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**Solitary rectal ulcer syndrome** **complicating** **sessile serrated adenoma/polyps: A case report and review of literature**

Sun H *et al.* Solitary rectal ulcer syndrome

Hui Sun, Wei-Qi Sheng, Dan Huang

**Hui Sun, Wei-Qi Sheng, Dan Huang,** Department of Pathology, Fudan University Shanghai Cancer Center, Shanghai 200032, China

**Hui Sun, Wei-Qi Sheng, Dan Huang,** Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China

**ORCID number:** Hui Sun (0000-0002-7145-6991); Wei-Qi Sheng (0000-0002-8726-277X); Dan Huang (0000-0002-7001-1325).

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**Correspondence to: Dan Huang, MD, PhD, Doctor, Professor, Teacher,** Department of Pathology, Fudan University Shanghai Cancer Center, 270 Dong An Road, Shanghai 200032, China. dianehuangfdcc@gmail.com

**Telephone:** +86-21-64175590

**Fax:** +86-21-64174774.

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**Abstract**

Solitary rectal ulcer syndrome (SRUS) is a rare benign condition, which can mimic many other diseases because of similarities in clinical, endoscopic and histological features. Sessile serrated adenoma/polyp (SSA/p) is a premalignant lesion in colon and rectum. The misdiagnosis of SSA/p in SRUS patients has been concerned, but the case of SRUS arising secondary to SSA/p was firstly reported. We herein report a case of a 59-year-old man presented with an ulcerative nodular lesion in rectum, accompany by the symptom of feces, diarrhea and constipation. Magnetic resonance imagining revealed a thickening of the rectal mucosa-submucosa. Histologically, it was characterized by the hyperplastic lamina propria and diffusely serrated crypts. Then further immunohistochemistry staining showed the loss of *HES1* and *MLH1* expressions in the epithelium cells in serrated area. The patient with SRUS has histological changes of SSA/p, suggesting a potential of tumor transformation in certain SRUS. The recognition of SRUS uncommonly accompanied by serrated lesions should at least be considered by pathologist and clinician.

**Key words:** Solitary rectal ulcer syndrome; Mucosal prolapse; Sessile serrated adenoma/polyp; Magnetic resonance imagining; *HES1;* Case report

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**Core tip:** We reported a 59-year-old man presenting with blood and mucus in the feces, diarrhea and constipation. A subsequent endoscopy of the rectum revealed a 5 cm size ulcerative nodule in the anterior wall of the rectum, 5 cm from the anal verge. Abdominal magnetic resonance imagining revealed a thickening of the mucosa-submucosa with the suspicious for rectal carcinoma. The surgical resection of rectum was performed. But the final pathology described an unusual case of solitary rectal ulcer syndrome complicating sessile serrated adenoma/polyp.

Sun H, Sheng WQ, Huang D. Solitary rectal ulcer syndrome complicating sessile serrated adenoma/polyps: A case report and review of literature. *World J Clin Cases* 2018; In press

**INTRODUCTION**

Solitary rectal ulcer syndrome (SRUS) is an uncommon benign disease, which is characterized by chronic defecation disorder. Along with the recognition of this disease, it has become clear that SRUS may not be solitary, ulceration or indeed confined to the rectum[1]. SRUS can resemble other conditions in its clinical presentation, endoscopic appearance and histopathologic feature[1-3]. Histologically, SRUS shows a characteristic fibromuscular proliferation within the lamina propria accompanied by the thickening of the muscularis mucosae. In some cases, there were focal serrated glands and dilated “diamond-shaped” crypts because of embedding artifact and architectural distortion[4,5]. These distorted crypts were the common reason for misinterpretation as sessile serrated adenoma/polyp (SSA/p)[6,7]. The majority of literatures on the SRUS morphology have concentrated on its hyperplastic polyp (HP)-like architecture distinction from true serrated lesions[7,8], so that a diagnosis of SRUS indicates the pathologists that this lesion with serrated changes has no neoplastic potential. On the contrary side, we herein report a case of SRUS complicating SSA/p, highlighting the need for careful histological assessment of serrated lesions in the polypoid mucosal prolapse with serrated architecture.

**CASE REPORT**

***Clinical history***

A 59-year-old man visited a local hospital for treatment of a 3-year history of occult blood and mucus in the feces, and with a long history of intermittent episodes of diarrhea and constipation. The patient had no history of steroid use, chronic liver disease, viral hepatitis, autoimmune diseases, or neoplasm. Physical examination was unremarkable except for an induration area palpable on the anterior wall of the rectum 5 cm from the anal verge. Occult blood was detected in his feces. The other laboratory studies were normal, and carcinoembryonic antigen was not elevated. A subsequent endoscopy of the rectum revealed a 5 cm size ulcerative nodule in the anterior wall of the rectum, 5 cm from the anal verge (Figure 1A). Initial endoscopic biopsy was performed in the local clinic and histopathologic finding was a rectal adenoma with low-grade dysplasia. After three months, the repeated colorectal endoscopy showed an ulcerative rectal mucosa and granulation tissue with no evidence of malignancy. However, the findings of abdominal magnetic resonance imagining (MRI) revealed a thickening of the mucosa-submucosa with the suspicious for rectal carcinoma (Figure 1B). In addition, clinical symptoms persisted despite medical treatment. Therefore, surgical resection of rectum was performed. The final pathology report was no malignancy seen. Thus, the patient was referred to our hospital for the pathology consultation.

***Pathological findings***

Grossly, a well-demarcated, superficial ulceration with polypoid mucosa involved almost the entire circumference of the rectum 5 cm from the anal dentate line. The ulcerative nodular lesion measured as 5 cm × 4 cm in length and width (described in the pathological report at the local clinic).

Histological examination revealed the fibromuscular obliteration in the lamina propria combined with a superficial ulcer, surrounded with a large amount of serrated crypts (Figure 2A). These irregular glands showed a saw-toothed pattern or a diamond-shaped architecture involving the basal of crypts (Figure 2B). The epithelial cells lined in the crypts were mucin hypersecretion and slight nuclear stratification (Figure 2C), showing pathological characteristics of SSA/p. Around the SSA/p area, micro-vesicular hyperplastic polyps (MVHPs) were found, showing the earliest lesions of serrated dysplasia (Figure 2D).

Immunostaining of Hes1 showed loss of expression in the serrated glands, while nuclei staining in the normal adjacent epithelium and interstitial inflammatory cells (Figure 3A). Similarly, there was superficial loss of MLH1 expression in the crypts with serrated architectures (Figure 3B). However, other mismatch repair genes, such as *MSH2*, *MSH6* and *PMS2*, were seen nuclear positive in all cells. The stains of β-catenin were diffuse positive along the cell membranes, and P53 was focal nuclear positivity. The Ki-67 proliferative staining was increased in the crypts of SSA/p (Figure 3C), compared with the basal staining in glands of MVHPs (Figure 3D).

**DISCUSSION**

SRUS is a poorly understood syndrome that originally described in 1829 since Cruveihier covered four cases of unusual rectal ulcers[9]. Further the term “SRUS” was widely accepted after characterized by Madigon and Morson[10] in the late 1960s. This syndrome usually manifests as rectal bleeding, prolonged excessive straining, copious mucus passing, and abdominal pain[11]. Ulcers and polyps have been the common endoscopic findings in 90% patients[12,13]. However, some of the clinical and endoscopic presentations in SRUS patients can be completely nonspecific, and up to 26% of patients may be asymptomatic[1,14]. Hence, it is difficult to distinguish SRUS from malignancy or other diseases based on symptoms, endoscopic features or image findings[15]. Misdiagnosis of SRUS as malignancy can lead to unnecessary surgery. Herein, we presented a 59-year-old man originally suspected of rectal malignancy, subsequently an abdominoperineal resection of the rectum was performed and the final diagnosis was SRUS with SSA/p. In the endoscopy, our case looked like the malignant. However, MRI images showed not a mass but a thickening of the mucosa-submucosa. This is a point of differentiation between SRUS and cancer in imaging techniques. Until now, the conservative measures (diet and bulking agents) and biofeedback therapy were the first steps in SRUS treatments. Surgery usually act as the final opinion for the patients who repeatedly relapse[16].

SRUS accompanied by SSA/p is extremely rare, and is an accurate differential diagnosis is difficult to achieve. In our case, the histopathologic alterations of SRUS are characteristic and include the hyperplasia of the smooth muscle and thicken of muscularis mucosae. Moreover, colonic crypts around the ulcer were no longer rounded but have diffusely serrated changes. These hypermucinous glands showed crypt dilatation and crypt flattening at the base. Surrounding with typical HPs, these serrated changes are reminiscent a diagnosis of SSA/p. The differential diagnosis included inflammatory cloacogenic polyp with SRU, which was inflammatory polyps of the anorectal transition zone[17]. Since previous studies have reported the distortion and entrapment of the crypts were the common reasons for misinterpretation of SSA/p[5,8]. However, the tumor location, diffuse HPs around and the striking features of SSA/p confirmed the final diagnosis of SRUS coexist with SSA/p in our case.

Previous research illustrated that loss of Hes1 in immunostaining could distinguish SSA/p from regenerative epitheliums or HPs[18]. Interestingly, we found Hes1 expression were deficiency in the serrated glands. As the downstream target of Notch signaling pathway, Hes1 might involve in the regulation of molecular activation and tumorigenesis of SRUS with SSA/p. Besides, some investigators showed that MLH1 deficient was association with the progression of sessile serrated lesions[19]. Moreover, previous study have reported that some of SRUS with HP-like architectures presented focal loss of MLH1 expression, suggesting a potential of preneoplastic change in some SRUS[8]. Similar results were obtained within our case, which showed the serrated crypts were no staining of MLH1 while other mismatch repair genes preserved. Likewise, it was discovered that the proliferation marker Ki67 were of value in assessing for SSA/p. The Ki-67 proliferative zone tended to be distributed diffusely within the base of the SSA/p crypts, but partially within the epithelium of the normal or HP glands[20]. For our case, the basal cells within serrated crypts demonstrated diffuse staining of Ki-67, which consistent with the features of SSA/p.

Little is known regarding the biologic characteristics and natural history of serrated lesions in SRUS. It is generally accepted that inappropriate and paradoxical contraction of pelvic floor, which causes straining on defecation and compression the rectum mucosa of prolapse, further results in ulceration and polyps in SRUS patients[21-23]. The repeated trauma and repair were commonly observed in SRUS, which may be the reason of neoplastic transformation. Further studies are needed to clarify the pathogenic relationship between SRUS and tumors. Our case presented the loss of HES1 and MLH1 in serrated crypts, which hypotheses that HES1 and MLH1 may act as a molecular trigger in the formation of serrated neoplasia in SRUS.

In summary, we described an unusual case of SRUS complicating SSA/p. Loss of HES1 and MLH1 expression were revealed in the serrated crypts, suggesting the alterations in molecular pathways promoted the SSA/p progression in certain case of SRUS. The pathologist and clinician must be aware the potential for serrated lesions developed in SRUS, it may occur in other clinical behaviors.

**ARTICLE HIGHLIGHTS**

***Case characteristics***

Solitary rectal ulcer syndrome (SRUS) is an uncommon benign disease. It has been reported previously, but the case of SURS arising secondary to sessile serrated adenomas/polyp (SSA/p) was firstly reported.

***Clinical diagnosis***

Rectal ulcer.

***Differential diagnosis***

Rectal cancer.

***Laboratory diagnosis***

Blood and mucus was detected in his feces.

***Imaging diagnosis***

Thickening of the rectal of mucosa-submucosa.

***Pathological diagnosis***

SRUS with SSA/P.

***Treatment***

Mainly take medical therapy, if not relieved, take surgical management.

***Related reports***

A review of solitary rectal ulcer syndrome has been reported in the *Journal of Gastrointestinal Endoscopy* from Ala I Sharara.

***Term explanation***

SRUS: Solitary rectal ulcer syndrome; SSA/p: Sessile serrated adenomas/polyp.

***Experiences and lessons***

This case will contribute to improvements in our understanding of the SRUS with SSA/P. This case may also serve as a reminder to gastroenterologists, surgeons and pathologists who encounter SRUS cases in their clinical practice to consider a diagnosis.

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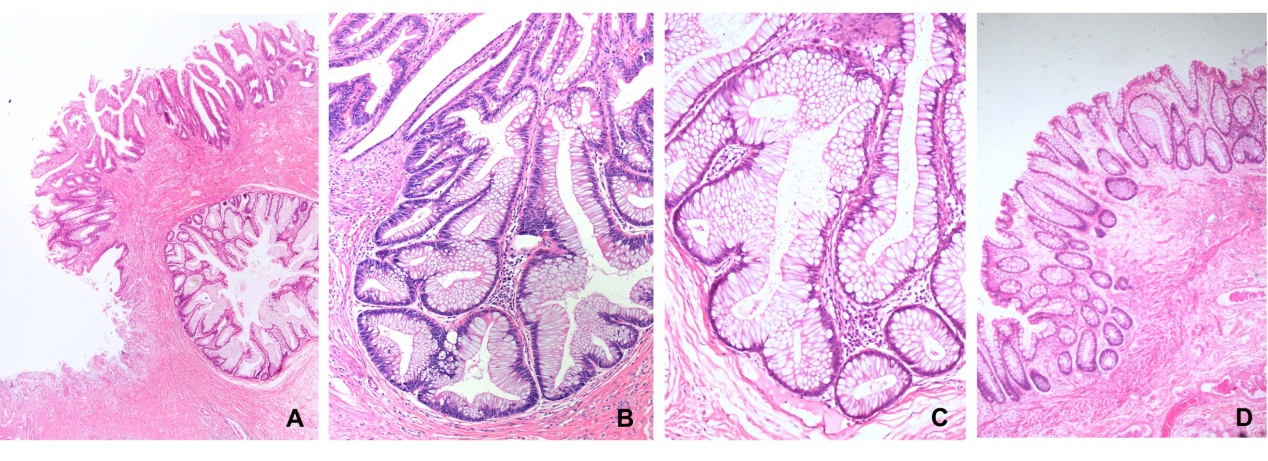
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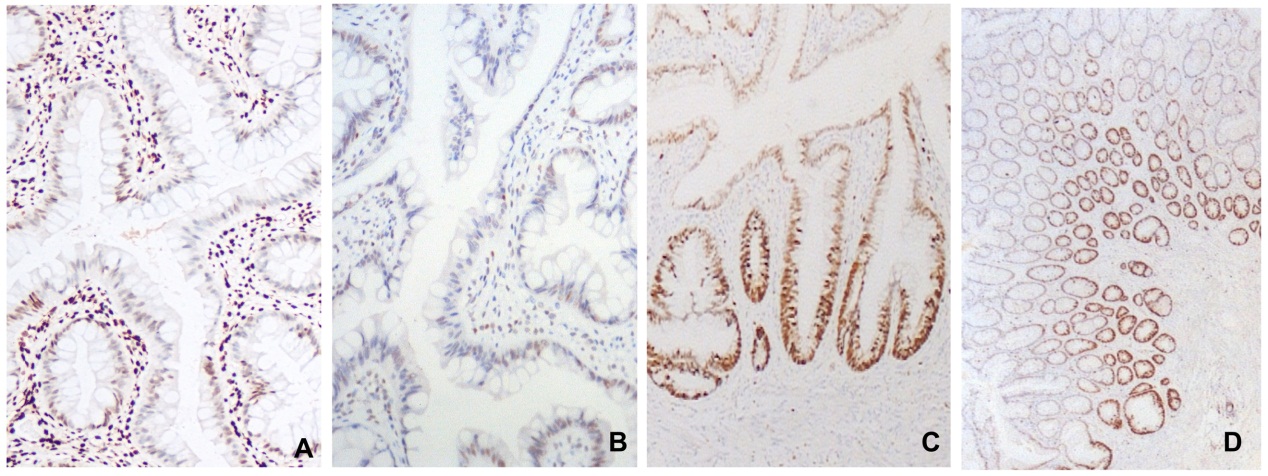
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**Figure 1 Endoscopic and magnetic resonance imaging of solitary rectal ulcer syndrome with sessile serrated adenomas/polyp.** A: Endoscopic imaging revealed a large ulcerative nodule in the anterior wall of the rectum; B: Magnetic resonance imagining showed focal thickening of the anterior rectal wall and irregularities in the mucosal surface.



## Figure 2 Histopathologic findings of solitary rectal ulcer syndrome with sessile serrated adenomas/polyp. A: Low power magnification showing a superficial ulcer and fibromuscular obliteration of the lamina propria with a few dilated and serrated crypts (H and E, original magnification: × 20); B: High power magnification showing the diffusely architectural distortion with the crypt dilatation and basal flattening (H and E, original magnification: × 100); C: High power magnification showing hypermucinous changes of crypt glands, but without epithelial dysplasia (H and E, original magnification: × 100); D: Medium power magnification showing microvesicular hyperplastic polyps around sessile serrated adenomas/polyp.



**Figure 3 Immunohistochemistry of solitary rectal ulcer syndrome with sessile serrated adenomas/polyp.** A: High-power Hes1 immunohistochemistry showing loss or very weak of nuclear expression in crypts from sessile serrated adenomas/polyp (SSA/P) changes (Immunohistochemistry, original magnification: × 100); B: High-power MLH1 immunohistochemistry showing reduced number of surface epithelial cells expressing MLH1 protein were observed in serrated crypts (Immunohistochemistry, original magnification: × 100); C: High-power Ki67 immunohistochemistry showing strong nuclear positive was increased within the surface epithelium of solitary rectal ulcer syndrome with SSA/P architecture (Immunohistochemistry, original magnification: × 100); D: Immunohistochemistry staining of Ki67 showed the basal staining in glands of micro-vesicular hyperplastic polyps.