ACG CASE REPORTS JOURNAL

CASE REPORT | COLON

Can a Solitary Juvenile Polyp Be Regarded as a Nonmalignant Polyp?

Kumiko Fukami, MD[1], Makoto Furihata, MD, PhD[1], Shintaro Yano, MD[1], Hiroki Okawa, MD[1], Shinjiro Nishi, MD[1], Yoichi Nakatsu, MD[1], Yusuke Nomoto, MD[1], Shingo Ogiwara, MD, PhD[1], Tsuneo Kitamura, MD, PhD[1], Shigeki Tomita, MD, PhD[2], and Taro Osada, MD, PhD[1]

[1]*Department of Gastroenterology, Juntendo University Urayasu Hospital, Urayasu-shi, Chiba, Japan*
[2]*Department of Pathology, Juntendo University Urayasu Hospital, Urayasu-shi, Chiba, Japan*

ABSTRACT

Juvenile polyps (JPs) are common, developing mostly as solitary, hamartomatous lesions in the colorectum, and principally affect pediatric patients. Solitary JPs are recognized as benign, with a negligible malignant transformation rate. Primary signet ring cell carcinoma is a rare type of colorectal cancer (0.1%–2.6%) that presents mostly at an advanced stage in younger patients and affects the right-sided colon, with extensive lymphatic invasion and peritoneal dissemination, resulting in a poorer prognosis compared with conventional colorectal cancer. We report a rare case of signet ring cell carcinoma in a solitary JP treated with endoscopic mucosal resection.

INTRODUCTION

Recently, the US Multi-Society Task Force on Colorectal Cancer provided guidelines for preventing colorectal cancer (CRC).[1-3] The guidelines provided comprehensive guidance on monitoring patients with juvenile polyposis syndrome (JPS) caused by a germ line pathogenic variant of *SMAD4* or *BMPR1A*. In the guidelines, JPS is associated with a risk factor of CRC carcinogenesis, whereas solitary juvenile polyps (JPs) are generally not regarded as premalignant. One study of 78 JPs from 12 patients with JPS and 34 patients with JPs reported that dysplasia was present in 31% of the polyps from patients with JPS, but in none of the polyps from patients with JPs.[3,4] Thus, JPs has been considered not to be a precancerous condition to the present, whereas patients with JPS are at increased risk of cancer principally in the stomach and colon with a cumulative lifetime risk of CRC reaching 38.7%.[3,5] Therefore, how to manage these similar pathogenic conditions has been markedly different. We question whether gastroenterologists should regard solitary JPs as non-neoplastic and report a case that provides evidence to the contrary.

CASE REPORT

A 45-year-old man tested positive for fecal occult blood on routine screening during an annual medical checkup and underwent colonoscopy, which revealed a pedunculated lesion in the rectum, 10 mm in diameter, with erythematous changes and erosions (Figure 1). We diagnosed the lesion as a solitary JP owing to the mucosal surface pattern of a round, lobulated, hyperemic head with white patches with no abnormal vascularity or surface pattern on narrow band imaging (Figure 1). Endoscopic mucosal resection was performed. Histopathology of the resected specimens showed diffuse signet ring cell carcinoma (SRCC) at the polyp head, including multilobulation, mixed with normal elements of the existing colonic mucosa, with dilated epithelial glands filled with mucoid and proliferative connective tissue periodic acid-Schiff staining (Figure 2). The mucinous fluid in the tumor cells was immunohistochemically positive for *p53* and periodic acid-Schiff staining (Figure 2). We diagnosed rectal SRCC in situ, occurring in a solitary JP. To support the plausibility of the polyp being JP and to examine the mucous trait in SRCC, immunohistochemical staining for MUC5AC was performed. Immunohistochemical staining for MUC5AC was

ACG Case Rep J 2022;9:e00936. doi:10.14309/crj.0000000000000936. Published online: December 26, 2022

Correspondence: Kumiko Fukami, MD (kumimnpi@yahoo.co.jp).

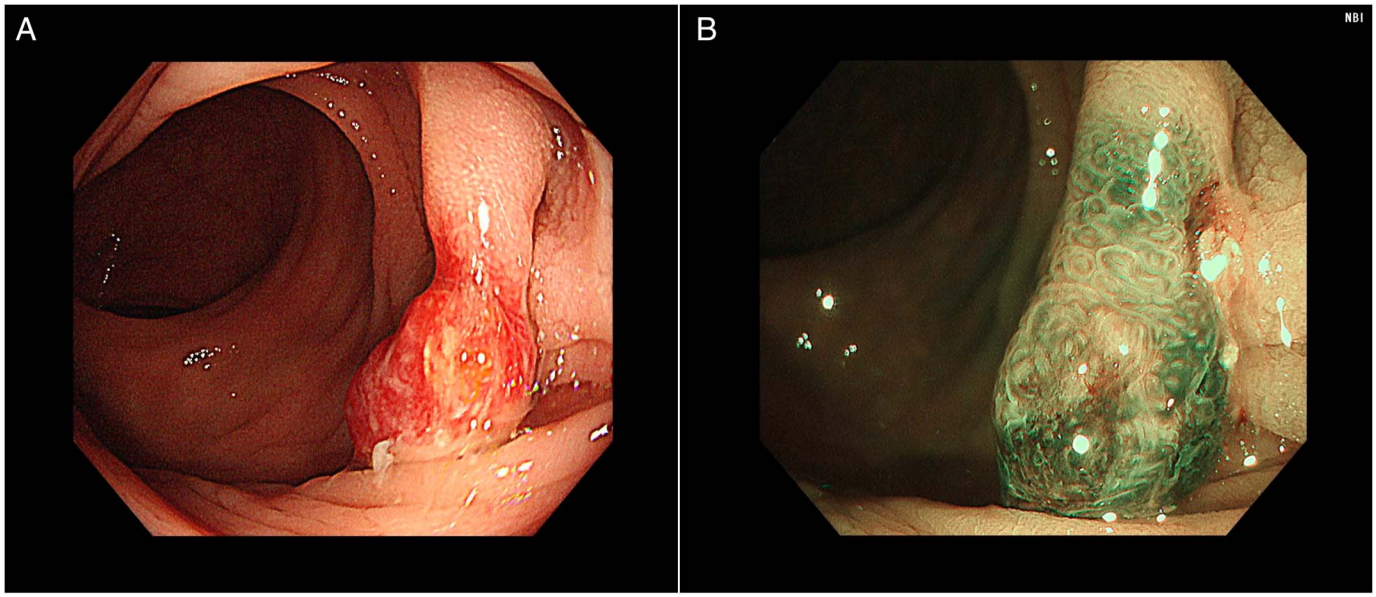

Figure 1. Colonoscopy showing a pedunculated rectal polyp measuring 10 mm in diameter. The surface of the lesion is erythematous and erosive with white patches (A). Narrow band imaging by high-definition endoscopy showing no abnormal vascularity or malignant surface pattern (B).

strongly positive in the periphery of the polyp head and positive in the cystic dilatated gland and SRCC (Figures 3 and 4). Low-grade adenoma coexisted at the polyp head (Figure 5). No recurrence was seen on colonoscopy at the 12-month follow-up.

DISCUSSION

The term JP was first coined by Horrilleno et al in 1957, and Morson revealed them to be hamartomas.[6–8] Solitary JPs are commonly perceived to have a low risk of recurrence and negligible malignant potential. Contrariwise, Ibrahimi et al

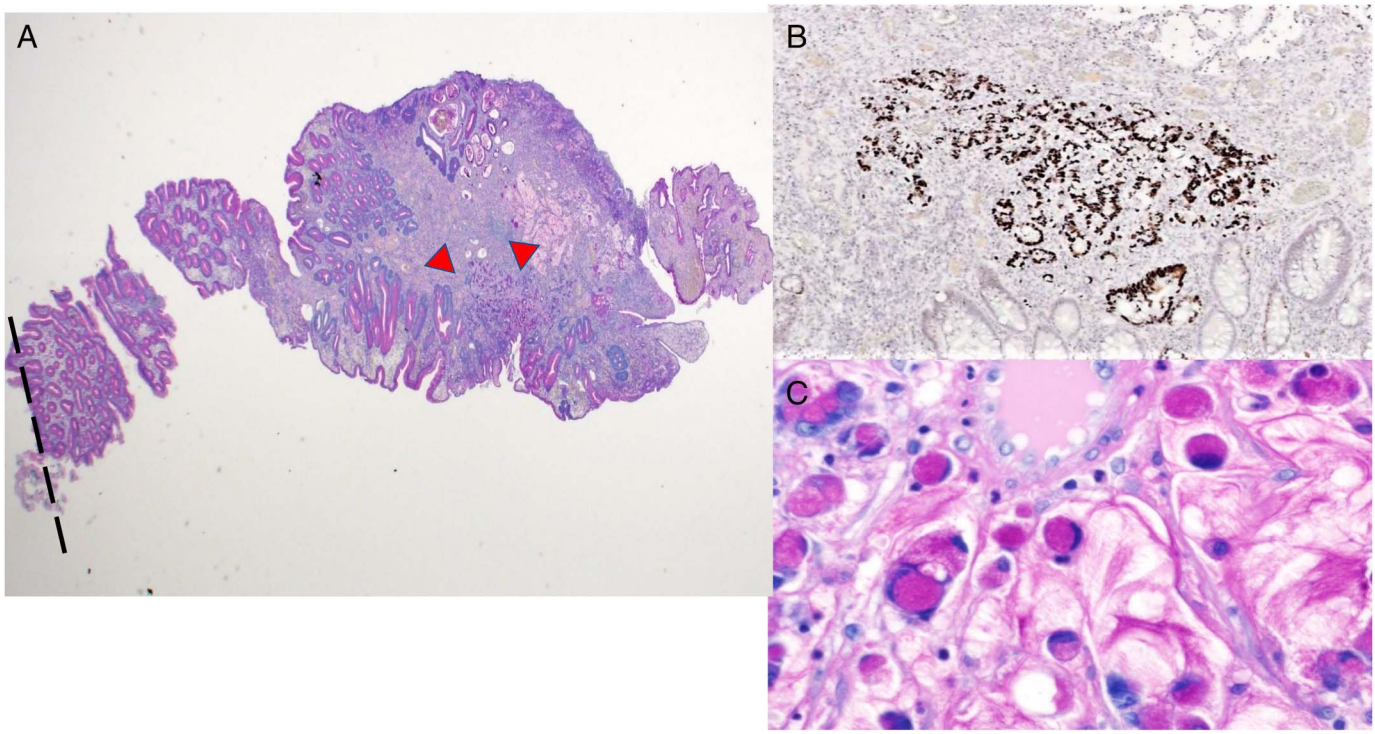

Figure 2. Periodic acid-Schiff (PAS) staining showing mucin-abundant neoplasm at the polyp head (A) (red arrows) with the resection margin (black dotted line). The signet ring cell carcinoma component with mucinous cytoplasm showing strong *p53* positivity on immunohistochemistry (B) and PAS staining (C) (A: ×20, B: ×40, C: ×200).

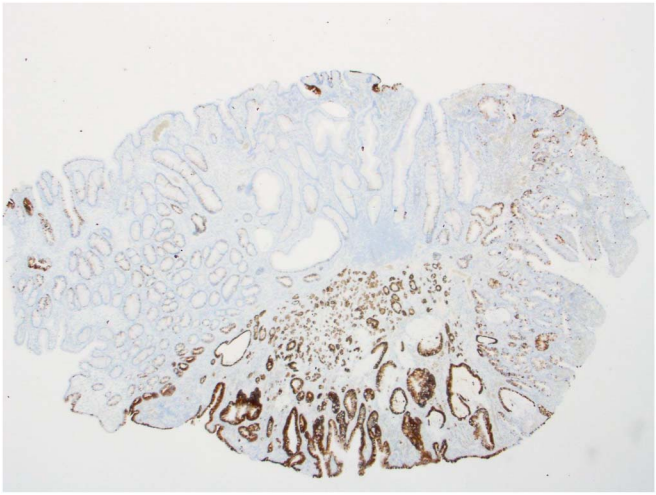

Figure 3. Immunohistochemical staining for *MUC5AC* is strongly positive in the periphery of the polyp head (×40).

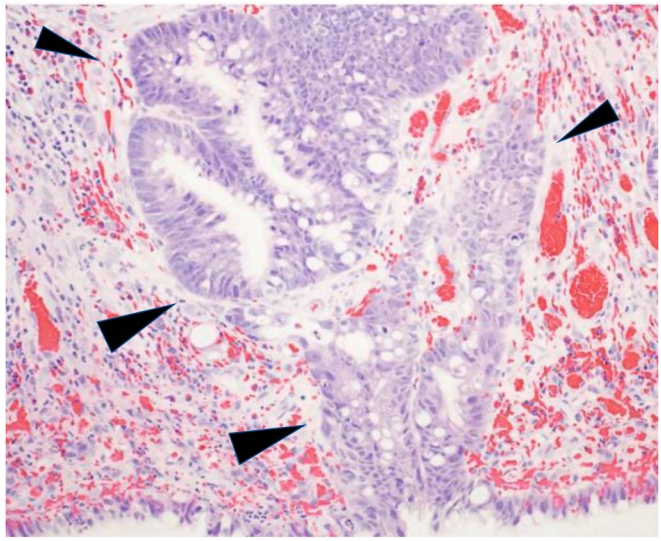

Figure 5. Noninvasive low-grade neoplasia coexisted at the polyp head (black arrows) (×200).

proposed that solitary JPs have a malignant potential, even in the absence of JPS, and right-sided sporadic JPs have a greater potential to undergo dysplastic transformation from adenoma to carcinoma.[9] Moreover, the largest single-center study concerning malignancy potential of JPs in adults in the Asian-Pacific area has been published most recently. Importantly, they found an incidence of 0.9% (1/107) of cancer and 6.5% (7/107) of low-grade intraepithelial neoplasia in JPs exclusive of JPS. They emphasized that carcinogenesis in JPs may be by an adenoma-carcinoma sequence.[10] Although first observed in 1951, a comprehensive understanding of colorectal SRCC is lacking. However, 2 subtypes have been identified: $MSI^+/CIMP^+/BRAF^+/CD3^+/PD\text{-}L1^+$ hypermethylated genotypes in the proximal colon and hypomethylated genotypes in the distal colorectum.[11] The morphological findings studied in 27 early-stage colorectal SRCC cases had either polypoid (37.0%) or flat and depressed types (63%).[2] To date, only 2 cases of JPs have been reported among polypoid-forming SRCC; however, both cases implicated the *de novo* carcinogenesis pathway because no adenomatous component was observed. To the best of our knowledge, our case is the first reported case of SRCC occurring in a JP with an adenomatous component.[6,12]

Did SRCC occur incidentally in solitary JPs in our case? We speculated the carcinogenesis pathway in this case as (i) a solitary JP-like hamartoma that developed during childhood; (ii) adenoma developed as a premalignant lesion; and (iii) SRCC developed by adenomatous transformation according to the adenoma-carcinoma sequence as the carcinogenesis pathway, considering the *p53* mutation. Whether both the periphery of the polyp and SRCC have gastric differentiation with MUC5AC expression is incidental or gastric differentiation coincides in the definite site remains to be solved.[13] In consideration of previously published cases, newly published reports by Ibrahimi et al and Dong et al, and this case, we believe that it is necessary for clinicians to recognize the possibility that neoplasms can occur even in solitary JPs and that the traditional wisdom that solitary JPs do not harbor malignant potential should be reconsidered.[6,9,10,12]

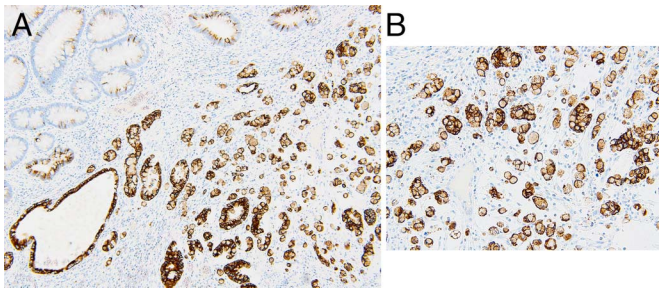

Figure 4. Immunohistochemical staining for MUC5AC is positive in both the dilatated gland (A) and SRCC (B). (A: ×40, B: ×100).

DISCLOSURES

Author contributions: K. Fukami and M. Furihata conceived the idea and wrote the manuscript. S. Yano, H. Okawa, S. Nishi, and Y. Nakatsu collected data and references. K. Fukami and Y. Nomoto interpreted the data. S. Tomita made the pathological judgment. S. Ogiwara, T. Kitamua, and T. Osada reviewed the manuscript and provided critical intellectual input. All authors reviewed and approved the submitted version of the manuscript. K. Fukami is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received June 25, 2022; Accepted November 14, 2022

REFERENCES

1. Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th edn. Mosby: Edinburgh, 2004, pp 805–11.

2. Kim JH, Park SJ, Park MI, et al. Early-stage primary signet ring cell carcinoma of the colon. *World J Gastroenterol.* 2013;19(24):3895–8.
3. Boland CR, Idos GE, Durno C, et al. Diagnosis and management of cancer risk in the gastrointestinal hamartomatous polyposis syndromes: Recommendations from the US multi-society task force on colorectal cancer. *Am J Gastroenterol.* 2022;117(6):846–64.
4. Wu TT, Rezai B, Rashid A, et al. Genetic alterations and epithelial dysplasia in juvenile polyposis syndrome and sporadic juvenile polyps. *Am J Pathol.* 1997;150(3):939–47.
5. Brosens LAA, van Hattem A, Hylind LM, et al. Risk of colorectal cancer in juvenile polyposis. *Gut.* 2007;56:965–7.
6. Kim HJ, Kang MK, Lee HS, Kim DS, Lee DH. Signet ring cell carcinoma arising from a solitary juvenile polyp in the colon. *J Korean Soc Coloproctol.* 2010;26(5):365–7.
7. Horrilleno EG, Eckert C, Ackerman LV. Polyps of the rectum and colon in children. *Cancer.* 1957;10(6):1210–20.
8. Morson BC. Precancerous lesions of upper gastrointestinal tract. 1962;5: 337–44.
9. Ibrahimi N, Septer SS, Lee BR, Garola R, Shah R, Attard TM. Polyp characteristics of nonsyndromic and potentially syndromic juvenile polyps: A retrospective cohort analysis. *J Pediatr Gastroenterol Nutr.* 2019;69(6):668–72.
10. Dong J, Ma TS, Xu YH, et al. Characteristics and potential malignancy of colorectal juvenile polyps in adults: A single-center retrospective study in China. *BMC Gastroenterol.* 2022;22(1):75.
11. An Y, Zhou J, Lin G, et al. Clinicopathological and molecular characteristics of colorectal signet ring cell carcinoma: A review. *Pathol Oncol Res.* 2021;27: 1609859.
12. Kang SH, Chung WS, Hyun CL, et al. A rare case of a signet ring cell carcinoma of the colon mimicking a juvenile polyp. *Gut Liver.* 2012;6(1): 129–31.
13. Barros R, Mendes N, Howe JR, et al. Juvenile polyps have gastric differentiation with MUC5AC expression and downregulation of CDX2 and SMAD4. *Histochem Cell Biol.* 2009;131(6):765–72.