Case Report

A case of acute radiation enteritis

—recommendation to perform colonoscopy together with histopathological examination—

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(Received: July 26, 2017; Accept: August 15, 2018.)

Abstract

Acute radiation enteritis is often self-limiting and reversible as long as radiotherapy ceases within a short period. Colonoscopy is thus rarely performed and the endoscopic findings have not been fully investigated. We encountered a case of acute radiation enteritis in which colonoscopy was performed. The patient was a 68-year-old man with prostatic cancer under hormone therapy. Back pain due to metastasis to the pelvic area developed, and radiotherapy was adopted. However, watery diarrhea began 4 days after the initiation of radiotherapy. Colonoscopy revealed mucosal erythema, edema, and epithelial friability with mucus adhesion in the sigmoid colon. Biopsied specimens showed shedding of superficial epithelium, atrophy of crypts, and infiltration of inflammatory cells into the lamina propria. On the basis of endoscopic and histopathological findings as well as the clinical pictures, acute radiation enteritis was diagnosed. Symptoms gradually improved after radiotherapy was suspended. Follow-up colonoscopy confirmed recovery to normal-appearing intestinal mucosa. When symptoms suggestive of colitis develop shortly after initiating radiotherapy, colonoscopy together with histopathological examination should be actively performed to achieve definitive diagnosis of acute radiation enteritis.

Introduction

Radiotherapy is utilized in the treatment of malignant tumors. However, radiation-related disorders often develop in the intestine, secondary to irradiation to the abdominal area especially to the pelvis. Such complications are generally classified into two subtypes: early disorder related directly to the radiation, and characterized by epithelial cell damage; and late disorder related to secondary disturbances in the microcirculation, and characterized by arteriosclerosis and fibrosis. Such disorders have been termed acute and chronic radiation enteritis, respectively.²

Acute radiation enteritis develops shortly after starting radiotherapy. Abdominal pain and diarrhea develop in 20-70% of patients within the first 2 weeks of treatment. As for the correlation between radiation dose and onset of symptoms, the irradiation threshold is reportedly 30-60 Gy. Symptoms are often self-limiting and improve on cessation of treatment.²³⁻⁵. Radiation injures the intestinal mucosa, causing epithelial atrophy and mucosal blood flow reduction.⁶ However, the intestinal epithelium can regenerate from stem cells present in the base of crypts when radiotherapy is

Keywords: Acute radiation enteritis, Colonoscopy, Diarrhea, Radiotherapy
suspended within a short period. In contrast, chronic radiation enteritis develops several months after completing radiotherapy, and is associated with irreversible outcomes\(^5\).

Endoscopic and pathological findings have been precisely reported and diagnostic criteria for chronic radiation enteritis have been established\(^6\). On the other hand, not only the diagnostic criteria but also detailed findings concerning acute radiation enteritis have yet to be fully reported\(^7\). This is probably because patients rarely have opportunities to undergo colonoscopy due to the reversible pathogenic features described above.

We present herein a case of acute radiation enteritis in which colonoscopy was performed, and compared the findings with the few previously reported cases\(^11,12\), and discuss the features of endoscopic findings referring to the histopathological findings.

**Case report**

A 68-year-old man presented to the urology department of our hospital complaining of poor urinary flow, frequent urination, and weakness of the lower limbs. He was diagnosed with prostatic cancer via prostate biopsy, and hormone therapy was commenced. Back pain developed during treatment. Bone scintigraphy revealed metastasis to the pelvis, and radiotherapy was initiated. However, watery diarrhea at a frequency of more than 20 times/day developed 4 days after starting radiotherapy. Although the patient showed no abdominal pain or hematochezia, diarrhea did not improve. He was then referred to our department of gastroenterology. Laboratory studies revealed a high serum level of prostate-specific antigen level at 3,664 ng/ml (reference range, <3.0 ng/ml), consistent with the presence of prostatic cancer. The serum concentration of alkaline phosphatase was also high at 660 IU/L (reference range, 100-325 IU/L), suggestive of metastasis to the pelvic bone. No significant pathogenic bacteria were detected in fecal cultures. Administration of antidiarrheal agents proved ineffective.

Colonoscopy was performed 7 days after the onset of diarrhea. Findings included mucosal erythema, edema, and epithelial friability with mucus adhesion in the sigmoid colon (Fig. 1). Epithelial biopsies were examined histopathologically, revealing atrophic or nearly absent

![Fig. 1](image)  
**Fig. 1** Colonoscopy performed 7 days after onset of diarrhea, showing erythematous and edematous mucosa with mucus adhering to the epithelium of the sigmoid colon.

![Fig. 2](image)  
**Fig. 2** Histology of a biopsied specimen from the sigmoid colon. A) Photomicrograph showing injured glands scattered (arrows) in the mucosa (hematoxylin and eosin stain, 100 × original magnification). B) Photomicrograph showing irregular nuclear changes in flattened epithelial cells (arrows) (hematoxylin and eosin stain, 400 × original magnification).
mucosa comprising small, irregular glands with mucous depletion. Epithelial cells were flattened with bizarre changes in unclear appearance. Mild infiltration of neutrophils, lymphocytes and plasma cells into the mucosal lamina propria was observed, and crypt abscesses were also identified in the injured glands (Fig. 2). Acute radiation enteritis was diagnosed on the basis of these endoscopic and histopathological findings, as well as the fact that symptoms had developed shortly after the initiation of radiotherapy. After radiotherapy was suspended, the frequency of diarrhea decreased and the symptom resolved completely by 14 days after cessation of irradiation. Colonoscopy performed 2 months after suspending radiotherapy showed normal appearance of the intestinal mucosa.

**Discussion**

Chronic radiation enteritis comprises irreversible changes caused by microcirculation injury due to arteriosclerosis and fibrosis. Various endoscopic findings have been reported, leading to the proposal of several endoscopic classifications. On the other hand, few reports have described endoscopic findings concerning acute radiation enteritis. Acute radiation enteritis is often overlooked because the symptoms are likely to be mild and reversible when treatment is ceased within a short period. To the best of our knowledge, four case reports published since 2000 have described cases of acute radiation enteritis (Table 1). However, endoscopic findings were described in only two of these, showing mucosal erythema, edema, and pallor with friability. In our institution, more than 100 patients each year receive radiotherapy to the pelvic area. Most of those patients actually suffer from mild diarrhea within the first 2 weeks of treatment. However, none of those patients had undergone colonoscopy or discontinuation of radiotherapy in the last 3 years until the present case was encountered.

Although the mechanisms of acute radiation enteritis have not yet been fully elucidated, irradiation causes radiation-related intestinal damage through the induction of proinflammatory cytokines. Recently, injury to the endothelium of the microvasculature supplying the intestine has also been reported as contributory. Histopathological changes observed in acute radiation enteritis include the following: transient mucosal atrophy, submucosal edema, infiltration of polymorphonuclear leukocytes and plasma cells to the lamina propria, and crypt abscess in the deep epithelium. Karyorrhexis is seen in nuclei with mitotic arrest. However, epithelial cells can regenerate to regress when the submucosal damage is not particularly severe. Ulceration or fibrosis thus rarely develops in acute radiation enteritis. Reflecting these pathological features, the endoscopic findings could be diffuse mild inflammation characterized by mucosal erythema and edema. The present case also showed crypt abscesses on pathological examination with mucous secretion from the crypts, reflected by mucus adhering to the epithelial mucosa on colonoscopy. The lack of correlation between some of the endoscopic and pathological findings might thus have been partly due to the reversibility of inflammation from acute radiation enteritis.

Meanwhile, patients who require radiotherapy tend to be compromised hosts with impaired immune function, which is also reduced by the administration of anticancer drugs. Acute radiation enteritis should thus be differentiated from both the cytomegalovirus (CMV)

<table>
<thead>
<tr>
<th>Author</th>
<th>Site of lesion</th>
<th>Endoscopic findings</th>
<th>Symptoms</th>
<th>Interval from start of radiotherapy to onset</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetreault-Lafamme et al. 2015 [12]</td>
<td>Sigmoid colon</td>
<td>Thickening sigmoid wall with edema, and telangiectasia</td>
<td>Abdominal pain, diarrhea</td>
<td>Not described</td>
<td>Surgery</td>
</tr>
<tr>
<td>Ue et al. 2016 [14]</td>
<td>Small intestine</td>
<td>Not described</td>
<td>Abdominal pain</td>
<td>24 days</td>
<td>Surgery</td>
</tr>
</tbody>
</table>
enteritis likely to develop in compromised hosts, and drug-induced enteritis caused by taking anticancer drugs. The ability to discriminate acute radiation enteritis from these diseases on the basis of endoscopic and pathological findings would thus be useful. CMV enteritis displays erosion or ulcer as one of the diagnostic criteria on colonoscopy, and requires pathological and/or serological confirmation. Colitis arising secondary to administration of anticancer drugs often shows ulcers extending longitudinally on colonoscopy and ischemic changes on histopathological examination. In the present case, none of these findings suggestive of CMV enteritis or drug-induced enteritis were observed.

On the contrary, endoscopic and pathological criteria to diagnose acute radiation enteritis have yet to be fully established. Findings observed in the present case were consistent with those reported previously. Mucosal erythema, edema, epithelial friability, and possibly mucus adhesion might be characteristics of acute radiation enteritis on colonoscopy. Accumulation of more cases would help establish the diagnostic criteria for examinations. However, the essential factor in the diagnosis of acute radiation enteritis is the fact that the patient is receiving radiotherapy.

Conclusion

The present case suggests that colonoscopy together with subsequent histopathological examination should be actively performed to reach a definitive diagnosis of acute radiation enteritis when symptoms suggestive of colitis such as diarrhea develop shortly after the initiation of radiotherapy.

References

急性放射線性腸炎の1例
——大腸内視鏡検査と病理組織学的検査施行の報告——

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池崎 修1) 三井 達也1) 三浦 みき1) 櫻庭 彰人1) 
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急性放射線性腸炎は自臨内であり放射線治療の終了とともに改善することが多い。このため大腸内視鏡検査が行われることは稀であり、その内視鏡所見が詳細にまとめられた報告は少ない。今回、急性放射線性腸炎で大腸内視鏡検査を施行した1例を経験した。症例は前立腺癌に対するホルモン療法中であった68歳の男性である。骨盤転移による下痢が出現し、放射線治療が開始された。治療4日後から水様性の下痢が始まり、大腸内視鏡検査を施行したところ、S状結腸の粘膜は発赤し浮腫状で、易出血性であり、粘液も付着していた。生検による病理組織では、表層上皮が脱落し間質は萎縮、また粘膜固有層に炎症細胞浸潤が認められた。臨床経過と内視鏡および病理組織所見より急性放射線性腸炎と診断した。放射線治療の中止により症状は次第に改善し、中止14日後の大腸内視鏡検査でも正常粘膜に復していることを確認した。放射線治療の開始後早期に腸炎症状が出現した時は、病理組織学的検査を含む大腸内視鏡検査を積極的に行い、急性放射線性腸炎の確定診断に努めるべきである。

Keywords: 急性放射線性腸炎，大腸内視鏡，放射線療法，下痢