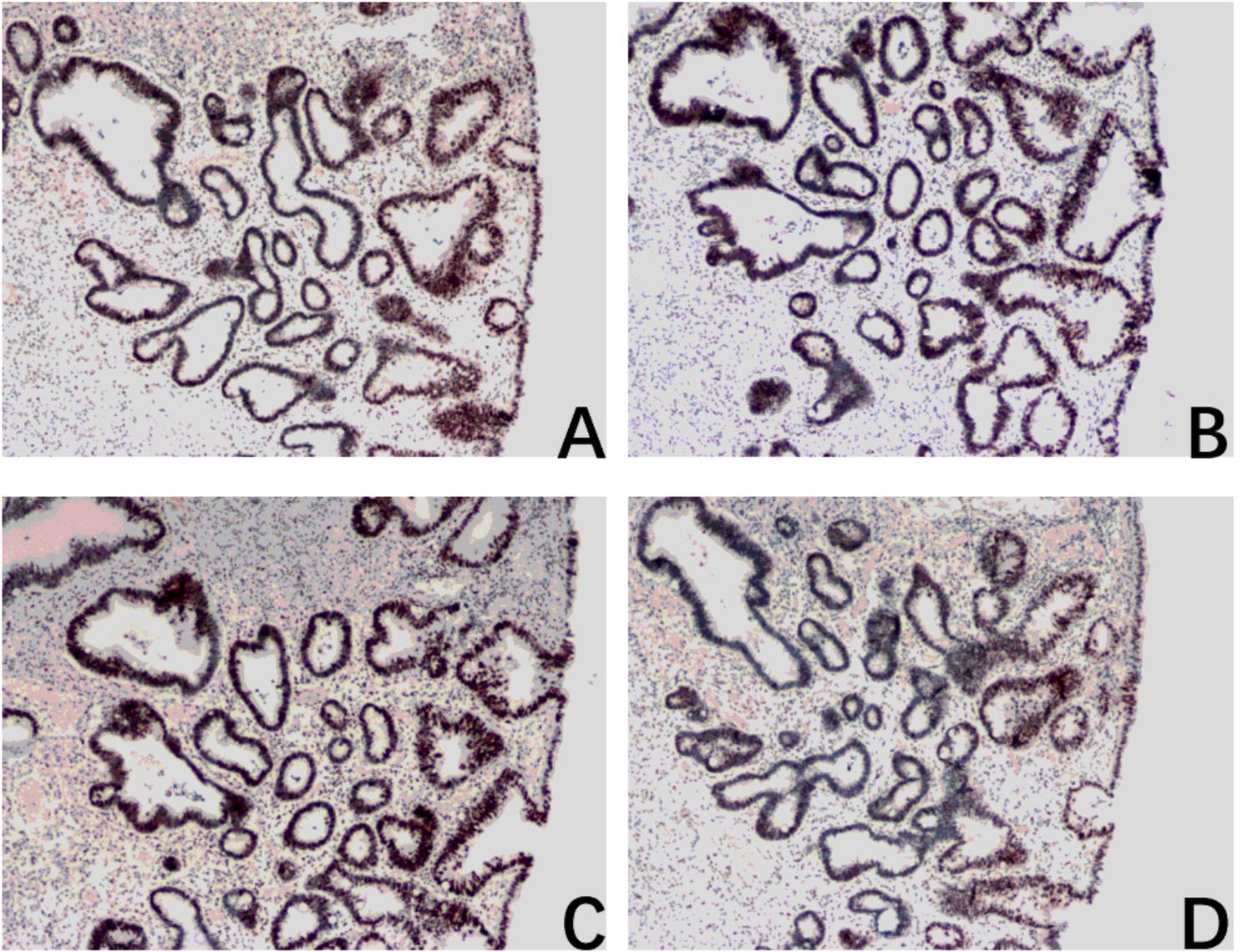


Figure 2

Juvenile polyp with carcinogenesis. Immunohistochemical staining positive for A: MLH1 ($\times 40$), B: MSH2 ($\times 40$), C: MSH6 ($\times 40$), and D: PMS2 ($\times 40$).

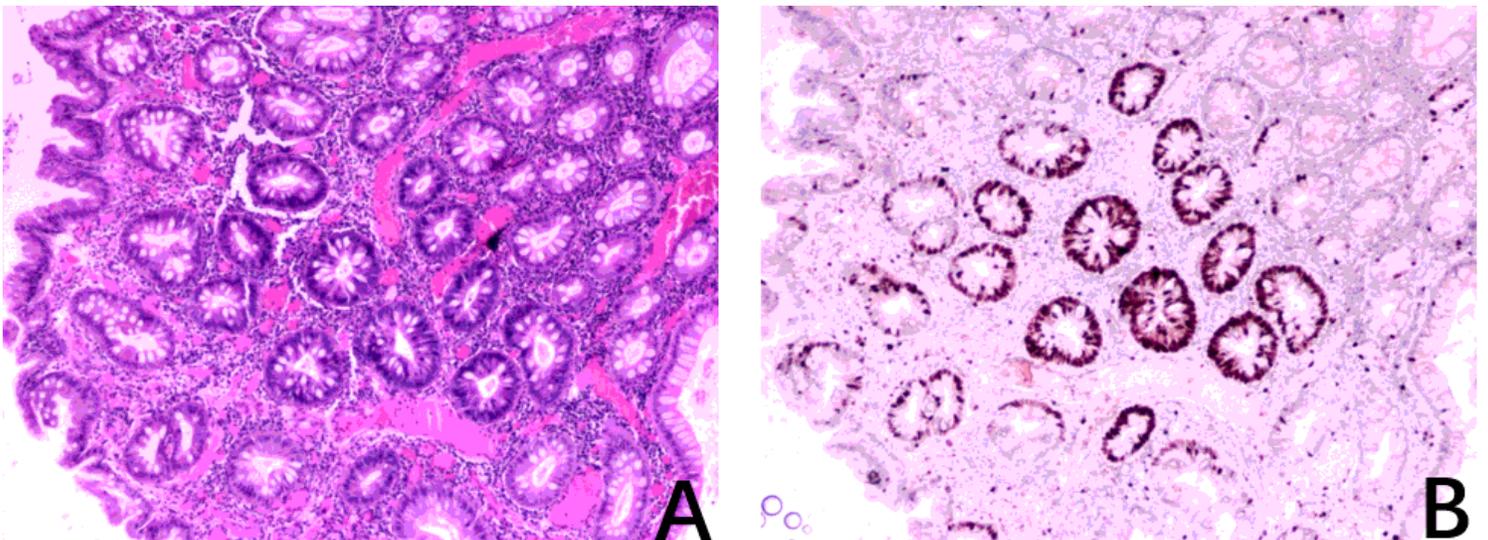


Figure 3

Juvenile polyp with low-grade intraepithelial neoplasia. A Hematoxylin and eosin staining ($\times 40$). B Immunohistochemical staining for Ki-67 was 40% ($\times 40$).

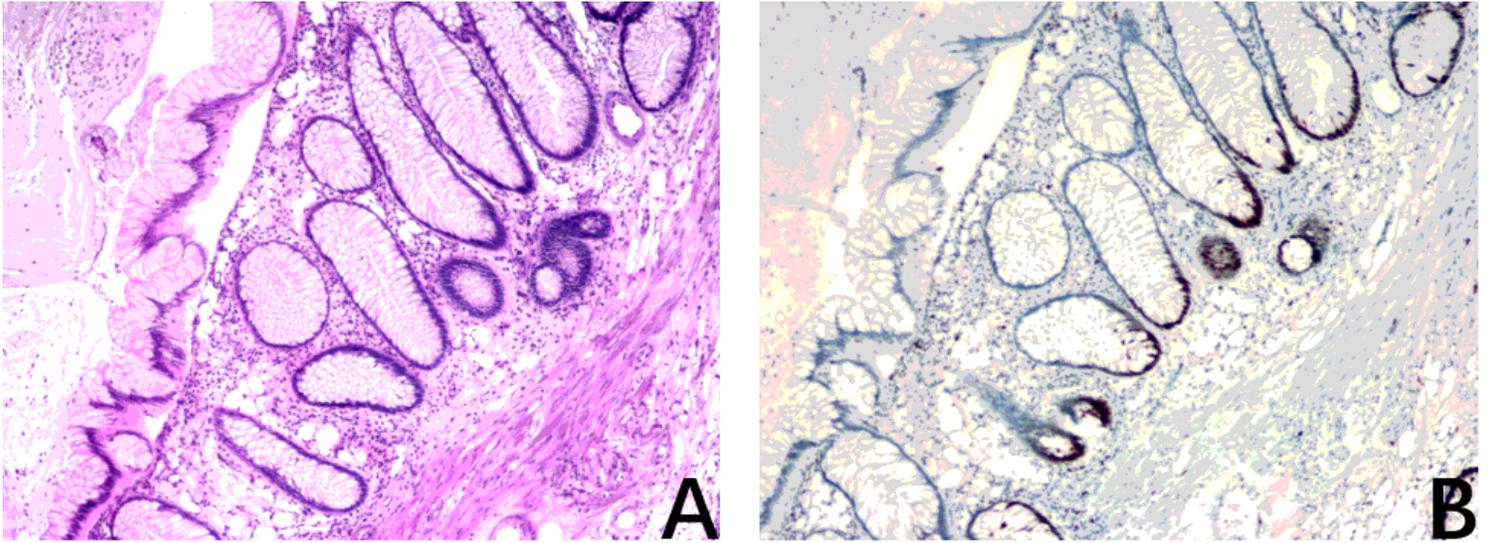


Figure 4

Simple juvenile polyp. A Hematoxylin and eosin staining ($\times 40$). B Immunohistochemical staining for Ki-67 was 20% ($\times 40$).