Case Analysis

Overview of Radiation-Related Colovesical or Rectovesical Fistula: Experience from 18 Patients at the Chang Gung Memorial Hospital in Kaohsiung

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Background. Adjuvant irradiation is currently the standard treatment for many malignant neoplasms; however, late complication due to radiation is a clinically common problem. This report presents our experience with long-term follow up for radiation-related colovesical or rectovesical fistula at the Kaohsiung Chang-Gung Memorial Hospital.
Methods. Eighteen patients (16 female, 2 male), from 1989 to 2003, with radiation-related colovesical or rectovesical fistula were retrospectively analyzed. The clinical course, pathologic findings, associated treatment, and outcomes were assessed.
Results. Patients were diagnosed with rectal cancer (n = 2, 11.1%), cervical cancer (n = 12, 66.7%), bladder cancer (n = 2, 11.1%), endometrial cancer (n = 1, 5.5%), and simultaneous bladder and cervical cancers (n = 1, 5.5%). The diagnostic tools included barium enema, cystography, abdominal computed tomography, colonoscopy and fistulography. And the sensitivity rate is 55.6%, 44.4%, 42.9%, 33.3% and 0% respectively. Six patients received diverting colostomy including 1 concomitant ileal conduit, 10 patients received Hartmann's procedure including 2 concomitant small bowel segmental resections, and 1 patient received repair of fistula through laparotomy. Almost all patients received symptom relief after operation, but 3 patients developed recurrent fistulas.
Conclusion. The barium enema is the most accurate diagnostic tool. Additionally, a combination of gastrointestinal and urological surgery is usually needed because of the nature of fistulas. One-stage operations should be limited to younger patients in good nutritional states and without severe inflammation, radiation injury, intestinal obstruction, or other major medical problem such as advanced malignancy.
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Adjuvant irradiation is currently the standard treatment for many malignant neoplasms. Gynecological cancer is the most common pelvic malignancy receiving radiotherapy, followed by gastroin-

testinal malignancies, male genital cancer, and carcinomas of the bladder.[1,2]

Late-onset radiotherapy-induced complications occur in 51% of patients, including bowel and urinary bladder complications in 41% and 21%, respectively.[3] Chronic gastrointestinal complications include cramping abdominal pain, diarrhea, or cachexia, or may present acutely as bowel obstruction or fistula.[4] Radiation-related mortality in small bowel disease is 32%, while that for colonic disease is 4%.[5] Urological complications include cystitis, hematuria, ureteral stenosis, and fistula formation.[6,7]

Long-term follow up data for radiation-induced colovesical or rectovesical fistula is important because radiation may lead to late-onset complications. Detecting and identifying the long-term complications associated with radiation is also crucial. This report presents our experience with long-term follow up for radiation-related colovesical or rectovesical fistulas at the Kaohsiung Chang-Gung Memorial Hospital.

Patients and Methods

A total of 18 patients were retrospectively enrolled from 90 patients with enterovesical fistulas. Patients were excluded because of benign disease (n = 33), cancer invasion (n = 35), and enterovesical fistulas (n = 4). Medical records for the remaining 18 patients (16 female, 2 male) with radiation-related colovesical or rectovesical fistula between 1989 and 2003 were retrospectively analyzed. The last follow up was in June 2008. The mean age was 61.5 years old (range 36-75 years). Fifteen patients (83.3%) received operations and adjuvant radiotherapy, 1 underwent surgery and concurrent radiochemotherapy, and 2 received radiotherapy only. The mean radiation dose was 4648 cGy (range 500-9900 cGy). The patients' demographic data is shown in Table 1.

Results

Among the 18 patients (16 women and 2 men) with radiation-related colovesical or rectovesical fistulas, the mean age was 61.5 (10.9) years (range 36-75

years) with female predominance (88.9%). Patients were diagnosed with rectal cancer (n = 2, 11.1%), cervical cancer (n = 12, 66.7%), bladder cancer (n = 2, 11.1%), endometrial cancer (n = 1, 5.5%), and simultaneous bladder and cervical cancers (n = 1, 5.5%). All patients received radiotherapy with or without surgical intervention (15 patients underwent surgery and 1 received concurrent chemotherapy). Seven patients showed recurrent cancer or distant metastasis at the time of the diagnosis of fistula. The mean duration from diagnosis of previous disease to the diagnosis of colovesical or rectovesical fistula was 8.8 years (range 3-18 years). Six patients had systemic diseases, including 3 with diabetes mellitus, 1 with hypertension, and 2 with both diseases.

The clinical symptoms are summarized in Table 2. We found fecaluria in 6 patients (33.3%), fever or chillness in 8 patients (44.4%), dysuria in 5 patients (27.8%), hematuria in 3 patients (16.7%), urine from the rectum in 2 patients (11.1%), urine leakage from the abdominal wound in 2 patients (11.1%), stool from the vagina in 1 patient (5.6%), bloody stool in 1 patient (5.6%) and abdominal pain in 2 patients (11.1%). Pneumaturia was not recorded in any of the patients.

Urine analysis was done in only 16 patients; of

Table 1. Demographic data of 18 patients with colovesical or rectovesical fistula

Mean age (years)	61.5 (10.9)	n = 18
Male	2	11.1%
Female	16	88.9%
Predisposing disease		
Cervical ca	12	66.7%
Bladder ca	2	11.1%
Rectal ca	2	11.1%
Endometrial ca	1	5.6%
Cervical and bladder ca	1	5.6%
Underlying disease		
DM	5	83.3%
HTN	3	50%
Treatment		
Medication	1	5.6%
Hartmann's procedure	10	55.6%
Segmental resection of small bowel	2	11.1%
Ileal conduit	1	5.6%
Diverting stoma	6	33.3%
Repair of fistula	1	5.6%

Table 2. Clinical symptoms of 18 patients with colovesical or rectovesical fistula

Symptoms		
Fever or chills	8	44.4%
Fecaluria	6	33%
Dysuria	5	27.8%
Hematuria	3	16.7%
Abdominal pain	2	11.1%
Urine from anus	2	11.1%
Urine from abdominal wound	2	11.1%
Stool from vagina	1	5.6%
Bloody stool	1	5.6%

Table 3. Diagnostic examination made in 18 patients

Diagnostic tool	No. of patients with positive finding of fistula	No. of patients receiving examination	Sensitivity (%)
Barium enema	5	9	55.6%
Cystography	4	9	44.4%
Abdominal CT	3	7	42.9%
Colonoscopy	1	3	33.3%
Fistulography	0	3	0

these, 13 patients (81.2%) had WBC > 5/mm^3 and 3 had WBC < 5/mm^3. Urine cultures were taken for 16 patients, 10 of which proved to have gram-negative bacterial infections. The most common pathogen was *Escherichia coli* (80%), followed by *Pseudomonas aeruginosa* (30%), *Proteus* sp. (10%), and *Klebsiella pneumoniae* (10%). Six patients (37.5%) showed renal insufficiency. The mean white count was 10,606/ mm^3 (range 4600-19,800/mm^3). Abdominal CT was performed in 7 patients, of which 3 were positive for fistula. Seven patients underwent cytoscopy with 3 positive findings of fistula. Cystography was performed in 9 patients, of which 4 positive findings of fistula were seen. Barium enema was done in 9 patients with 5 positive findings of fistula. Colonoscopy was done in 3 patients with 1 positive findings of fistula. Fistulography was done in 3 patients without positive findings of fistula. Positive prediction rates of different diagnostic tools are summarized in Table 3.

All patients received surgical intervention, and different procedures were chosen. Six patients received diverting colostomy including 1 concomitant ileal conduit, 10 patients received Hartmann's procedure including 2 concomitant small bowel segmental resections, and 1 patient received repair of fistula via the abdomen. The orifice of the fistula was found at the intestinal end in 13 patients, including 6 at the rectum, and 7 at the colon respectively. Postoperatively, 1 patient had short bowel syndrome. Sixteen patients have stoma present after the operation, and no reconstruction was done in any of these cases, no matter with or without urological surgery (ileal conduit). Three mortalities were noted at 3 months of follow up in this group. Almost all patients received symptom relief after operation, but 3 patients developed recurrent fistulas.

Discussion

Colovesical fistula is a rare disease and is one of the late-onset complications of pelvic radiotherapy. The etiologies of colovesical fistula are known to be cancer invasion, irradiation, diverticulitis, inflammatory bowel disease, or others. In one study, the underlying pathology included diverticular disease (62%), carcinoma (27%), and inflammatory bowel disease (6%).[8] In Hayne et al.'s study,[9] more than 75% of patients receiving pelvic radiotherapy experienced acute anorectal symptoms and up to 20% suffered from late-phase radiation proctitis. About 5% developed other chronic complications such as fistulas, stricture, and disabling fecal incontinence.

Solkar et al. retrospectively reviewed 50 cases of colovesical fistula with etiologies of diverticular disease, Crohn's disease, and pelvic malignancy.[10] The most common clinical presentations were fecaluria, pneumaturia, or both. In our study, pneumaturia was never recorded. However, this may be due to the difficulty in recognizing the symptom by patients.

Predisposing factors of radiation-induced complications include radiation dosage, type and mode of delivery, pelvic inflammatory disease, hypertension, diabetes, arteriosclerotic heart disease, and age greater than 50 years.[11] In our study, the mean age of the patients was 61.5 years. Some of our patients had systemic diseases such as diabetes mellitus and hypertension. The mean total dose of radiation to treat pelvic cancer was 4648 cGy. Hong et al. concluded that low-pelvic RT alone (range 40-60 Gy [median 50 Gy]) significantly reduces the complications in node-nega-

tive, high-risk, Stage I-IIA cervical cancer patients.[12]

The lag time from radiotherapy to the development of fistulas was previously unclear. In our study, the mean time for induction of colovesical fistulas was found to be 8.8 years after radiotherapy, which may suggest long-term follow up to confirm this late-onset complication of radiotherapy.

Traditionally, cystoscopy and barium enema examination are most commonly used modality to confirm the presence of colovesical fistulas.[13] Cystoscopy would demonstrate abnormalities in 90% of cases and the fistulas might be declared in 33% of cases (Fig. 1). Biopsies should also be taken to exclude a urological malignancy as the cause of fistula. Barium enema

shows a fistula in only a third of the cases and can help determine underlying colorectal disease. More recently, computed tomography (CT) has been proposed to be an effective diagnostic investigative tool; it has a diagnostic accuracy of more than 90%. Jarrett and Vaughan described that abdominal CT helps confirm the diagnosis and provides important anatomical information by revealing the intraluminal and extraluminal pathological status.[14] In a review study by Sarr et al., the most common abnormal findings in CT included intravesical gas (90%), focal bladder wall thickening (90%), and an extraluminal mass (75%) (Fig. 2).[15] Although the scan did not always show the fistulous tract, it accurately predicted the correct location in all cases.
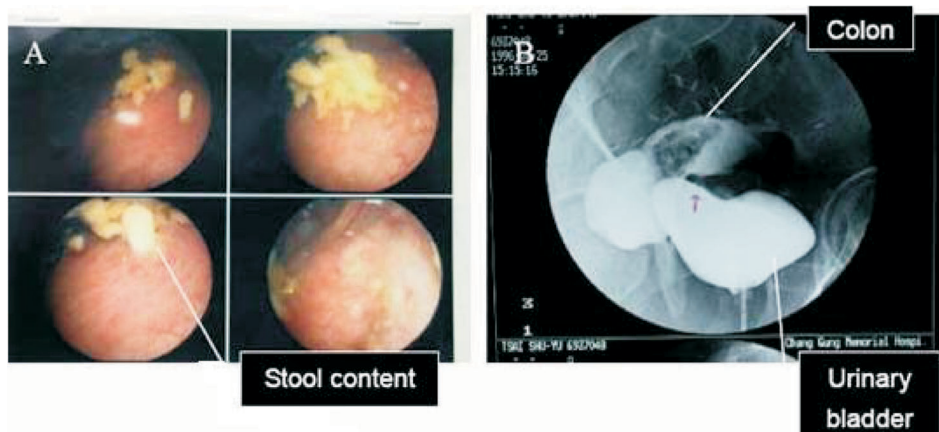

Fig. 1. A. Cytoscopy images showing stool content in the urinary bladder. B. Colon shown by contrast through the urinary bladder.
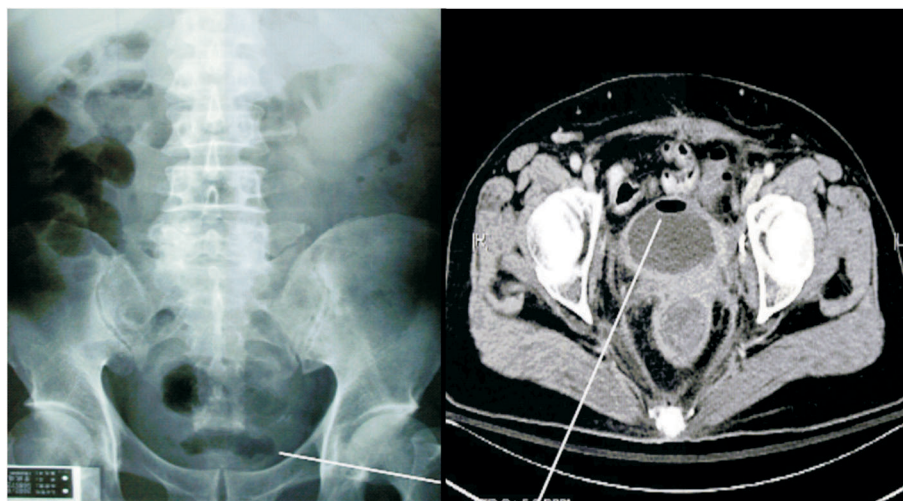

Fig. 2. KUB and abdominal CT images showing intravesical air. Intravesical air and thickening of urinary bladder wall are the typical CT findings for enterovesical fistula.

Daniels et al. recommended cystoscopy and urine cytology for fecal material as first-line investigations in all patients with a suspected enterovesical fistula.[16] CT scanning and barium enema should not be first-line investigations, but may be performed subsequently to help determine etiology and to plan surgery. Other methods had also been used to confirm the presence of colovesical fistulas. Volkmer et al. used transrectal 3D ultrasound with contrast media to detect fistulas.[17] Wrong surgical choice may leave residual disease for enterovesicle fistulas and therefore, definite confirmation of the location of fistulas before operation is very important.

The purpose of surgery is to reduce gastrointestinal and urological symptoms. The principle of surgical procedure is to separate the gastrointestinal and genitourinary tracts or can even be primary closure of the fistula. The procedure may consist of one stage, which was first described in 1972, or multiple stages, depending to the condition of the patients.[18-20] The one-stage method is currently the management of choice in patients with no sepsis, obstruction, or organ impairment and in those with a normal nutritional status, especially in patients with an inflammatory cause of the fistula, diverticular, or granulamatous bowel disease. Staged repairs may be more judicious in patients with advanced malignancy, radiation changes, severe inflammation, large pelvic abscesses, or inadequate bowel preparation.[21,22]

The most common selected procedure to treat colovesical or rectovesial fistulas is sigmoid colectomy followed by Hartmann's procedure and anterior resection.[21-23] However, this course of action should be limited to younger patients in good nutritional states and without severe inflammation, radiation injury, intestinal obstruction, and other major medical problems such as advanced malignancy.[23] In our practice, less invasive procedures were favored because of the fragility of radiation-injured tissue. Segreti et al. concluded that there were no statistically significant differences between patients treated with loop or end colostomy with regard to early morbidity or survival.[24] In our study, 10 patients received end colostomy and 6 patients received loop colostomy. There is not enough data to support which procedure is superior, but there is evidence that loop colostomy leaves residual dis-

ease. There were 3 patients with recurrent fistulas after treatment, 1 of which underwent medical treatment only, and 1 who received repair of fistula via the abdomen.

In summary, colovesical or rectovesical fistula is a late-onset complication following radiotherapy for pelvic malignancies due to either tumor recurrence or the effect of radiation. Several kinds of diagnostic tools may help confirm the presence and nature of the fistula, and therefore careful choosing of the appropriate tool is important. Diverting stoma is usually the preferred procedure. Additionally, a combination of gastrointestinal and urological surgery is usually needed because of the nature of fistulas.

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病例分析

放射治療相關之大腸/直腸-膀胱廔管：
高雄長庚 18 例的經驗回顧

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背景　目前放射治療已經廣泛應用在多種癌症的治療，且放射治療相關的遲發性併發症也是臨床上常見的問題。本篇文章針對本院對放射治療相關之大腸/直腸-膀胱廔管的經驗與長期追蹤結果提供分享。

方法　本研究蒐集自 1989 至 2003 年間，在本院有紀錄之放射治療相關的大腸/直腸-膀胱廔管，吾人等分析其臨床上的病史、病理診斷、治療、以及治療的成果。

結果　在這 18 例病患中，分別因以下原因接受放射治療；直腸癌 (n = 2, 11.1%)、子宮頸癌 (n = 12, 66.7%)、膀胱癌 (n = 2, 11.1%)、子宮內膜癌 (n = 1, 5.5%)，另有一位同時患有膀胱癌及子宮頸癌 (n = 1, 5.5%)。常用的診斷工具包括鋇劑攝影、膀胱攝影、腹部電腦斷層、大腸鏡和廔管攝影，檢查的敏感度分別為 55.6%，44.4%，42.9%，33.3% 和 0%。共有 6 名患者接受分流性大腸造廔，其中有一位同時接受人工膀胱手術；有 10 名患者接受 Hartmann's 手術，其中有兩位同時接受部分小腸切除，有一位接受經腹部廔管修補手術。幾乎所有患者在接受手術治療之後都得道症狀緩解，但有 3 例發生廔管復發。

結論　鋇劑攝影是正確率最高的診斷工具。考量疾病的成因，腸道及泌尿道的合併手術經常是必要的。一次性手術僅侷限於少部分病患適用；年輕、營養狀況佳、沒有進行性的發炎、沒有放射線相關損傷、沒有腸阻塞或其他主要內科疾病，如侵犯性的癌症。

關鍵詞　放射線、結腸-膀胱廔管、直腸-膀胱廔管。