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# Small bowel perforation after radiotherapy for cervical carcinoma

## 以放射治療法醫治子宮頸癌後出現小腸穿孔

Radiotherapy is the treatment of choice for carcinoma of the uterine cervix. We report on a 62-year-old Chinese woman with cervical carcinoma, in whom a small bowel perforation developed 5 months after radiotherapy. Ten centimetres of small bowel, including the perforation site, were resected. No bowel adhesion was detected during the operation. The postoperative course was uneventful, and the patient was discharged home 7 days after surgery. Histological examination confirmed post-irradiation injury. The presenting complaints of patients with bowel perforation following radiotherapy vary, and signs of peritonitis may be absent. Emergency physicians must be alert for these complications in patients who have been treated with radiotherapy.

放射治療是治療子宮頸癌的首選方法。我們報告一名 62 歲患子宮頸癌的華裔婦 人,在完成放射治療後五個月出現小腸穿孔。該小孔以及附近10厘米的部位均以 手術切除;過程中未有發現孔粘連的情況。病人在手術後接受常規治療,並於手術 後第七天出院。組織學檢查確定該穿孔是照射造成的損傷。因接受放射治療而出現 腸穿孔的患者,其徵狀各有不同,患者亦可能不會出現腹膜炎症狀。急症室醫生為 曾接受放射治療的病人診斷時,必須加倍警惕上述併發症的出現。

### **Case report**

A 62-year-old Chinese woman presented to the Accident and Emergency Department at the North District Hospital in May 2002 because of the sudden onset of colicky pain in the lower abdomen. She had a history of carcinoma of the cervix and had completed a course of radiotherapy 5 months before presentation; she had not undergone abdominal surgery. In addition, the patient had consulted with a private practitioner shortly before presentation, and had received an analgesic intramuscularly.

At the time of presentation, there was no vomiting, diarrhoea, constipation, urinary symptoms, vaginal discharge, or adnexal tenderness. Physical examination revealed a body temperature of 37.5°C, blood pressure of 157/60 mm Hg, and heart rate of 64 beats per minute. The abdomen was soft and bowel sounds were audible; tenderness was detected over the lower abdomen, but loin tenderness was absent. Urinalysis showed a leukocyte level of 10 to 25 /µL and a protein level of 5 g/L. The patient was given an intramuscular injection of ketorolac 30 mg for pain relief, and she was admitted to the observation ward because of persistent lower abdominal pain. The provisional diagnosis was lower urinary tract infection. The differential diagnosis included recurrence of cervical carcinoma, early-stage appendicitis, and non-specific abdominal pain.

After 4 hours of observation, the patient's abdominal pain partially resolved. However, a fever developed, as did tenderness and distention of the lower abdomen. Abdominal ultrasonography revealed free fluid in Morrison's pouch and among dilated loops of bowel (Fig 1). The chest X-ray showed free gas under the right hemi-diaphragm and a dilated bowel (Fig 2).

The patient was admitted to the surgical ward with a provisional diagnosis of peritonitis. Laparotomy was performed and showed a 0.5-cm perforation in the distal jejunum. A large amount of turbid fluid was present in the peritoneal cavity.

#### Key words:

Cervix neoplasms; Intestinal perforation; Peritonitis; Radiotherapy

#### 關鍵詞:

子宮頸癌; 腸穿孔; 腹膜炎; 放射療法

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Fig 1. Abdominal ultrasonogram showing free peritoneal fluid and dilated bowel

There were post-irradiation changes of part of the ileum and jejunum. Ten centimetres of small bowel, including the perforation site, were resected, and no bowel adhesion was detected during the operation. The postoperative course was uneventful, and the patient was discharged home 7 days after surgery.

Histological examination of the resected specimen showed a 5-mm transmural perforation. The intestinal wall around the perforation appeared friable and haemorrhagic. There were no enlarged lymph nodes. Microscopic examination showed transmural necrosis of the intestinal wall at the perforation site, with granulation tissue, submucosal fibrosis, and abnormal stromal cells around the site. The submucosal vessels showed intimal thickening, foamy histiocyte aggregations, and hyalinisation of the muscular wall. These changes were compatible with postirradiation injury of the gastrointestinal tract—in particular, with late-stage injury—that is, intimal hyperplasia and collagenous hyalinisation with thickening of the media layer of vascular wall.<sup>11</sup>

#### Discussion

Gastrointestinal complications of radiotherapy are classified into two distinct groups: early complications, which occur during or immediately after treatment, and late complications, which can occur months or years after radiotherapy. Late complications, such as bowel obstruction or perforation, or fistula formation, are thought to be secondary effects of radiation-induced endarteritis and diffuse collagen deposition. Fibrotic change in the submucosal and subserosal layers is another factor leading to late-stage complications of irradiation.

Late-stage complications may appear from a few months to 20 years or more after radiation therapy.<sup>1,2</sup> A retrospective study by Ramirez et al<sup>3</sup> showed that the median time to sigmoid perforation following radiation therapy for cervical



Fig 2. Chest X-ray showing free gas under diaphragm

carcinoma was 13 months (range, 3-98 months). The mean time from the onset of gastrointestinal symptoms to perforation was reported in the same study to be 90 days. In contrast, Sher and Bauer<sup>4</sup> and Rao et al<sup>5</sup> reported cases of acute perforation with a 14-year latency period. Sher and Bauer<sup>4</sup> even reported a case of perforation that occurred 37 years after radiotherapy.

Many factors influence the development of complications following radiotherapy.<sup>1,2,4,6</sup> The dose and type of radiation, the use of chemotherapy, and the combined use of external beam and intracavitary radiation are important factors. Patients with a history of abdominal surgery, pelvic inflammatory disease, or diverticulosis are also more susceptible than others to experience radiation-induced bowel complications. One mechanism that complications arise may be that after abdominal surgery or infection, adhesions may form, which may reduce bowel motility and hold a portion of bowel in an unfavourable position during radiotherapy.<sup>6</sup> Shibata et al<sup>2</sup> found that 33% of patients with complications of radiotherapy had previously undergone abdominal surgery. Other predisposing factors include underlying cardiovascular diseases. For example, DeCosse et al<sup>7</sup> demonstrated a significant association between hypertension, diabetes, and cardiovascular disease and the subsequent development of radiation enteritis.

The presentation of bowel perforation after radiotherapy varies. According to Ramirez et al,<sup>3</sup> only 19% of the patients showed signs of acute peritonitis. Abdominal pain was a

common complaint but only 9% of patients described it as severe. Marks and Mohiudden<sup>10</sup> attributed the delay in presentation of acute symptoms to possible encasement of the viscera by fibrinous envelopes that coat and insulate the peritoneum. As a result, peritonitis is partially or completely masked, perhaps explaining the atypical presentation of the patient in our case.

The presenting complaints of patients with bowel perforation following radiotherapy vary and tend to be atypical. Signs of peritonitis may be equivocal or even absent. Thus, emergency physicians must consider this disease entity as a possible complication among patients who have been treated with radiotherapy.

#### References

- Deitel M, Degani C, Alexander MA. Major gastrointestinal problems after radiotherapy: management and nutritional considerations. Int Surg 1977;62:334-7.
- 2. Shibata HR, Freeman CR, Roman TN. Gastrointestinal complications

after radiotherapy for carcinoma of the uterine cervix. Can J Surg 1982; 25:64-6.

- Ramirez PT, Levenback C, Burke TW, Eifel P, Wolf JK, Gershenson DM. Sigmoid perforation following radiation therapy in patients with cervical cancer. Gynecol Oncol 2001;82:150-5.
- 4. Sher ME, Bauer J. Radiation-induced enteropathy. Am J Gastroenterol 1990;85:121-8.
- Rao SP, Anderson V, Shlasko E, Miller ST, Choi K, Rabinowitz S. Intestinal perforation 14 years after abdominal irradiation and chemotherapy for Wilms tumour. J Pediatr Hematol Oncol 1996;18:187-90.
- Maruyama Y, Van Nagell JR Jr, Utley J, Vider ML, Parker JC. Radiation and small bowel complications in cervical carcinoma therapy. Radiology 1974;112:699-703.
- DeCosse JJ, Rhodes RS, Wentz WB, Reagan JW, Dworken HJ, Holden WD. The natural history and management of radiation induced injury of the gastrointestinal tract. Ann Surg 1969;170:369-84.
- Galland RB, Spencer J. Natural history and surgical management of radiation enteritis. Br J Surg 1987;74:742-7.
- 9. Meissner K. Late radiogenic small bowel damage: guidelines for the general surgeon. Dig Surg 1999;16:169-74.
- Marks G, Mohiudden M. The surgical management of the radiationinjured intestine. Surg Clin North Am 1983;63:81-96.
- Environmental and nutritional diseases. In: Cotran RS, Kumar V, Robbins SL. Robbin pathologic basis of disease. 5th ed. Philadelphia: WB Saunder; 1994:405.