

Case Report

Rectourethral fistula during bevacizumab administration for cecum cancer after prostate brachytherapy: A case report.

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Rectourethral fistula is rare complication after ^{125}I low-dose-rate prostate brachytherapy, and gastrointestinal fistulas are widely recognized as a complication of bevacizumab. To our knowledge, this is the first case of rectourethral fistula during bevacizumab administration for cecum cancer after prostate brachytherapy. A 75-year-old man visited our hospital because of urinary retention and fecaluria. He had been receiving chemotherapy for one year against recurrence of cecum cancer. The chemotherapy regimens were bevacizumab and capecitabine plus oxaliplatin. He had undergone laparoscopic ileocecal resection for cecum cancer 1.5 years earlier. Eight months after the operation, recurrence was recognized. He had a history of prostate cancer and had received ^{125}I low-dose-rate prostate brachytherapy for prostate cancer 17 years earlier. Computed tomography revealed air bubble from the rectum to the prostate and urethra. To prevent urinary tract infection, laparoscopic transverse colostomy and percutaneous cystostomy were performed. Although the patient's quality of life subsequently improved, the performance status declined remarkably. He was therefore transferred to another hospital and received the best supportive care. Rectourethral fistula is a rare but serious complication after ^{125}I low-dose-rate prostate brachytherapy. The introduction of bevacizumab to patients who have received this therapy should be carefully considered.

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Introduction

Rectourethral fistula is a rare complication after ^{125}I low-dose-rate prostate brachytherapy, with a reported incidence of <1% [1]. While gastrointestinal fistulas are widely recognized as a complication of bevacizumab, there are few reports of rectourethral fistula. To our knowledge, this is the first case of rectourethral fistula during bevacizumab administration for cecum cancer after prostate brachytherapy.

Case Report

A 75-year-old man visited our hospital because of urinary

retention and fecaluria. He had been receiving chemotherapy for one year against recurrence of cecum cancer. The chemotherapy regimens were bevacizumab and capecitabine plus oxaliplatin (CapeOX). He had undergone laparoscopic ileocecal resection for cecum cancer 1.5 years earlier, and the final stage had been IIIa at that time. Eight months after the operation, recurrence was recognized by computed tomography (CT). He had a history of prostate cancer, hypertension and angina. He had received ^{125}I low-dose-rate prostate brachytherapy for prostate cancer 17 years earlier. A routine laboratory evaluation showed a white blood cell count of 12,800/ μl , hemoglobin 6.7 g/dl, C-reactive protein (CRP) 15.55 mg/dl, urea nitrogen (BUN) 23 mg/dl, creatinine 1.07 mg/dl, total protein 7.1 g/dl, albumin 2.4 g/dl and carci-

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noembryonic antigen (CEA) 6.4 ng/ml. CT revealed air bubble from the rectum to the prostate and urethra (Fig. 1), multiple liver metastases, lymph nodes metastasis and peritoneal dissemination. To prevent urinary tract infection, laparoscopic transverse colostomy and percutaneous cystostomy were performed. Although the patient's quality of life subsequently improved, the performance status declined remarkably. He was therefore transferred to another hospital and received the best supportive care.

A)



B)



Figure 1. CT scan (A: axial view, B: sagittal view). Computed tomography (CT) revealed air bubbles from the rectum to the prostate and urethra.

Discussion

Given the positional relationship between the prostate and the rectum, damage to the rectal anterior wall is considered inevitable when radiotherapy is performed on the prostate. Radiation injures small blood vessels and produces ischemia, fibrosis and hypoxia [2,3]. Rectourethral fistula is a rare complication after ^{125}I low-dose-rate prostate brachytherapy, with a reported incidence of <1% [1], but it is a serious complication. The utility of hyperbaric oxygen therapy for radiation enteritis and rectal ulcer has been demonstrated [4], but its utility against rectourethral fistula after prostate brachytherapy is unclear. For rectourethral fistula after radiotherapy, urinary tract changes due to cystocele fistula and ostomy construction should be considered first. After evaluating the condition, a curative procedure should be considered [5]. Rectourethral and rectovaginal fistula closure using the perineal approach with pedicled gracilis muscle interposition is a useful operation with a high success rate. However, the curative rate after radiation treatment is lower than that of untreated patients [2, 6].

Bevacizumab is an indispensable presence in chemotherapy for colorectal cancer. It is a humanized antivascular endothelial growth factor monoclonal antibody [7] and inhibits tumor angiogenesis [8]. Significant side effects of bevacizumab include hypertension, proteinuria, intestinal perforation and retardation of wound healing [9]. There have been several reports on the incidence of rectovaginal fistula [10-13] and sigmoid-vaginal fistula [14] during bevacizumab administration. However, rectourethral fistula during bevacizumab administration is very rare, as the interposition of prostate and connective tissue between the rectum and the urethra make it difficult for rectourethral fistula to form.

Several risk factors of bowel perforation from bevacizumab are reported [15-19]. Intact primary tumor, NSAIDs use, diverticulosis, recent endoscopy, bowel obstruction, colitis, peptic ulcer disease and abdominal irradiation are related to perforation. In these reports, all of irradiation therapy were stereotactic body radiation therapy (SBRT) and not brachytherapy.

Malnutrition easily occurs in patients undergoing chemotherapy. In another study, hypoalbuminemia was shown to be a predictive factor for fistula formation in recurrent cervical cancer [20]. The patient's serum albumin was 2.4 g/dl, which is considered to be a state of malnutrition. In the present case, prostate brachytherapy, bevacizumab administration and malnutrition were all related to the occurrence of disease. In conclusion, rectourethral fistula is a rare but serious complication after ^{125}I low-dose-rate prostate brachytherapy. The

rectal mucosa and nutritional status should be carefully considered before introducing bevacizumab to patients who have received this therapy.

Competing interests

The authors declare that they have no competing interests.

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