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SELECTIVE SEROTONIN REUPTAKE INHIBITORS AND SOLITARY RECTAL ULCER SYNDROME: A BLOODY RELATIONSHIP

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ABSTRACT

Introduction: Solitary rectal ulcer syndrome (SURS) is a poorly understood and uncommon benign disorder of the lower gastrointestinal tract. It presents with various symptoms, often misinterpreted as inflammatory bowel disease. To date, there is no association between the use of selective serotonin reuptake inhibitors (SSRIs) and SURS.

Case description: A 29-year-old male on paroxetine for six months and with a non-contributory surgical history presented to the clinic due to three months of haematochezia, abdominal pain and mucoid discharge. Physical examination and a review of systems were unremarkable; a colonoscopy demonstrated a suspicious ulcerated lesion in the rectum, which was identified as SURS on biopsy. The patient was advised lifestyle and dietary modifications. In addition, paroxetine was discontinued, and patient was switched to venlafaxine, a serotonin–norepinephrine reuptake inhibitor. Subsequently, the patient's symptoms resolved gradually, and he did not report any signs of recurrence on follow-up.

Conclusion: Literature confirms that SSRIs can increase the occurrence of GI ulceration yet focuses specifically on upper gastrointestinal bleeding rather than rectal bleeding. This finding raises the need for further research.

KEYWORDS

Solitary rectal ulcer syndrome, SSRIs, gastrointestinal bleed, platelet dysfunction

LEARNING POINTS

- SURS is often underdiagnosed or misdiagnosed as inflammatory bowel disease.
- The pathophysiology and aetiology behind SURS remain obscure.
- This case points to a potential correlation between SSRIs use and SURS development.

INTRODUCTION

Solitary rectal ulcer syndrome (SURS) is a benign disorder of the lower gastrointestinal tract. It is relatively uncommon, with a prevalence of 1 per 100,000 adults per year[1]. In the adult population, there is no higher risk of the disease with gender or increased age, occurring almost equally among

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adult men and women of the same age[2]. SURS is characterised by difficult and painful defecation, a sensation of incomplete evacuation and is sometimes associated with lower GI bleeding[2]. Due to its vague symptoms that most often hint towards other, more prevalent disorders, SURS is often underdiagnosed or misdiagnosed as inflammatory bowel disease. Therefore, diagnosing SURS requires a combination of clinical symptoms, imaging and histopathology findings[3]. The pathophysiology and aetiology of SURS are poorly understood. However, it is thought that rectal prolapse and chronic severe constipation are risk factors for the disease[4]. Finally, the treatment of SURS ranges from lifestyle changes to surgery, with the choice of treatment depending on the severity of the symptoms[5]. Here, we document the case of a previously healthy patient on selective serotonin reuptake inhibitors (SSRIs) presenting for rectal bleeding, who was found to have SURS. Our goal is to find out whether paroxetine was the main orchestrator behind SURS development in our patient.

CASE DESCRIPTION

A 29-year-old male patient sought medical care for recurrent haematochezia, rectal pain and mucoid discharge of one-month's duration. He denied any family history of gastrointestinal disorders or malignancies. He also denied tenesmus, melena, haematemesis, diarrhoea or constipation. Past surgical history is non-contributory; regarding his past medical history, he began paroxetine (20 mg once daily) therapy two years previously for six months duration, for treatment of generalised anxiety disorder. During this course, patient exhibited symptoms of rectal bleeding and mucoid discharge but disregarded his symptoms, which resolved shortly after his paroxetine course ended. However, one year following his first course of SSRI, the patient's generalised anxiety disorder relapsed, and he consulted his psychiatrist again. He received another course of paroxetine (20 mg once daily), which resulted in recurrence of his rectal symptoms, but they were much more severe and surfaced after three months of treatment. The patient presented to the ER with severe rectal pain and mucoid discharge. He reported having experienced the same symptoms while on his first course of paroxetine, but they were less severe and less frequent. On presentation the abdomen was soft, non-distended, without guarding or rebound tenderness. A review of systems, a complete blood count and inflammatory markers were unremarkable. The patient was referred for a colonoscopy, which showed the presence of a suspicious ulcerated lesion in the rectum *(Fig. 1)*. A biopsy was taken and sent for histopathologic analysis, which revealed fibromuscular obliteration of the lamina propria and hypertrophied muscularis mucosa and glandular crypt abnormalities, yielding the diagnosis of SURS. Subsequently, the patient was recommended lifestyle and dietary modifications. In addition, paroxetine was halted, and the patient continued a course of venlafaxine, a serotonin–norepinephrine reuptake inhibitor, as recommend by his psychiatrist. The patient's symptoms resolved completely, and he did not report any signs of recurrence on follow-up; a follow-up colonoscopy was completely normal.

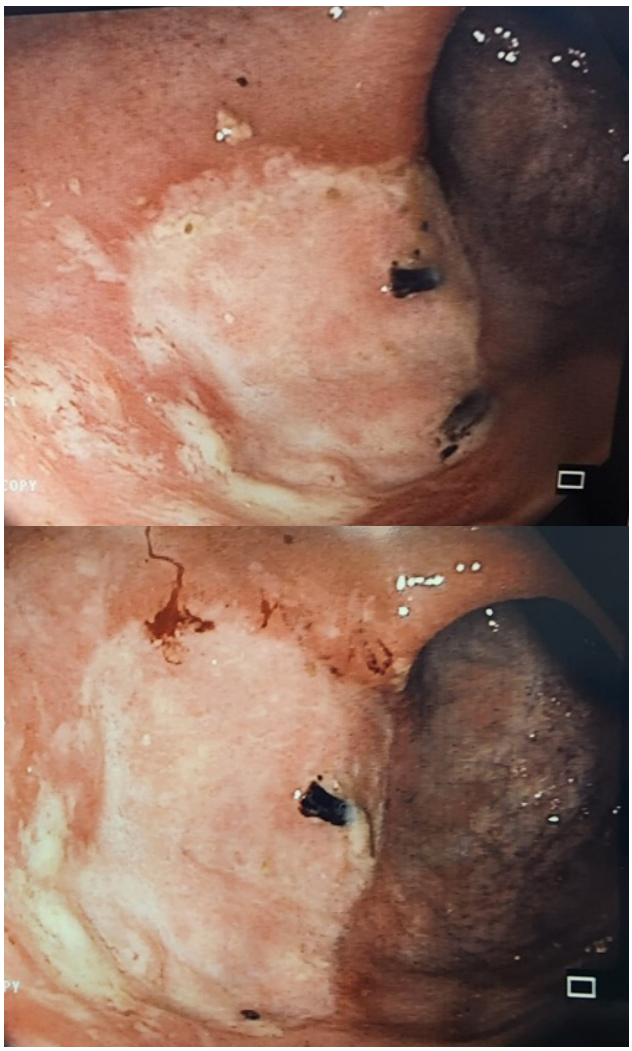

Figure 1. Colonoscopy images showing the ulcerative lesion found in the rectum of our patient.

DISCUSSION

To date, the literature lacks any documented cases of SSRI-induced SURS. Although our case may be a coincidence rather than an actual correlation, it is not a surprising finding, considering that SSRIs are known to cause gastrointestinal bleeding[6]. Paton and Ferrier[6] mention four studies assessing the relationship between SSRI use and GI bleeding. Two studies had odds ratio values of 3.0 (95% confidence interval [2.1–4.4]) and 3.6 (95% confidence interval [2.7–4.7]), implying statistically significant results and showing that SSRI use is associated with an approximative three-fold increase in GI bleed[6].

Literature has offered some mechanisms explaining the relationship between SSRI use and possible GI bleeding. The inhibition of the serotonin transporter protein responsible for the uptake of serotonin by the platelets and the SSRI-induced increase in gastric acidity play major roles in inhibiting platelet aggregation and GI ulceration respectively[7-9]. This association between SSRIs and GI

QUESTIONS	SCORE
1. Are there previous conclusive reports on this reaction?	+1
2. Did the adverse event occur after the suspected drug was administered?	+2
3. Did the adverse reaction improve when the drug was discontinued, or a specific antagonist was administered?	+1
4. Did the adverse reaction reappear when the drug was re-administered?	+2
5. Are there alternative causes (other than the drug) that could have caused the reaction on their own?	0
6. Did the reaction appear when a placebo was given?	0
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1
10. Was the adverse event confirmed by any objective evidence?	+1
TOTAL	**+8**

Interpretation: definite ≥9; probable 5–8; possible 1–4; doubtful 0

Table 1. The Naranjo score[10].

bleeding has been widely reported in the literature, but no case of SSRI-induced SURS has been documented.

In our case we aim to find if there is an association between SSRI use and SURS development and will do so by calculating the adverse drug reaction probability scale (Naranjo score). The Naranjo score was first developed at the University of Toronto in 1981[10]. It is a simple questionnaire that consists of ten separate questions used to assess if a specific clinical outcome was the result of an adverse drug reaction. The Naranjo score components and the findings of our case are illustrated in *Table 1*.

In our case, the Naranjo score was 8, indicating a 'probable adverse drug reaction'. Note that this 'probable' association has some limitations: consideration of other confounding factors, and the lack of prior documented cases make our interpretation questionable. However, the association should not be ruled out and further prospective studies must investigate our suggested correlation.

Little is found in the literature about the pathophysiology of SURS. SURS can present in wide range of overlapping symptoms and clinical findings, which make the diagnosis even harder as well as the treatment strategies[11]. From anal pain, difficult defecation to lower GI bleeding, SURS diagnosis remains challenging[4]. In a study conducted by Gouriou et al., 102 patients with histologically confirmed SURS were included. The study aimed to find clinical characteristics of patients with SURS and find associations between symptom, anatomy and anorectal physiology. It was found that about a third of the participants were females and with psychiatric disorders, mostly anxio-depressive disease[11]. This raises our attention to the possibility of an association between psychiatric disorders and SURS; up until now, this association has still not been studied. According to Gouriou et al, the identification of psychiatric disorders while diagnosing SURS is crucial for the treatment as it requires rehabilitation, dealing with severe pain, and accepting the treatment and diagnosis[11]. All of these would have probably been heightened in psychiatric patients. However, psychiatric disorders might have played a role in the development of SURS rather than affecting the clinical course of the disease. Psychiatric disorders and more specifically mood disorders are associated with change in eating and behavioural habits. These lifestyle modifications would impact gut health and bowel habits—chronic constipation is identified as a major cause in the formation of rectal ulcers and subsequent development of SURS[4]. As an adverse effect of paroxetine or as result of chronic psychiatric disorders, further studies must target this association and find clear interpretations.

CONCLUSION

The pathophysiology and aetiology behind SURS remain obscure. Our case presentation and review of the present literature aim at finding a new potential cause behind SURS. Literature confirms that SSRIs can increase the occurrence of GI ulceration yet focus specifically on upper gastrointestinal bleeding rather than rectal bleeding. A large-scale prospective study involving patients on SSRIs assessing the development of lower GI bleed is needed to confirm or deny our suggested correlation. In addition, the association between SURS and psychiatric disorders needs to be further studied, which might reveal a cause–effect relationship or impact subsequent treatment strategies.

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