Morphological and mucus secretion criteria for
differential diagnosis of solitary ulcer syndrome
and non-specific proctitis

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SUMMARY  Over a four-year period 21 cases of solitary ulcer syndrome (SUS) were studied for their
clinical, histological, and mucus secretion patterns and compared with histological and mucus
secretion patterns of 78 cases of non-specific proctitis collected over the same period. Normal
mucus composition was found in non-specific proctitis while abnormalities of mucins with predomi-
nance of sialomucins were associated with SUS. Although histology remains the most important
investigation in the diagnosis of SUS, mucin changes provide valuable additional evidence.

Solitary ulcer syndrome (SUS) and non-specific proctitis both present with symptoms which are
common to most anorectal diseases.¹–³ The sig-
moidoscopic appearance and particularly the histo-
logical features of the rectal mucosa are used to
differentiate these two conditions. We investigated
the mucin-staining patterns in the rectal biopsies of
patients with these diseases to see if this provided
useful additional information.

Patients and methods

The clinical features were studied closely and the
histology of the rectal mucosa and the mucin secre-
tion patterns were compared, in 78 patients with
non-specific proctitis and 21 cases of SUS, seen over
a four-year period (1975-9). Patients had non-
specific proctitis if on sigmoidoscopy inflammation
was limited to the rectum with normal mucosa
above this and a normal barium enema. All patients
had a rectal biopsy which showed a variable inflam-
matory infiltrate in the lamina propria by mono-
nuclear or mixed cells with occasional crypt abscesses.
Distorted crypts and hyperplasia were also observed.
There was no evidence of ulcerative colitis, Crohn's
disease or an infective type of proctitis. A clinical
diagnosis of SUS was made in patients who had a
normal barium enema but in whom rectal examina-
tion revealed induration and sigmoidoscopy showed
either an ulcer without other evidence of inflamma-
tion or a localised area of hyperaemia with abnormal
perineal descent or prolapse of the rectal mucosa.

All rectal biopsies were routinely fixed in 10%
formol saline and paraffin sections were stained with
haematoxylin and eosin and van Gieson's stain. To
assess the amount and types of mucins the following
techniques were used: periodic acid-Schiff (PAS)⁴
and high iron-diamine-alcian blue (HID-AB)⁵ which
distinguish between neutral, sulpho- and sialomucins.
The histological criteria for SUS¹ were based on the
presence of mucosal ulceration, increased fibroblasts
in the lamina propria with minimal inflammation
and thickened muscularis mucosae with tendency of
individual fibres to point toward the lumen. Distorted
crypts, hyperplasia and mucus depletion were seen
in some cases.

The histology of 21 patients with SUS was
reviewed without the knowledge of previous results
and other clinical details. All cases were then
classified into three groups:
A: Patients with definite clinical diagnosis of SUS
supported by accepted histological criteria.
B: Patients who were suspected to have SUS on
clinical grounds but the histological features were
equivocal.
C: Patients with clinical appearances suggestive of
SUS, in whom the histology showed non-specific
changes.

In the normal rectal mucosa, mucus secretion con-
tains predominantly sulphomucins (normal mucin
Table 1  **Histological features and mucin patterns in 21 cases of solitary ulcer syndrome (SUS)**

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<tr>
<th><em>Histology</em></th>
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<td>Lamina propria</td>
<td>☑</td>
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<td>Fibroblasts</td>
<td>☑</td>
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<td>Smooth muscle</td>
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<td>Inflammation</td>
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<td>Mucosal erosion</td>
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<td>Crypt distortion</td>
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<td>Epithelial hyperplasia</td>
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<td>Thickening of muscularis mucosae</td>
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<tr>
<td>Sialomucins</td>
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Group A, B, C
(see text)

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+ = present.
? = doubtful.
* = Rutter and Riddell (1975).

**Results**

Among the patients who suffered from SUS common symptoms were: rectal and lower abdominal pain; altered bowel habit; increased frequency being commoner than constipation; and passage of mucus rectally which sometimes took the form of rectal discharge. Rectal bleeding was found in 12 cases, single ulcer was seen in nine cases and four patients had a history of attending a psychiatric clinic with depression or anxiety. History of coexisting ano-rectal disease such as fissure in ano, fistulae, piles, or rectal prolapse was found in 10 patients. External prolapse of the rectal mucosa was seen in six cases. Patients with non-specific proctitis had a similar clinical picture except a history of rectal bleeding was invariable. Of 78 patients with non-specific proctitis, 12 had a history of attending a psychiatric clinic and none of them had an associated ano-rectal disease.

The histological features for each of the SUS patients are shown in Table 1. In the 78 cases of non-specific proctitis the morphological changes consisted in hyperaemia, mild to severe inflammatory infiltrate in the lamina propria including neutrophils and formation of crypt abscesses in a few cases, associated or not with decreased mucin secretion, and crypt distortion. In none of the specimens was there erosion, significant increase in fibroblasts or the presence of smooth muscle fibres in the lamina propria. Epithelial hyperplasia was not a feature. No specific causes for the proctitis could be found and both ulcerative colitis and Crohn's disease were excluded.

When the mucus secretion pattern of SUS and non-specific proctitis was compared, marked differences in mucin composition appeared (Table 2).

Mucin secretion in rectal biopsies from patients with SUS was frequently abnormal (Tables 1 and 2). Sialomucins were predominant in all cases in group A (Fig. 1) and in six out of seven cases in group B (the latter patients had suggestive clinical features of SUS but equivocal histology). In contrast, patients in group C showed a normal mucin pattern in six out of eight cases. It is interesting to note that three patients in group A and B who had excessive sialomucins in the initial biopsies showed a normal histology and normal mucins, on subsequent rectal biopsies when they were in remission.

In non-specific proctitis, the pattern of mucin secretion was normal in all but two cases (Figs. 2 and 3; Table 2). On careful review, one of these two cases had a single ulcer seen on sigmoidoscopy without surrounding inflammation and almost certainly had SUS while the second patient showed gross perineal descent.

Mucin secretion was reduced (visual assessment) in a small number of patients with both non-specific proctitis (10 in 72) and SUS (2 in 21).
Fig. 1  Rectal mucosa in solitary ulcer syndrome showing (a) crypt hyperplasia, moderate mucus depletion, increased fibroblasts and muscle fibres pointing toward the lumen (haematoxylin and eosin), (b) mucus contains small amounts of sulphated material revealed by weak high iron-diamine staining and (c) a higher proportion of sialomucins shown in a parallel section stained by the high iron-diamine-alcian blue method. Compare intensity of staining in b with Figs. 2b and 3b × 80.

Fig. 2  Rectal mucosa in active non-specific proctitis showing (a) inflammation in the lamina propria with formation of a small crypt abscess (haematoxylin and eosin), and (b) preservation of mucus secretion which consists mainly of sulphomucins stained strongly with high iron-diamine × 130.
Morphological and mucus secretion criteria for differential diagnosis of solitary ulcer syndrome

From our observations it is clear that SUS and non-specific proctitis present with very similar symptoms, although there was an increased incidence of psychiatric illness and anorectal diseases such as piles, prolapsed rectum, fissure and fistulae in patients with solitary ulcer. The latter fact was also commented upon by Rutter and Riddell and Rutter.2 The value of sigmoidoscopy and rectal biopsy in the diagnosis of SUS is well established1-3 but there remain a number of cases in which histological appearances are not conclusive. The presence of sialomucins further supports the diagnosis of SUS in the presence of suggestive clinical features and equivocal histology as in patients in group B. The differences in mucin patterns with predominance of sialomucins in SUS in contrast with a normal mucus secretion in non-specific proctitis, helps in the differential diagnosis of these two conditions.

At present, the interpretation of the mechanism(s) involved in the mucin changes observed in SUS can only be speculative, as the cause of this entity is as yet unknown.

Some of the histological features, such as tall crypts, high mitotic activity with elongation of the proliferative zone, and decreased mucus secretion but no atypia, suggest a reactive hyperplastic process to mucosal damage. Ischaemia, trauma and alterations in autonomic nerve control have been implicated as possible factors.1 2 These factors may alter the composition of colonic mucus either by a direct effect on glycoprotein synthesis8 7 and/or indirectly through increased proliferative cell capacity.9-10 It is known that changes in glycoprotein synthesis take place along the crypt in parallel with cell differentiation;11 12 neutral mucins or incomplete glycoproteins being synthesised by immature cells which later mature with the addition of acid radicals to the carbohydrate chain.

In SUS the higher proportion of immature cells within the enlarged proliferative crypt zone, possibly associated with decreased or selective uptake of glycoprotein precursors due to ischaemia, could explain the variations in the mucin composition described. Although the role of injury in the quantitative and qualitative changes in mucus production seems valid,10 14 it fails to explain normal patterns of mucus secretion in other conditions causing reactive hyperplasia—for example, (a) in idiopathic proctitis even when inflammation is severe; (b) in reactive as opposed to dysplastic epithelia in ulcerative colitis;15 (c) in reactive hyperplasia at the anastomotic site in rats which had undergone colonic surgery.16 Ischaemia may play a role in the particular mucin changes found in SUS. Mucin studies in ischaemic lesions may help to clarify this point.

Although changes of mucin pattern do not occur in most cases of reactive hyperplasia they have been reported in colonic mucosa in association with malignancy.15 17-21 Increased sialomucins were observed in the "transitional" mucosa adjacent to carcinoma and in patches of uninvolved mucosa distant from it;15 17 22 in familial polyposis coli,23 and in rats with dimethyldihydroza-induced colorectal carcinoma.16 24 These findings strongly suggest an association between abnormal glycoproteins and carcinogenesis, and is supported by biochemical
Solitary ulcer syndrome is the first condition, not associated with malignancy, which shows predominance of sialomucins. This may raise doubts about the value of excess sialomucins as a marker of colonic malignancy. We believe that this is not the case.

The colonic epithelial cells produce a sulphated glycoprotein through a complex process of synthesis involving many sugar precursors and specific enzymes. Many factors can alter this process to produce incomplete or abnormal glycoproteins. At present histochemical methods used to study these changes are of low specificity and only distinguish between neutral, sulphated and acid non-sulphated sialomucins but give no information on the other components of the carbohydrate molecule. Further investigation is needed to find a profile of the changes which may occur in the various sugars and sialic acid derivatives in different conditions, before the value of mucin patterns to differentiate a reactive from a neoplastic process can be firmly established.

As a conclusion, variations in mucin composition seem to be a useful parameter to differentiate SUS from non-specific proctitis, and may also help in the diagnosis of SUS when histology is equivocal.

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References

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