

## **Radiation Therapy of Esophageal Carcinoma: Correlation of Clinical and Radiographic Findings**

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**Abstract.** Seventeen patients with esophageal carcinoma treated by radiation therapy (RT) at our hospital between 1981 and 1984 had initial diagnostic esophagrams and 1 or more repeat esophagrams after completing RT. Total regression of the tumor was observed radiographically in 10 patients (59%) with a normal esophagus (24%) or benign-appearing residual stricture (35%) at the site of the previous lesion. Partial regression was observed in 4 patients, and progression of the tumor in 3. No correlation was found between the size, stage, or morphology of the lesion and its response to therapy. Although local recurrences were relatively uncommon, patient survival was often limited by the development of distant metastases. Fourteen of 15 patients with clinical follow-up initially had significant relief from dysphagia as the tumor regressed. However, 9 of those patients had recurrent or increased dysphagia over a subsequent 3–9-month period. Exacerbation of symptoms did not necessarily indicate recurrent carcinoma; it also resulted from benign radiation strictures, opportunistic esophagitis, or other complications of RT detected on esophagography.

**Key words:** Esophagus, carcinoma – Esophagus, radiotherapy.

Radiation therapy (RT) has long been advocated as a viable alternative to surgery for treating esophageal carcinoma. As a palliative form of treatment, RT may provide significant relief from dysphagia for 2 or more months in 50–77% of

patients with advanced local disease and/or distant metastases [1–5]. It may also be used as the definitive treatment for esophageal cancer with 5-year survival rates comparable to or slightly worse than those of surgery [1, 6–9]. However, RT avoids the short-term morbidity and mortality associated with surgery. As a result, some investigators believe that it should be the primary modality for treating this disease [6, 8].

Although numerous clinical studies have been published on this subject, little has been written about the radiologic assessment of esophageal carcinoma treated by RT. Anecdotal cases have been reported in which esophagrams taken before and after treatment showed regression of the tumor [1, 6, 10–13]. While these lesions may recur, local recurrences have rarely been documented radiographically. Furthermore, no attempt has been made to correlate the clinical and radiographic findings after RT. We therefore performed a retrospective study to review our experience with patients with esophageal carcinoma treated by RT.

### **Materials and Methods**

Records of the Department of Radiation Therapy at our hospital revealed 63 patients with biopsy-proven esophageal carcinoma who were treated by RT during a 4-year period between 1981 and 1984. Thirty-five patients received combined treatment with RT and surgery, while 28 patients were treated only by RT. Seventeen of the latter patients had initial diagnostic esophagrams and 1 or more repeat esophagrams after completion of therapy. An average of 2 posttreatment esophagrams (range, 1–6) were performed on each patient. While double-contrast technique was employed in most patients, several had single-contrast esophagrams, since they were too sick or debilitated to cooperate for a double-contrast examination.

The initial diagnostic esophagrams of those 17 patients were reviewed to determine the appearance, size, and location of the tumor as well as the presence and degree of esophageal obstruction. Serial esophagrams after RT were then reviewed in chronological sequence to determine whether there was pro-

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gression, regression, and/or recurrence of tumor following treatment. Medical records were also reviewed to determine the presenting clinical findings and the indications for RT. Sixteen patients had squamous cell carcinomas and 1 had adenocarcinoma arising in Barrett's mucosa. The initial metastatic work-up included chest radiographs, chest and abdominal CT scans, liver scans, and/or bone scans.

Eleven patients who had no apparent metastatic disease underwent radical RT in an attempt to cure. Although surgery has generally been employed as the definitive treatment for esophageal carcinoma at our institution, 9 of those patients were considered poor surgical candidates, and 2 patients refused surgery. In all 11 cases, RT was administered by a 6 MeV linear accelerator. These patients received an average total radiation dosage of 6,190 rads (range, 5,940–6,800) over an average period of 48.9 days (range, 41–69 days). Four of those patients also received adjuvant chemotherapy. The remaining 6 patients who had extensive metastases underwent palliative RT administered by a 15-MeV (4 cases) or 6-MeV (2 cases) linear accelerator. These patients received an average total radiation dosage of 4,725 rads (range, 3,900–6,000 rads) over an average period of 28 days (range, 16–48 days).

Of the 17 patients who had serial esophagrams, follow-up clinical data after treatment were available in 15 cases. The average length of follow-up was 13.4 months (range, 1–44 months). Both the initial clinical response and subsequent patient course were correlated with the radiographic findings. Five patients underwent endoscopy and biopsy during the post-treatment period. The esophagus was also examined at autopsy in 2 patients who died following RT.

## Results

### Clinical Findings

**Before Treatment.** Ten patients with esophageal carcinoma treated by RT were men and 7 were women. The average patient's age was 62.5 years, with a range of 49–87 years. All but 1 patient had dysphagia. Other presenting clinical findings included weight loss (9 cases), substernal chest pain (5 cases), odynophagia (4 cases), hematemesis (1 case), hoarseness (1 case), and sore throat (1 case). The average duration of symptoms was 2.5 months (range, 1–12 months). Initial medical work-up revealed extracervical spread of tumor in 6 patients with metastases to the mediastinum (4 cases), liver (2 cases), celiac or distant lymph nodes (2 cases), and/or lung (1 case). The remaining 11 patients apparently had localized esophageal disease.

**After Treatment.** Follow-up clinical data in 15 patients (the other 2 were lost to follow-up) showed that 14 experienced significant relief from dysphagia within several weeks to months after initiation of RT. However, dysphagia subsequently recurred or increased over a 3–9-month period in 9 of those patients. Further follow-up data revealed that 6 patients had died between 1 and 34 months after completion of RT with a mean survival of

14.2 months. All had widespread metastases. Examination of the esophagus at autopsy revealed no evidence of local recurrence in 1 case and residual tumor in the esophagus in another. Nine other patients were still alive during an average follow-up period of 12.9 months. Two of those patients were asymptomatic 17 and 19 months after RT, respectively. A repeat endoscopic examination in 1 showed no evidence of recurrent tumor. Three other patients had mild dysphagia and 4 had severe dysphagia at the last clinical follow-up between 1.5 and 44 months after completion of RT. Endoscopic biopsies in 4 of those patients confirmed the presence of residual or recurrent esophageal cancer in 3.

### Radiographic Findings

**Before Treatment.** The initial diagnostic esophagram revealed obvious esophageal carcinoma in all 17 patients. Two were located in the cervical esophagus, 4 in the proximal thoracic esophagus, 8 in the midthoracic esophagus, and 3 in the distal thoracic esophagus. Six patients had annular lesions, 6 had infiltrating lesions (see Figs. 2A, 7A, and 8A) and 5 had polypoid intraluminal masses (see Figs. 3A and 5A). Esophageal obstruction was present in 3 patients (2 low-grade and 1 high-grade), and all 3 had annular carcinomas. The average length of the lesion was 5.4 cm (range,

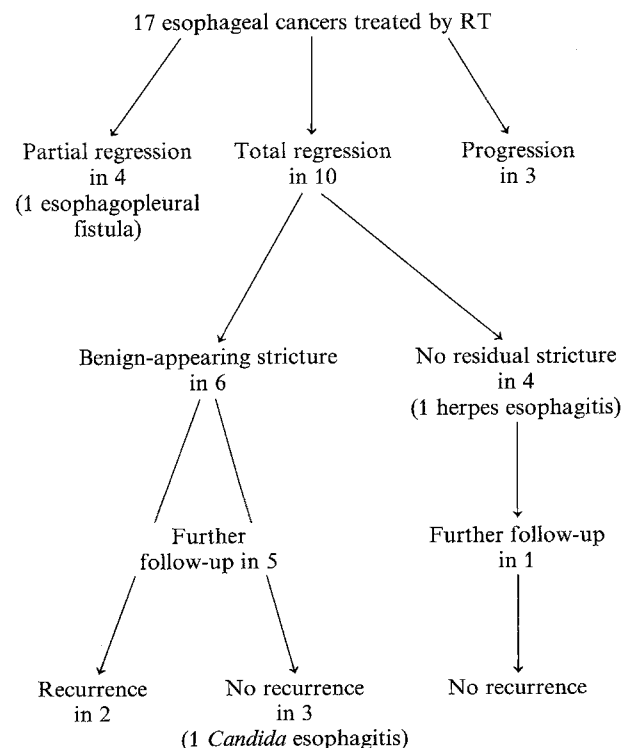
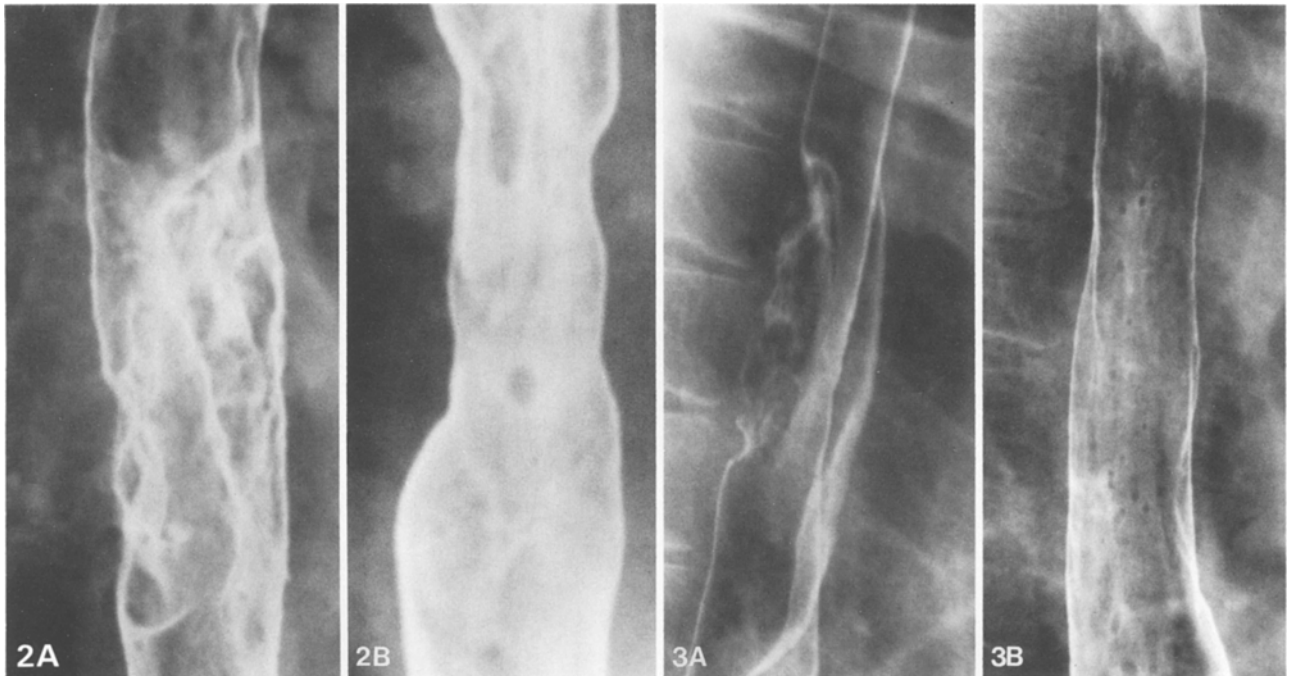
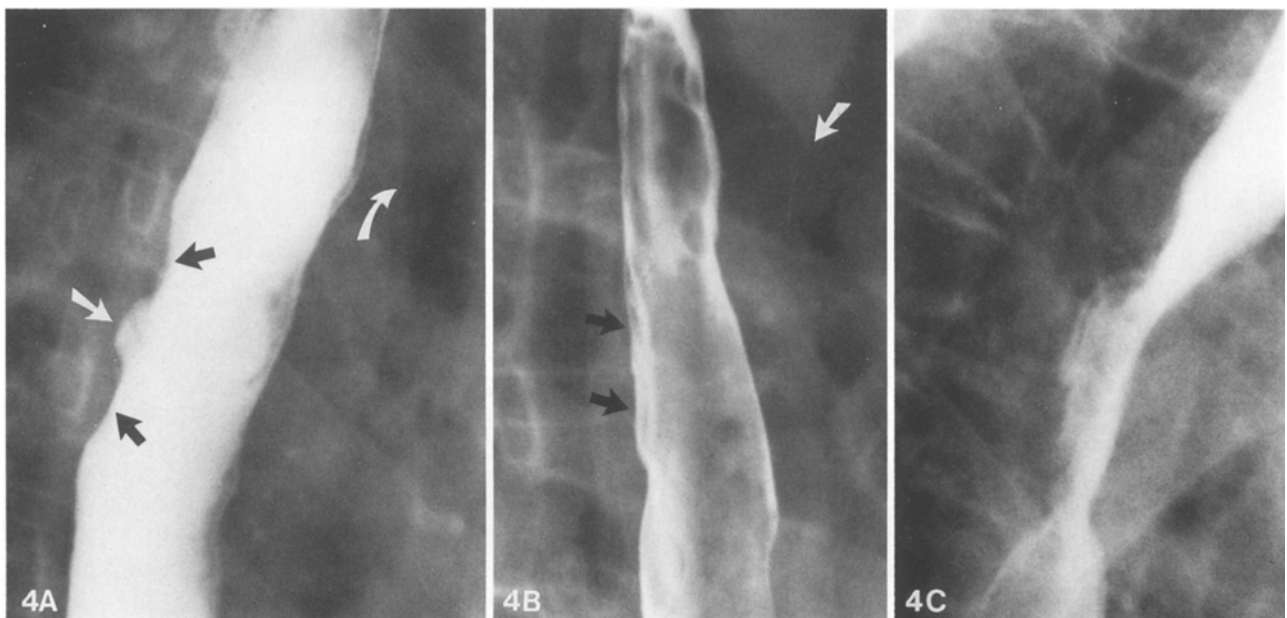


Fig. 1. Radiologic response of esophageal carcinoma to RT.

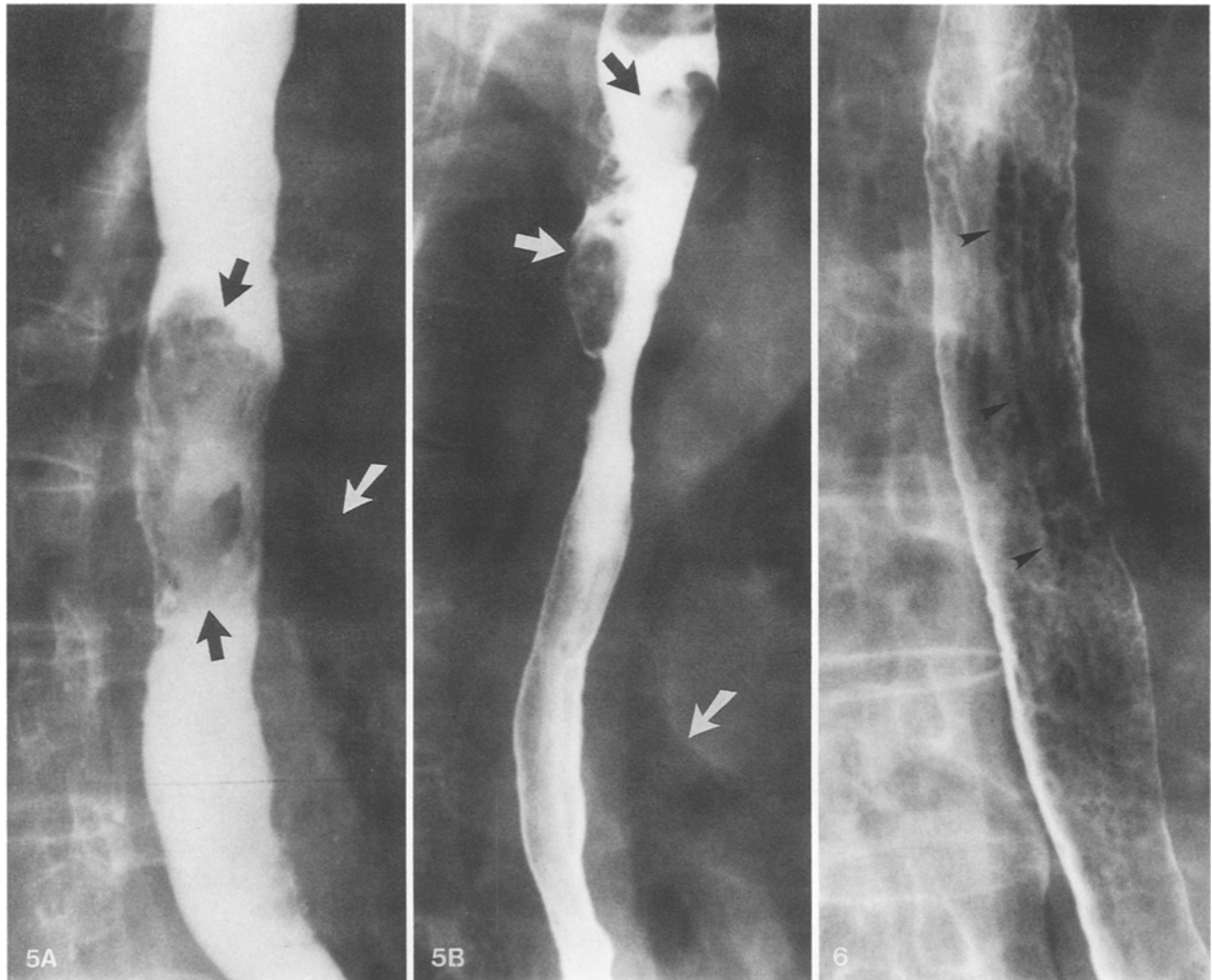


**Fig. 2.** **A** Infiltrating carcinoma in midesophagus. **B** Benign-appearing stricture at site of original lesion 3 months after RT.

**Fig. 3.** **A** Polypoid carcinoma in proximal thoracic esophagus. **B** Normal-appearing esophagus without evidence of stricture or residual tumor 2 years after RT.



**Fig. 4.** **A** Relatively flat carcinoma (*black arrows*) with central ulceration (*straight white arrow*) in midesophagus just below level of left mainstem bronchus (*curved white arrow*). **B** Early stricture with flattening of posterior esophageal wall (*black arrows*) but no evidence of residual tumor 6 weeks after RT. *White arrow*, left mainstem bronchus. **C** Irregular narrowing and ulceration of esophagus 4 months later, due to recurrent carcinoma.



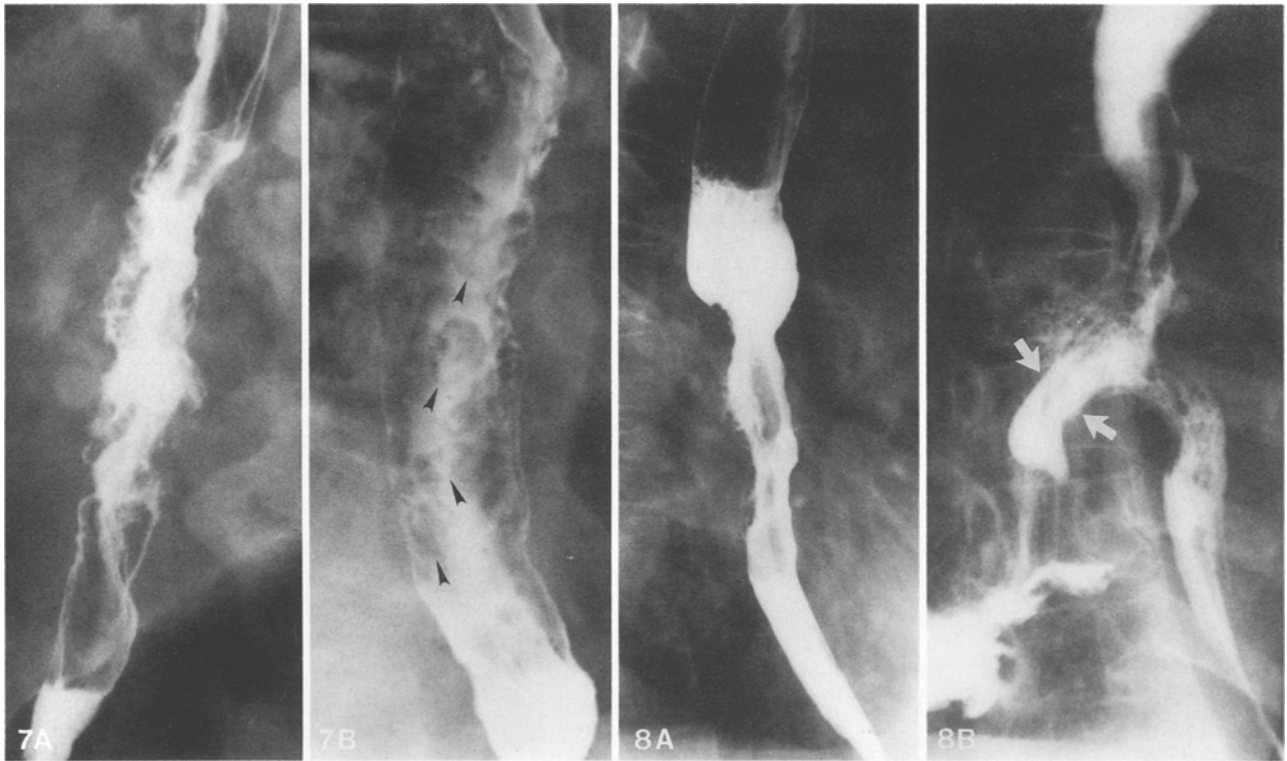
**Fig. 5. A** Polypoid carcinoma in midesophagus (*black arrows*) at level of left mainstem bronchus (*white arrow*). (Note apparent contrast collections outside esophagus due to barium spilled on patient's gown.) **B** Proximal extension of tumor beyond radiation portal 7 months later (*short arrows*), with regression more distally at level of left bronchus (*long arrow*).

**Fig. 6.** Double-contrast esophagram to evaluate recurrent dysphagia 6 weeks after RT for distal esophageal cancer shows irregular mucosa with multiple plaque-like defects in midesophagus due to proven *Candida* esophagitis. Note characteristic longitudinal orientation of plaques (*arrowheads*). Other radiographs of distal esophagus revealed mild residual stricture at site of the previous tumor.

3.5–9 cm). Nine patients had lesions 5 cm or less in length and 8 had lesions greater than 5 cm.

**After Treatment.** Repeat esophagrams after completion of RT revealed total regression of the tumor in 10 of 17 or 59% of patients (Fig. 1). Six of those patients had a benign-appearing residual stricture with smooth, tapered, often symmetrical narrowing at the site of the previous lesion (Fig. 2). In 2 cases, the findings at endoscopy and autopsy confirmed the benign nature of the stricture. The other 4 patients had a normal-appearing esophagus (Fig. 3). The average interval between the ini-

tial diagnostic esophagram and the first repeat study showing total regression was about 6 months, although the tumor disappeared radiographically as early as 1 week after completion of RT in 4 cases. Six of 10 patients with total regression on esophagography had additional barium studies over a subsequent 6–12-month period; 4 had no evidence of recurrent tumor, but the remaining 2 had irregular narrowing, mass effect, and ulceration within a previously benign-appearing stricture, presumably due to recurrent carcinoma (Fig. 4). In both cases, the original lesion had rapidly regressed within 1 week after RT was com-



**Fig. 7.** **A** Infiltrating, ulcerated carcinoma in distal esophagus. **B** Repeat esophagram to evaluate recurrent dysphagia 1 $\frac{1}{2}$  years after RT shows disappearance of tumor. However, discrete, centrally umbilicated plaques (*arrowheads*) can be seen in distal esophagus due to proven herpes esophagitis.

**Fig. 8.** **A** Infiltrating, partially obstructing carcinoma in midesophagus. **B** Repeat esophagram 3 months after RT shows esophago-pleural fistula (*arrows*) with focal extravasation of water-soluble contrast from region of irradiated tumor into right pleural space.

pleted. Thus, 2 of 4 patients with early regression later developed recurrent local disease.

Repeat esophagrams revealed partial regression of the tumor in another 4 patients with a significant decrease in the size of the lesion compared to pretreatment studies. The average follow-up period was only 3.3 months in these cases. The remaining 3 patients had progression of the tumor on repeat esophagrams during an average period of 4 months following RT. Two of those patients had proximal extension of tumor beyond the radiation portal (Fig. 5), and 1 had intraluminal growth of the tumor within the radiation portal, which caused progressive obstruction.

The location of the tumor significantly affected its radiosensitivity. All 6 carcinomas in the cervical or upper thoracic esophagus totally (5 cases) or partially (1 case) regressed following RT, whereas 3 of 11 carcinomas in the mid or distal esophagus underwent progression despite RT. In contrast, the size of the tumor correlated poorly with its response to therapy. Of 9 lesions 5 cm or smaller, 5 totally regressed, 2 partially regressed, and 2 pro-

gressed following RT. Of the remaining 8 lesions greater than 5 cm in length, 5 totally regressed, 2 partially regressed, and 1 progressed following RT. Similarly, the morphology of the tumor was not a predictive factor; annular, infiltrating, and polypoid esophageal cancers all underwent varying degrees of regression or progression following therapy. However, 3 of 4 patients with polypoid lesions had a normal-appearing esophagus following tumor regression (Fig. 3).

#### *Correlation of Clinical and Radiographic Findings Following RT*

Of 14 patients whose dysphagia significantly improved following RT, 13 had total (9 cases) or partial (4 cases) regression of their esophageal cancer on follow-up barium studies. A dramatic clinical response to RT therefore correlated closely with regression of the lesion on esophagography. However, 9 of the 13 patients whose dysphagia initially improved due to regression of tumor had increased dysphagia over a subsequent 3–9-month period.

One of those patients had recurrent carcinoma on follow-up esophagography. However, 2 patients had opportunistic infection of the esophagus due to *Candida* or herpes esophagitis without evidence of recurrent tumor (Figs. 6 and 7). One patient who complained of coughing on swallowing developed an esophagopleural fistula (Fig. 8). The remaining 5 patients had either a normal esophagus (2 cases) or a benign-appearing residual stricture (3 cases). Thus, recurrent or increased dysphagia following RT correlated poorly with the development of recurrent carcinoma.

Of 6 patients with known metastatic disease at the time of therapy, 3 had total and 3 had partial regression of their cancer on follow-up barium studies. Of 11 patients with apparently localized esophageal disease, 8 had total (7 cases) or partial (1 case) regression and 3 had progression of tumor following RT. Thus, the local response of the lesion to RT did not depend on the stage of the tumor at the time of therapy. However, total regression of the tumor was observed radiographically in 5 patients who subsequently died from distant metastases.

## Discussion

Radiation therapy (RT) may be employed as the primary modality for either palliative or definitive treatment of esophageal carcinoma. Polypoid squamous cell carcinomas under 5 cm in the cervical or upper thoracic esophagus are thought to be the most radiosensitive lesions [5, 9, 14, 15]. Partial or total regression of the cancer reportedly occurs in about two-thirds of patients who undergo this form of treatment [13, 16, 17]. As a result, most patients experience significant relief from dysphagia in the initial months following therapy [1–5]. However, various studies in the medical literature have shown that these lesions recur locally in 50–85% of cases [6, 9, 18]. Recurrent tumor usually develops between 6 and 12 months following RT, but occasionally as long as 30 months after therapy [11]. Even when the tumor is eradicated locally, these patients frequently die from widespread metastases to the liver, lungs, or mediastinum [9, 13, 19–21]. Increased morbidity and mortality may also be attributed directly to RT with complications such as esophageal ulceration, perforation, and fistula formation reportedly occurring in 7–25% of cases [5, 18]. As a result, RT has been associated with an average patient survival of 9–10 months [1, 3].

The effects of RT on esophageal carcinoma have not been well documented in the radiologic

literature. Several authors have reported anecdotal cases in which radiologic studies after completion of RT revealed dramatic regression of tumor with a normal-appearing esophagus or slight residual stricture at the site of the previous lesion [1, 6, 10–12]. However, it is thought to be extremely difficult to differentiate a benign stricture from residual or recurrent carcinoma on posttreatment barium studies [6, 9]. Pearson reported 3 patients who underwent operations for apparent radiologic recurrences but had no evidence of tumor at surgery [6]. He also described cases of recurrent tumor in the submucosa that had a benign radiologic appearance [6]. Others have suggested that any persistent stricture after RT probably represents recurrent cancer [9]. Thus, radiologists have not had a major role in evaluating these patients.

In our study, esophagography revealed partial or total regression of 14 of 17 or 82% of esophageal carcinomas treated by RT. Lesions in the cervical or upper thoracic esophagus were more radiosensitive than those in the mid or distal esophagus. However, no correlation was found between the size, stage, or morphology of the lesion and its response to therapy. In 10 patients, or 59% of those treated by RT, repeat esophagrams revealed a normal esophagus (24%) (Fig. 3) or benign-appearing residual stricture (35%) (Fig. 2) at the site of the previous lesion. These strictures had smooth, tapered borders without evidence of nodularity, mass effect, or ulceration to suggest residual tumor (Fig. 2). In 2 cases, the findings at endoscopy and autopsy confirmed the benign nature of these strictures. Thus, our experience suggests that mild residual strictures are frequently observed following tumor regression and that a persistent stricture does not necessarily indicate recurrent tumor (see Fig. 1).

The pathogenesis of these benign esophageal strictures following RT is uncertain. However, Pearson postulated that when a circumferential cancer involving the muscular layers of the esophageal wall is eradicated by RT, subsequent fibrosis in these muscular layers produces a stricture [11]. Conversely, he thought that a polypoid intraluminal cancer not densely infiltrating the muscular layers of the wall might regress without producing a stricture [11]. Our findings support this view, since 3 of 4 patients who had a normal-appearing esophagus after tumor regression originally had a polypoid lesion.

In our study, recurrent carcinoma was detected radiographically in only 33% of patients who underwent additional barium studies after the lesion had regressed (Figs. 1 and 4). Our findings suggest

that local recurrences may occur less frequently than previously reported. In both patients with recurrent tumor, however, the original cancer had rapidly regressed within 1 week after RT was completed. It is not surprising that lesions that regress rapidly may recur rapidly, since early regression indicates a high clonogenic compartment within the tumor.

While local recurrences were uncommon, 50% of patients with total regression on esophagography eventually died from distant metastases. Approximately half of those patients had apparently localized esophageal disease at the time of therapy. However, unrecognized lymph node metastases presumably were present at that time, with subsequent dissemination of tumor. Others have similarly found that local regression of tumor often occurs in patients who eventually die from distant metastases [9, 13, 19–21]. Thus, disappearance of the tumor on radiologic or endoscopic studies does not necessarily indicate a cure.

All but 1 of our patients with clinical follow-up had significant relief from dysphagia soon after completing RT. This dramatic clinical response correlated closely with regression of the lesion on esophagography. However, the majority of patients whose dysphagia initially improved had recurrent or increased dysphagia over a subsequent 3–9 month period. This exacerbation of symptoms often was not due to recurrent carcinoma but to benign radiation strictures or other causes such as opportunistic esophageal infection (i.e., *Candida* or herpes esophagitis) (Figs. 6 and 7) or a radiation-induced esophagopleural fistula (Fig. 8). Thus, radiologic studies to evaluate recurrent or increased dysphagia after initial regression of tumor may be extremely helpful in differentiating recurrent carcinoma from other esophageal complications in these patients.

In summary, total or partial regression of esophageal carcinoma can be recognized radiographically in the majority of patients treated by RT. In many cases, follow-up esophagrams may demonstrate benign residual strictures at the site of the previous lesion. Although local recurrences are relatively uncommon, patient survival is often limited by the development of distant metastases. Most patients initially experience significant relief from dysphagia as the tumor regresses. However, subsequent exacerbation of symptoms may result from not only recurrent carcinoma but also benign radiation strictures, opportunistic esophagitis, or other complications of RT that can readily be detected on esophagography. Our experience therefore suggests that serial radiologic studies after

completion of RT can significantly contribute to the evaluation and subsequent management of these patients.

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