

Histopathological Misdiagnosis of Solitary Rectal Ulcer Syndrome

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Abstract: Although, the clinicopathologic features of Solitary Rectal Ulcer Syndrome (SRUS) are well documented, the heterogeneous histologic features of lesions that the syndrome produces and its rare incidence may make for histologic misdiagnosis. The retrospective descriptive study was performed on patients presenting to No. 3 Special Pathology Laboratory of Tabriz Medical University from 1999-2000. There were 5 patients with SRUS. There were 5 patients (3 males and 2 females) with age range of 15-75 years. Of all cases, SRUS had been considered only in one case as clinical differential diagnosis. The patients had no history of previous important disease in their family. Their manifestations were anal pain and itching, anorectal pain and feeling of incomplete emptying, mild rectal bleeding at the end of defecation. SRUS is often underdiagnosed condition. It is often misdiagnosed as other digestive diseases such as cancer or inflammatory bowel disease. The diagnosis requires a high index of suspicion on the part of both the clinician and the pathologist. Also, serial cutting and examination of all slices is an important help for both pathologist and patient.

Key words: Solitary rectal ulcer syndrome, misdiagnosis, histopathology

INTRODUCTION

Solitary Rectal Ulcer Syndrome (SRUS) is an uncommon rectal disorder that can present with bleeding, passage of mucus, straining during defecation and a sense of incomplete evacuation (Jarrett *et al.*, 2004; Meurette *et al.*, 2008; Vaizey *et al.*, 1998; Dehghani *et al.*, 2008; Chong and Jalihal, 2006). Macroscopic evidence of ulceration is frequently, but not invariably, present (Jarrett *et al.*, 2004). The ulcerations may be single or multiple (Rao *et al.*, 2006; Felt-Berma and Cuesta, 2001; Perrakis *et al.*, 2005). Its incidence has been estimated to be one in 100 000 in adults. A few cases, however, have been reported in pediatric age groups (Dehghani *et al.*, 2008; Perrakis *et al.*, 2005; Crespo *et al.*, 2007). SRUS is localized not only in the rectum but in other colonic tracts. It more frequently appears in female, the age preferred by the disease is the one between twenties and thirties. The 68% of ulcers is localized in the anterior wall of rectum and their length varies from 4-15 cm. The SRU is a benign chronic disease that does not pass the muscularis mucosae (Zanghi *et al.*, 1995).

The etiology and pathophysiology remains obscure (Perrakis *et al.*, 2005; Martin de Carpi *et al.*, 2007; Choi *et al.*, 2005; Rao *et al.*, 2006). The macroscopic appearance varies from erythema to ulceration or polypoid lesions, usually on the anterior rectal wall, but sometimes it may be more extensive, even circumferential (Perrakis *et al.*, 2005).

SRUS is thought to be an ischemic injury from repeated mucosal trauma (Sood *et al.*, 2008). It is a clinical condition associated with functional anorectal evacuatory disorders (Choi *et al.*, 2005). Biofeedback therapy improves Functional Defecation Disorders (FDD), restores normal defecation dynamics and improves subjective parameters (straining, using digital maneuvers, blood and mucus in stool) and mucosal changes. These findings suggest a pathophysiological association between SRUS and FDD (Oztürk, 2007; Rao *et al.*, 2006). SRUS is often underdiagnosed condition (Jarrett *et al.*, 2004; Martin de Carpi *et al.*, 2007). As the clinical presentation varies, the diagnosis requires a high index of suspicion on the part of both the clinician and the pathologist (Dehghani *et al.*, 2008; Singh *et al.*, 2007). It is often misdiagnosed as a malignant ulcer. Histopathological features of SRUS are characteristic and pathognomonic nevertheless, the endoscopic and clinical presentations may be confusing (Torres *et al.*, 2007). Also, the condition is commonly misdiagnosis with other digestive diseases such as cancer or inflammatory bowel disease (Crespo *et al.*, 2007). Unless recognized, the diagnosis can be delayed and be mistaken for non-specific ulcer, inflammatory bowel disease or neoplasm. This can lead to inappropriate treatment being given (Chong and Jalihal, 2006). Symptomatic SRUS should always be considered in all patients with malignant looking rectal tumors (Perrakis *et al.*, 2005).

Treatment is designed to alleviate the underlying defecatory problems (Sood *et al.*, 2008). Current treatment includes the use of bulking agents, laxatives, sucralfate enema (Dehghani *et al.*, 2008), injection of corticosteroid (Dehghani *et al.*, 2008), bowel retraining with or without biofeedback and surgery (Meurette *et al.*, 2008; Chong and Jalihal, 2006; Bishop and Nowicki, 2002). The first-line therapy is biofeedback, employing a behavioral approach. In SRUS, this therapy has two aims: Firstly, habit training to impose a discipline about the number of visits a patient makes to the toilet, time spent in the toilet, straining, digitation, and laxative use and secondly, to normalize pelvic floor coordination (Jarrett *et al.*, 2004; Oztürk, 2007; Nagar, 2007). In patients with refractory symptoms, surgical treatment should be considered. Results of anterior resection and proctocolectomy are satisfactory for solitary rectal ulcer (Torres *et al.*, 2007). Surgical resection is usually required in patients with rectal stricture (Perrakis *et al.*, 2005; Choi *et al.*, 2005).

Because this is less frequent pathology and there are little reports on this syndrome and also it is often misdiagnosed and under-diagnosed condition, we performed this study to highlight the importance of high index of suspicion on the part of both the clinician and the pathologist for diagnosis of this syndrome.

MATERIALS AND METHODS

The retrospective descriptive study was performed on patients presenting to No. 3 Special Pathology Laboratory of Tabriz Medical University from 1999-2000. There were five patients with SRUS.

For all cases, the blocks from the mucosal biopsy of rectum at the site of solitary rectal ulcer were recut and stained with Van Gieson stain for collagen content. These were examined in conjunction with the original haematoxylin and eosin stain.

At least 2 slides with more than 4 sections for each patient were examined and the measurements were taken using the micrometer scale on the microscope stage.

Histological examination: The thickness of submucosa was measured in millimeters. The collagen content was quantified into three different grades: 1 = normal, 2 = mild or moderate collagen excess and 3 = severe collagen excess.

The clinical features were studied closely and the histology of the rectal mucosa and the mucin secretion patterns were compared.

RESULTS

There were 5 patients (3 males and 2 females) with age range of 15-75 years. Of all cases, SRUS had been considered only in one case as differential diagnosis. The patients had no history of previous were no important disease in their family. They denied using suppositories or any other medication.

The first case had 10 years old with a single ulcer in about 15 cm far from anus in an inflammatory background. This case was evaluated as inflammatory lesion. However, histological examination showed that in spite of inflammatory view, it has not attacked by inflammatory cells and there are only few inflammatory cells in lamina propria which mostly are mononuclear. The fibromuscular tissue has entered the lamina propria and has located between mucosal crypts (Fig. 1). There was moderate fibrosis in lamina propria. Although, the hyperplastic changes were not so severe, the high cell turnover was seen as elevated mucus columnar cells to Goblet cells ratio. Dysplastic like changes in a few glands may cause diagnostic challenges.

The second case had 75 years old and presented with anal pain and itching. Colonoscopy showed Grade 2 hemorrhoid and a superficial ulcer in rectum. Then, regarding the patient age, the lesion was evaluated as malignant lesion. Histological examination of one block showed a patch of superficial ulcer with acute inflammatory exudate and a granulation tissue around it having a few acute inflammatory cells infiltration. In the other block there were hyperplastic crypts and glands with thickened mucosal muscles (Fig. 2) and splicing of smooth-muscle fibers and their extension from the muscularis mucosae vertically upwards between crypts. Lamina propria was fibrotic and without inflammatory cells.

The third patients had presented with anorectal pain and feeling of incomplete emptying. The diagnosis of SRUS had been considered only in this patient. Histological examination of one block showed a patch of superficial ulcer with granulation tissue and acute inflammatory cell infiltration and in some parts, Goblet cells depletion. In the other block there were elongation of hyperplastic crypts with apparent Goblet cells with significant hypertrophy of muscularis mucosa and absence of inflammatory cells in lamina propria and mild hyperplasia of focal glands (Fig. 3).

The fourth case presented with a history of mild rectal bleeding at the end of defecation. Microscopy examination of solitary ulcer in rectum showed crypts with only regenerative epithelium in a markedly fibrotic lamina propria.

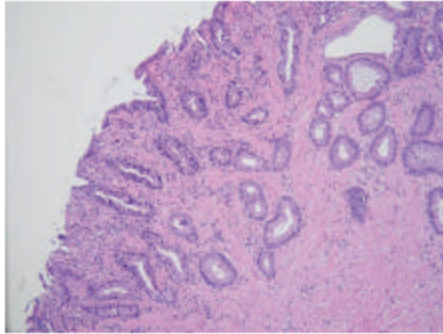


Fig. 1: Small magnification. A fibromuscular obliteration of the lamina propria can be observed

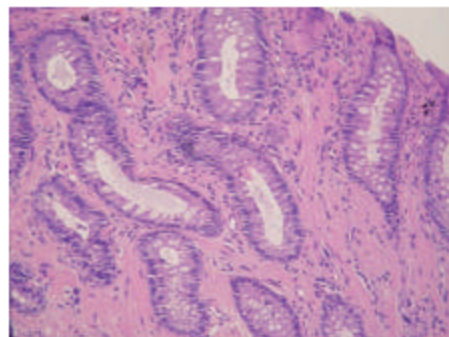


Fig 2: Great magnification. A thickened muscularis mucosae and the extension of smooth-muscle fibers from the muscularis mucosae vertically upwards between crypts may be observed

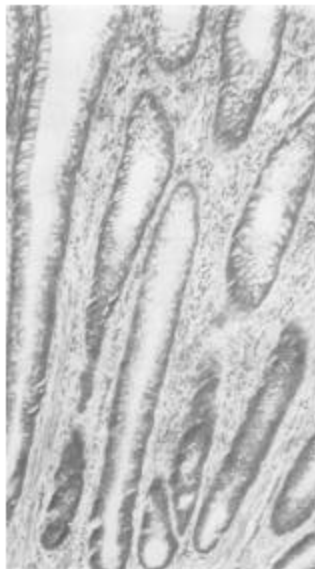


Fig 3: Rectal mucosa in solitary ulcer syndrome showing crypt hyperplasia, moderate mucin depletion, increased fibroblasts and muscle fibers pointing toward the lumen (haematoxylin and eosin)

The fifth patients had mild rectal bleeding at the end of defecation, feeling of incomplete emptying, and anorectal pain. Physical examination was normal except for the rectal exam, which revealed a firm zone on the left side of the rectum. Colonoscopy showed two small rectal polyps, internal hemorrhoids and a 2×2 cm patch of erythematous mucosa located on the left side of the rectum with well-delimited borders. These findings initially suggested inflammatory bowel disease, stercoral ulcer, or solitary rectal ulcer syndrome. Rectal biopsy showed a fibrous obliteration of the lamina propria, which was replaced with smooth muscle and collagen and a thickened muscularis mucosa with distortion of crypt architecture, all hallmarks of solitary rectal ulcer.

DISCUSSION

Solitary rectal ulcer syndrome is an uncommon benign condition characterized by rectal bleeding, passage of mucus, tenesmus, perineal and abdominal pain (Crespo *et al.*, 2007; Keshitgar, 2008). The most common symptom is the passage of small amounts of red blood on defecation (60%). Passage of mucus is reported in 18% of cases and constipation in 55%. A sense of incomplete defecation is common and patients usually have a feeling of unsatisfied defecation. Another common complaint is anorectal or abdominal pain. Diarrhea is seen in 20% of patients and up to 25% can be asymptomatic, incidentally discovered while investigating other diseases. Macroscopically, SRUS typically appears (57% of cases) as an isolated shallow ulcerating lesion (rounded, oval, or linear) on a hyperemic mucosa, most often located on the anterior or anterior-lateral wall of the rectum, that may range from 0.5-5 cm in diameter. Up to 30% of cases consist of multiple ulcers and can be located in the sigmoid or descending colon (Crespo *et al.*, 2007; Sharara *et al.*, 2005). Nearly all of these manifestations were seen in our series. In agreement with many authors (Chong and Jalihal, 2006; Perrakis *et al.*, 2005; Crespo *et al.*, 2007; Baba *et al.*, 2007; Ertem *et al.*, 2002), the term SRUS is a misnomer, as 20% of the endoscopic findings in this study showed multiple lesions.

Chong and Jalihal (2006) retrospectively reviewed the clinical, endoscopic characteristics and predictive profiles on 28 patients (14 males) with biopsy-proven SRUS with the mean age of 29.5±16.1 (range 10-81) years. Common symptoms reported included rectal bleeding (86%), abdominal pain (36%), mucus passage (25%) and constipation (14%). Digital manual evacuation was reported by 11%. Lesions were located anteriorly (38.5%), posteriorly (30.7%) and circumferentially (31.8%). The

lesions were multiple (34%), ulcerative (64.3%) and polypoidal/nodular (32.1%) (Chong and Jalihal, 2006). The rectal prolapse is a differential diagnosis of SRUS. Mucosal abnormalities in solitary rectal ulcer syndrome and complete rectal prolapse are now well characterized. In solitary rectal ulcer syndrome there is mucosal thickening with edema of the lamina propria, a variable degree of fibrosis and extension of smooth muscle fibers upwards between the crypts. The muscularis mucosa is usually hypertrophied. In complete rectal prolapse the features are histologically similar but usually less well developed. Possible abnormalities of the muscularis propria have not been investigated in either condition. Studying the rectal wall in these conditions may help elucidate the pathogenesis of these disorders. It may also help to resolve the question as to whether these 2 disorders are separate conditions, or 2 disorders on the same disease spectrum (Kang *et al.*, 1996).

Also, the condition is commonly misdiagnosed with other digestive diseases such as Crohn disease and idiopathic proctitis. Fibrosis of lamina propria is a tissue marker for differentiation of SRUS from Crohn disease and idiopathic proctitis (Levine, 1987). When the mucus secretion pattern of SRUS and non-specific proctitis was compared, marked differences in mucin composition appeared. Mucin secretion in rectal biopsies from patients with SRUS was frequently abnormal. The presence of sialomucins further supports the diagnosis of SRUS in the presence of suggestive clinical features and equivocal histology. The differences in mucin patterns with predominance of sialomucins in SRUS in contrast with a normal mucus secretion in non-specific proctitis, helps in the differential diagnosis of these two conditions (Ehsanullah *et al.*, 1982). Patients with SRUS frequently present with a mass that can be misinterpreted as cancer. The histopathology of SRUS may occasionally represent a characteristic but nonspecific mucosal reactive change to a deeper seated malignancy. The terminology solitary rectal ulcer syndrome/mucosal prolapse changes with a cautionary note may be useful for reporting biopsy results to emphasize the possibility of underlying primary or metastatic malignancy in the differential diagnosis (Li and Hamilton, 1998). Tsuchida *et al.* (1998) reported a case of carcinoma in solitary rectal ulcer syndrome. The lesion exhibited typical histological features of solitary rectal ulcer syndrome, with a well differentiated adenocarcinoma invading submucosal layers and some dysplastic glands. They believe that the adenocarcinoma represents a malignant transformation from solitary rectal ulcer syndrome, because similar to longstanding chronic idiopathic colitis, colorectal dysplasia and carcinoma may develop (Tsuchida *et al.*, 1998).

The site of colostomy and ileostomy histologically resemble SRUS because of mucosal prolapse and should be considered in differential diagnosis (Vaizey *et al.*, 1998). Also, the presence of excessive mucosal folds and their prolapse mimic the lesions of SRUS.

Daya *et al.* (1995) reported a unique case of rectal endometriosis mimicking SRUS. Several rectal biopsies were performed before the correct diagnosis of rectal endometriosis was made. The lesion had striking histological features resembling colitis cystica profunda. The definitive diagnosis of SRUS and localized Colitis Cystica Profunda (CCP) must depend upon the recognition of specific histopathologic features in rectal biopsy specimens from ulcer margins or otherwise abnormal mucosa (Levine, 1987; Daya *et al.*, 1995). However, the distinction between colonic and endometrial glands is very difficult on hematoxylin-and-eosin-stained slides. Endometrial stroma is identified only in repeated biopsy specimens. Although rare, rectal endometriosis should be considered in the differential diagnosis of solitary rectal ulcer syndrome (Daya *et al.*, 1995).

SRUS is a benign lesion of adults (Nincheri *et al.*, 1998) and children (Keshtgar, 2008) of either sex, which presents with chronic constipation, peculiar defecatory disorders, rectal prolapse and mild psychological abnormalities. The characteristic appearance of this disease is a neither being always ulcerate, nor always solitary lesion, but often with polypoid or granular feature, typically localized in anterior rectal wall, a few inches from anal channel. Distinctive histopathological features are localized mucosal distortion, hypertrophic proliferation of muscularis mucosae and obliteration of lamina propria by fibroblasts and muscle fibers from the muscularis mucosae (Nincheri *et al.*, 1998). Although, solitary rectal ulcer syndrome is rarely reported in children, it must be suspected in patients with rectal discharge of blood and mucus and previous disorders of evacuation. Martin *et al.* (2007) presented three children (aged 9, 10 and 14 years) with solitary rectal ulcer syndrome that had presented with rectal bleeding. A careful inquiry about evacuation habits and a high index of suspicion in children presenting with hematochezia helps to diagnose this possibly unrecognized or misdiagnosed entity in children. Endoscopy and histologic examination confirms this condition (Martín de Carpi *et al.*, 2007). Although, the syndrome is well-recognized in adults, the pediatric experience with this condition is limited and often remains unrecognized or misdiagnosed. There are few pediatric case reports in English literature (Ertem *et al.*, 2002). We retrospectively evaluated five patients with SRUS who had various

treatments. There were 5 patients (3 males and 2 females) with age range of 15-75 years. Of all cases, SRUS had been considered only in one case as differential diagnosis.

The underlying etiology of SRUS is not fully understood but it is likely to be secondary to ischemic changes in the rectum associated with paradoxical contraction of pelvic floor and external anal sphincter muscles and rectal prolapse (Keshtgar, 2008; Vaizey *et al.*, 1997). However, physiological and histological studies suggest a spectrum of disease, raising the possibility that this syndrome may result from more than one cause. In clinical practice some patients seem to have a behavioral disorder with excessive straining, whereas in others there is no history of straining. The encouraging results from the use of behavioral therapies for defecation disorders led us to explore whether some patients with SRUS might benefit from biofeedback retraining (Vaizey *et al.*, 1997).

Rectal bleeding, disordered defecation and anal pain are associated with a benign rectal lesion with typical histological findings. The macroscopic appearance ranges from hyperemia to ulceration or even a polypoid lesion and the lesions are not necessarily solitary. The histological features consist of mucosal thickening with edema of the lamina propria, fibrosis and extension of smooth muscle fibers upwards between the crypts. Full thickness rectal histology reveals architectural derangement of the muscularis propria in some patients (Vaizey *et al.*, 1997). Histologically, the presence of fibromuscular obliteration of the lamina propria with disorientation of muscle fibers is characteristic, which could be secondary to chronic mechanical and ischemic trauma and inflammation by hard stools and intussusception of the rectal mucosa. A misdiagnosis has been reported in one fourth of adult cases and the correct diagnosis usually delayed approximately 5-7 years (Ertem *et al.*, 2002). SRUS is a benign condition of the rectum that is found most often in young adults. Because the clinical presentation varies, the diagnosis requires a high index of suspicion of both the clinician and the pathologist. This entity either is rare in children or usually goes unrecognized or misdiagnosed in pediatric practice (Ertem *et al.*, 2002).

SRUS is a traumatic lesion of the anterior or circular rectal wall caused by straining due to functional disorders of defecation. Defecography, transrectal ultrasonography or anorectal manometry are suitable procedures that may be used to detect the causative disorder and should, therefore, be performed in patients with solitary rectal ulcer syndrome. Histopathological features of SRUS are characteristic and pathognomonic; nevertheless the endoscopic and clinical presentations may be confusing.

The lesions may mimic other rectal pathologies and lead to wrong diagnosis. Double contrast barium enema represents a useful radiologic method to diagnose solitary rectal ulcer, but air insufflation and pharmacological hypotonia prevent the functional study of rectal walls. Endoscopy permits to detect mucosal ulcerations, erythema, pseudopolyps and granular proctitis; biopsy provides an accurate diagnosis. Salzano *et al.* (1998) suggest combined defecography and videoproctography as a useful tool for evaluating solitary rectal ulcer syndrome as a whole; defecography is necessary to identify associated functional abnormalities, such as rectal prolapse and intussusception, not detectable by other instrumental and radiologic investigations and considered by many authors the likely cause of the disease (Salzano *et al.*, 1998).

Medical treatment is performed by high-fiber diet, but biofeedback training is very helpful. Conservative measures like high intake of fluids and fibers, laxatives, biofeedback and behavior modification therapy may be beneficial for treatment of constipation. Excision of rectal ulcer and surgery of overt rectal prolapse, however, may be required in refractory cases not responding to conservative treatments. A therapeutic role for botulinum toxin injection into the external anal sphincter for treatment of SRUS associated with constipation and paradoxical contraction of pelvic floor and external anal sphincter muscles in children, may exist. Surgical management is as an excisional surgery, as a rectopexy if there is prolapse. Fecal diversion and rectocolic resection are considered only for patients with obstinate and severe symptoms. Even in patients who seem to advocate a surgical approach it is important to heal a dyskinetic puborectalis muscle (Keshtgar, 2008; Nincheri *et al.*, 1998).

CONCLUSION

SRUS is often underdiagnosed condition. It is often misdiagnosed as other digestive diseases such as cancer or inflammatory bowel disease. The diagnosis requires a high index of suspicion on the part of both the clinician and the pathologist. Histopathological features of SRUS are characteristic and pathognomonic; nevertheless, the endoscopic and clinical presentations may be confusing. Unless recognized, the diagnosis can be delayed and be mistaken for non-specific ulcer, inflammatory bowel disease or neoplasm. This can lead to inappropriate treatment being given. SRUS should always be considered in all patients with malignant looking rectal tumors. Also, serial cutting and examination of all slices is an important help for both pathologist and patient.

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