CASE REPORT

Does chronic radiation enteritis pose a diagnostic challenge? A report of three cases

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We present three cases of late radiation enteritis, all admitted through the accident and emergency unit and managed in the surgical department. All presented with acute symptoms. Two had abdominal pain, nausea, and vomiting and in these two cases, plain radiology and computed tomography scans demonstrated small bowel obstruction. Exploratory laparotomies confirmed chronic radiation damage to the small bowel. The affected areas were resected and anastomoses were performed. The postoperative course was uneventful. The other patient presented with bleeding per rectum and a colonoscopy with biopsy of the rectum confirmed proctitis and radiation enteritis. This patient was treated conservatively and responded well. The key factor needed for successful diagnosis and management of chronic radiation enteritis is a high index of suspicion leading to appropriate use of imaging.

Introduction

About 15 to 20% of cancer patients currently receive radiotherapy in western countries including the United Kingdom. More efforts are now made to reduce or prevent radiation enteropathy, which develops in 5 to 20% of patients following abdominal and pelvic radiation.[1] In the past, preventive measures were not well developed, so we expect to see more patients with late radiation enteropathy. While immediate radiation effects manifest as acute gastro-intestinal symptoms and can be easily diagnosed, chronic effects present as vague symptoms and pose a major diagnostic challenge. We present three patients with complicated radiation enteropathy. Reaching the diagnosis was dependent on having a high index of suspicion and performing appropriate investigations.

Case report

Case 1

A 62-year-old man was admitted in February 2007 to the accident and emergency unit with a 3-day history of upper abdominal pain. He had a history of similar episodes over several years that had been investigated by the physicians with a range of tests that failed to determine the cause of his chronic pain. A diagnostic laparoscopy performed at that time showed scattered vasculitis of the terminal ileum, and no further surgical action was advised. He had a surgical history of a seminoma of the testis treated with deep X-ray therapy in 1975. The usual dose at that time was 3000 rad fractionated over 6 weeks targeting the pelvis and para-aortic lymph nodes.

On physical examination, he had a distended, soft abdomen with tenderness in the central and upper quadrants. There was no guarding, the bowel sounds were hyperactive and the rectal examination was normal. A full blood count showed mild anaemia (haemoglobin, 102 g/L). A plain X-ray of the abdomen revealed dilated small bowel loops, air in the large bowel and rectum, with some faecal loading. An abdominal computed tomographic (CT) scan confirmed a distal small bowel obstruction due to localised strictures, at which thickening of the terminal ileum wall was seen. On exploratory laparotomy, we found dilated small bowel loops up to a tight stricture located 50 cm from the ileocaecal (IC) valve. Another stricture was found 40 cm from the IC valve, with a contracted segment of bowel distal to the stricture (Fig a, b). The caecum and the rest of the bowel were normal. 50 cm of the affected terminal ileum was resected and an end-side ileocaecal anastomosis and appendectomy were performed. His recovery was uneventful, apart from loose bowel motions, and he was discharged home in good condition. A histological examination of the resected specimen revealed late radiation enteritis (RE).

Case 2

In August 2007, a 64-year-old woman presented with acute central abdominal pain

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從三個病例看慢性放射性腸炎是否難以診斷

本文報告三個晚期放射性腸炎的病例，所有病者都是由醫院急症室接收，並由外科治療。病者均有急性症狀，其中兩人出現腹痛、噁心和嘔吐，放射檢查和電腦斷層掃瞄顯示有小腸梗阻。開腹確定小腸受放射性腸炎破壞後，把受影響的小腸切除，並施以吻合術，術後康復過程順利。餘下一位病者則有便血，結腸鏡檢查及直腸活組織檢查證實患直腸炎和放射性腸炎，醫生採取保守的治療措施，病情進展良好。要準確診斷和治療慢性放射性腸炎，關鍵因素在於對病症高度警覺，採取懷疑的態度，加以適當運用成像術。

associated with nausea and vomiting. She had experienced recurrent episodes of abdominal pain over the past 7 years. She had been treated with fractionated external beam radiotherapy 27 years ago for ovarian carcinoma during which she received 3000 rad over 2 months.

On examination, her abdomen was distended and soft, with tenderness around the umbilicus, and her bowel sounds were hyperactive. A CT scan of the abdomen showed a thick small bowel wall with dilated proximal loops, and Crohn's disease was reported as the most likely cause. A magnetic resonance imaging enteroclysis revealed no abnormalities but a small bowel enema showed a relatively long stricture of the ileum (Fig c, d). At exploratory laparotomy the caecum and a segment of terminal ileum were found to be abnormal. Resection of the diseased caecum and terminal ileum was performed and an ileo-colic side-side anastomosis was accomplished. The patient developed a wound infection postoperatively, which was treated with free drainage and dressing and she recovered progressively. A histological examination of the resected bowel revealed late RE.

Case 3

A 70-year-old man presented in October 2007 with a first episode of fresh rectal bleeding 3 years after undergoing radiotherapy for prostatic carcinoma. He was given the standard treatment, including external radiation and bilateral 120-degree rotational arcs, with portals leaving 2-cm margins around the prostate to deliver 68-70 Gy to the prostate was the standard treatment. He also gave a history of chronic irregular bowel motions, lower abdominal cramps, and tenesmus.

Physical examination revealed a pale, obese man with no chest and abdominal abnormalities. A digital rectal examination indicated rectal fresh bleeding, irregular upper anal and lower rectal mucosa and definite prostate irregularities consistent with prostate cancer. He had mild anaemia, and an inconclusive abdominal radiograph. A CT scan and colonoscopy confirmed a thickening of the rectum and proctitis (Fig e, f). Histological examination of rectal biopsy specimens revealed RE. The patient was treated conservatively and recovered without further bleeding.

Discussion

Radiation enteritis is a known complication of

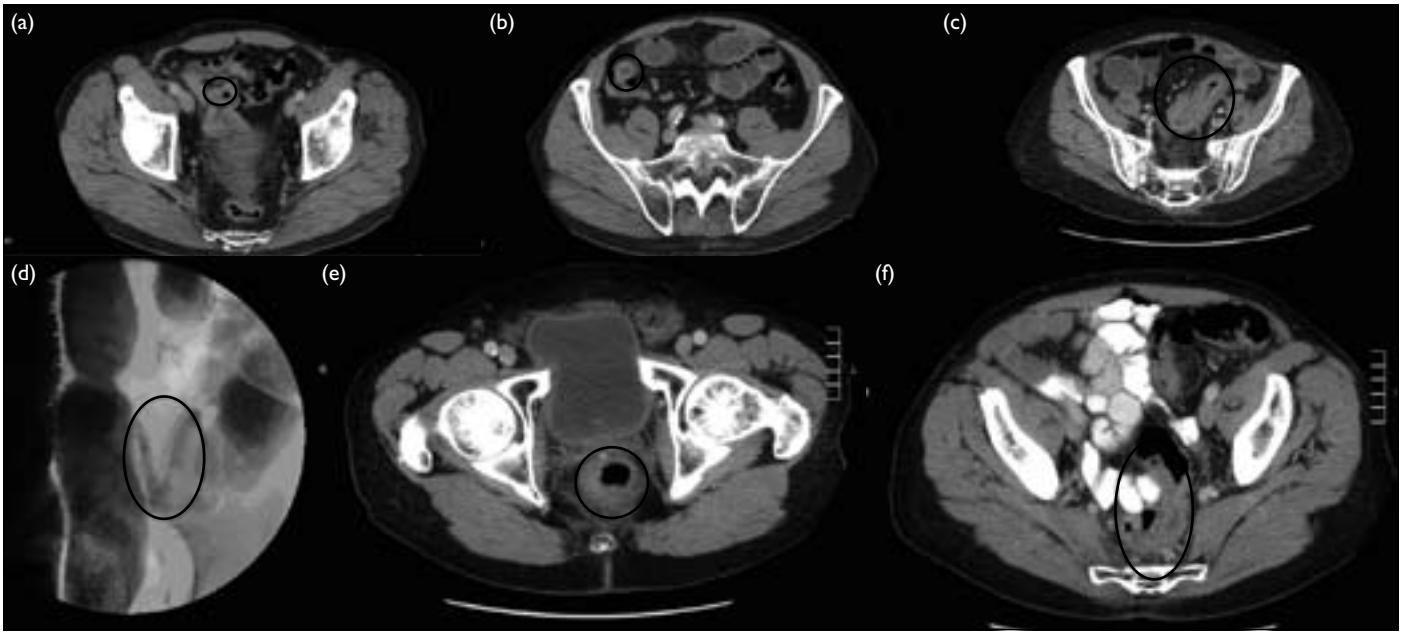

FIG. Computed tomographic scans
Case 1: showing (a) terminal ileum stricture (encircled) and (b) terminal ileum stricture (encircled) and adjacent dilated ileum loop; case 2: showing (c) thickened small bowel wall (encircled), dilated small bowel loops and (d) gastrograffin study showing a long small bowel stricture (encircled); case 3: showing (e, f) thick rectal wall (encircled)

radiotherapy to the gastro-intestinal tract. Despite high initial mortality and morbidity rates, life expectancies among patients with chronic RE and no recurrence of their neoplastic disease are good.[2] The incidence of RE has not been well documented but about 15% of patients are expected to develop a chronic problem. Another group will develop acute and self-limiting enteritis.[3] Although radiation therapy affects all layers of the bowel wall, radiation damage is more intense in the mucosa due to its rapid cellular proliferation.[4] It can induce a break in the cell cycle with subsequent villous atrophy and an acute inflammatory response and fibrosis. Alternatively, damage to low turnover cells (including stromal cells, smooth muscle and endothelium) in conjunction with progressive, obliterative vasculitis (which induces tissue ischaemia from vessel thrombosis) leads to fibrosis and necrosis of the bowel wall.[1]

Chronic RE can be a progression from acute RE or a late event, both of which can be directly related to dose fractionation frequency, field size, and mode of delivery (ie whether intracavity, brachytherapy, or external beam therapy). The incidence of RE increases significantly when chemotherapy (such as 5-fluorouracil or cisplatin) is used concurrently. The increased level of CTGF protein and mRNA associated with the accumulation of fibroblasts/myofibroblasts and collagen deposition are fibrogenic signals involved in the persistence of late intestinal radiation fibrosis.[5,6] The sections most frequently affected are the lower ileum, caecum, and rectosigmoid; the midgut and transverse colon are usually free of radiation effects.[7]

The presentation of RE is reflective of the stage of the disease. In acute RE, the patient usually has abdominal pain, nausea, vomiting, diarrhoea, and abdominal distension. In the chronic form, the main symptoms are those of intestinal obstruction followed by fistula formation, perforation, and bleeding. Some patients become underweight, and develop pernicious anaemia due to a malabsorption syndrome caused by chronic intestinal failure.

While the diagnosis of acute RE is usually straightforward, making a chronic RE diagnosis can be very challenging, especially when the presentation is late. The level of diagnostic challenge is related to the RE sites. As seen in the third case, there is no difficulty making an early diagnosis of radiation-induced proctitis. In the first two cases, however, the diagnosis was made late and was challenging because the RE was in the small bowel. A detailed history of the patient's radiation therapy course is a crucial component when assessing such a patient and reaching the right diagnosis. Early endoscopy may demonstrate friable mucosa, which later becomes dusky with oedema and inflammation or pale with telangiectatic vasculature. Smooth fibrotic strictures may be evident in chronic disease.[8]

Computed tomography is very helpful, as it shows up the diseased segment with a thickened wall and dilated proximal loops.[9] It may show strictures and can be used to exclude other bowel pathologies. Mechanical obstruction induced by adhesion bands and inflammatory disease such as Cohn's disease can have a similar CT appearance so differentiating RE from other pathologic conditions can be difficult unless patients give a good history of radiation therapy. Recent advances in diagnostic modalities such as capsule endoscopy can be also very helpful for diagnosing RE.[10] An incomplete series of investigations may lead to a delayed diagnosis of RE. This was the case with the first patient who underwent upper gastro-intestinal tests including several gastroscopies before referral. In the second case the patient presented with symptomatic RE to a gynaecologist because of her history of ovarian cancer. This led to a delayed diagnosis as gynaecological problems were excluded and RE was not considered. An early presentation to a surgeon can lead to an early diagnosis and definitive management, as happened in the third case.

Acute RE is usually managed conservatively and it is advisable to involve the radiation therapy physician. Resting, and slowing down bowel movement using medications, diet modification and, when needed, total parenteral nutrition[11,12] are useful measures. In chronic RE, the management is challenging. Marshall et al[1] reported the use of hyperbaric oxygen as a treatment for chronic RE and found a total response rate of 68% (43% complete and 25% partial response rate). Surgery is usually reserved for cases of chronic RE complicated by intestinal obstruction, enterocutaneous fistulae, intestinal stenosis, intestinal bleeding, and intestinal perforation.[13] Stricturoplasty may be an effective and safe means of conserving intestinal length in certain carefully selected patients with chronic RE and small-bowel strictures.[14] Bypass surgery is indicated in some patients, while in other patients, resection and primary anastomosis may be an appropriate choice.[15] Some authors even advocate a generous surgical resection rather than a conservative approach to chronic RE.[16]

Radiation proctitis-induced bleeding may settle spontaneously, while severe haemorrhagic radiation proctitis may require repeated blood transfusions. Argon plasma coagulation is a good option that reduces the bleeding in 80 to 90% of patients and even alleviates diarrhoea and urgency.[17]

Prevention of radiation enteritis

Data indicate that radioprotectant agents or measures have the potential to reduce intestinal mucosal injury

and may reduce both the acute and chronic side-effects of radiotherapy.[18] It has been reported that various surgical techniques such as the use of vicryl mesh and multifield irradiation can prevent acute and chronic RE. Pelvic exclusion using an intrapelvic silicone breast prosthesis[19,20] is another approach. Conformal radiotherapy can reduce the radiation dose to the adjacent structures and hence the risk of complications. In this type of radiation therapy, metal blocks are put in the path of the radiation beam, thus reducing damage to nearby structures and delivering a high dose to the tumour. The shape of the treatment volume is changed in three dimensions from a cuboidal structure to a sphere or a cylinder, thereby leading to a reduction in the treated volume of around 30% to 50%; all of this reduced volume is radiation affecting normal tissue.[21] These strategies should be considered in order to reduce or prevent RE.

Radiation enteritis can be a challenging condition and one that is difficult to diagnose, especially in a late presentation. Surgeons and physicians should suspect RE if there is a history suggestive of past radiotherapy. Surgery is the treatment of choice for complicated RE.

References

1. Marshall GT, Thirlby RC, Bredfeldt JE, Hampson NB. Treatment of gastrointestinal radiation injury with hyperbaric oxygen. Undersea Hyperb Med 2007;34:35-42.
2. Touboul E, Balosso J, Schlienger M, Laugier A. Radiation injury of the small intestine. Radiobiological, radiopathological aspects; risk factors and prevention [in French]. Ann Chir 1996;50:58-71.
3. Regimbeau JM, Panis Y, Gouzi JL, Fagniez PL; French University Association for Surgical Research. Operative and long term results after surgery for chronic radiation enteritis. Am J Surg 2001;182:237-42.
4. Fajardo LF. Pathology of radiation injury. New York: Mason publishers; 1982:47-76.
5. Vozenin-Brotons MC, Milliat F, Sabourin JC, et al. Fibrogenic signals in patients with radiation enteritis are associated with increased connective tissue growth factor expression. Int J Radiat Oncol Biol Phys 2003;56:561-72.
6. Nguyen NP, Antoine JE, Dutta S, Karlsson U, Sallah S. Current concepts in radiation enteritis and implications for future clinical trials. Cancer 2002;95:1151-63.
7. Meissner K. Late radiogenic small bowel damage: guidelines for the general surgeon. Dig Surg 1999;16:169-74.
8. Vasudeva R, Elraie K. Intestinal radiation injury. E-medicine website: http://www.emedicine.com/med/topic1184.html. Accessed Mar 2007.
9. Chen S, Harisinghani MG, Wittenberg J. Small bowel CT fat density target sign in chronic radiation enteritis. Australas Radiol 2003;47:450-2.
10. Romero Vázquez J, Caunedo Alvarez A, Rodríguez-Tellez M, Sánchez Yagüe A, Pellicer Bautista F, Herrerías Gutiérrez JM. Previously unknown stricture due to radiation therapy diagnosed by capsule endoscopy. Rev Esp Enferm Dig 2005;97:449-54.
11. Gavazzi C, Bhoori S, Lovullo S, Cozzi G, Mariani L. Role of home parenteral nutrition in chronic radiation enteritis. Am J Gastroenterol 2006;101:374-9.
12. Scolapio JS, Ukleja A, Burnes JU, Kelly DG. Outcome of patients with radiation enteritis treated with home parenteral nutrition. Am J Gastroenterol 2002;97:662-6.
13. Li N, Zhu WM, Ren JA, et al. Surgical management of chronic radiation enteritis [in Chinese]. Zhonghua Wai Ke Za Zhi 2006;44:23-6.
14. Dietz DW, Remzi FH, Fazio VW. Strictureplasty for obstructing small-bowel lesions in diffuse radiation enteritis—successful outcome in five patients. Dis Colon Rectum 2001;44:1772-7.
15. Tsai MS, Liang JT. Surgery is justified in patients with bowel obstruction due to radiation therapy. J Gastrointest Surg 2006;10:575-82.
16. Perrin H, Panis Y, Messing B, Matuchanski C, Valleur P. Aggressive initial surgery for chronic radiation enteritis: long-term results of resection vs non-resection in 44 consecutive cases. Colorectal Dis 1999;1:162.
17. Postgate A, Saunders B, Tjandra J, Vargo J. Argon plasma coagulation in chronic radiation proctitis. Endoscopy 2007;39:361-5.
18. Waddell BE, Rodriguez-Bigas MA, Lee RJ, Weber TK, Petrelli NJ. Prevention of chronic radiation enteritis. J Am Coll Surg 1999;189:611-24.
19. Tuech JJ, Chaudron V, Thoma V, et al. Prevention of radiation enteritis by intrapelvic breast prosthesis. Eur J Surg Oncol 2004;30:900-4.
20. Abhyankar A, Jenney M, Huddart SN, Tilsley DW, Cox R, Saad M. Use of a tissue expander and a polyglactic acid (Vicryl) mesh to reduce radiation enteritis: case report and literature review. Pediatr Surg Int 2005;21:755-7.
21. Crosby TD, Melcher AA, Wetherall S, Brockway S, Burnet NG. A comparison of two planning techniques for radiotherapy of high grade astrocytomas. Clin Oncol (R Coll Radiol) 1998;10:392-8.