Diagnostic Roentgenology of Radiotherapy Change

edited by
HERMAN I. LIBSHITZ, M.D.

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Dedication

To our patients
and to Susie.

Preface

Radiology is no longer a unified specialty. The diagnostic radiologist is now primarily concerned with the performance and interpretation of radiographic examinations while the therapeutic radiologist is now primarily concerned with the care and treatment of the patient with a malignancy. This division has resulted in benefit to our patients. Both have become more competent in their subspecialized area and both have been aided by improvements in techniques and equipment. Unfortunately, the relationship between the two is all too often the same as between the diagnostic radiologist and his colleagues in the other fields of medicine.

As in other areas that have become more subspecialized, discussion between various practitioners becomes more difficult. The basic education in both areas is no longer uniform. The common ground which had been present is split and the split is gradually widening. As the separation widens, the recognition of the roentgen appearance of radiation change is one area that can suffer. The internal dialogue that used to exist in the single individual who did both is no longer available. Our aim is to define the roentgen appearance of radiation change. We are neither radiation biologists nor radiation pathologists. While the roentgenographic appearance of any organ following irradiation is dependent on those changes caused by radiation at the cellular and tissue levels these areas will be considered only as they relate to the roentgenographic appearance.

The radiation therapist recognizes that normal tissue must be included in any treatment volume to totally encompass the lesion. As a result radiation damage occurs in this normal tissue. It is all too easy to refer to any changes caused by radiation as a complication of the therapy. At surgery some normal tissue is removed with the diseased. The analogous situation occurs in radiation therapy. It is better to refer to such changes as those expected following radiation therapy. Unfortunately, in either the surgical resection of malignancy or the sterilization of a malignancy by radiation, unexpected events can follow the treatment. These can truly be referred to as complications. It is our aim to define both changes that are expected as well as those sequelae that extend beyond this anticipated range.

When the anticipated changes of radiation therapy are identified the question of what represents either superimposed infection or recurrence of tumor is easier to answer. It is the identification of either of these that requires alterations or additions to the patient's therapeutic regimen. Confusing either recurrence of tumor or infection with the expected changes of irradiation can result in unnecessary diagnostic procedures or unwarranted therapeutic intervention.

It is hoped that this volume will be of value to both diagnostic and therapeutic radiologists and that our colleagues in other specialities of medicine and surgery who treat patients with malignancies will find it useful.

A volume of this sort, covering the entire range of diagnostic radiology, could not be written by an individual. The field has become too large. Were it not for my colleagues in the Department of Diagnostic Radiology at M. D. Anderson Hospital who have generously contributed their time, and especially their knowledge, this volume would not exist. The members of the Department of Radiotherapy also contributed generously of their time and knowledge and have made their records available to us. Too many other physicians to mention at our institution have also been of help with specific questions.

I should like to express particular thanks to

Gerald D. Dodd, M.D., and Sidney Wallace, M.D., for their encouragement and support and to Simon Kramer, M.D., and Martha Southard, M.D., of the Department of Radiotherapy, Thomas Jefferson University, Philadelphia, who taught me the importance of recognizing the effects of radiotherapy. Thanks, also, go to Miss Brenda Martin, my secretary, who kept track of all the parts of a multicontributor book. And, special thanks to my wife, Alison, for her understanding and tolerance.

H.I.L.

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Contents

chapter 1

Parameters Involved in Radiotherapy Complications

GILBERT H. FLETCHER, M.D.

An understanding of the irradiation factors related to radiotherapy complications will help the diagnostic radiologist to interpret roentgenologic findings and place them in a proper frame of reference.

There are two types of complications: (a) acute reactions during treatment and shortly thereafter, and (b) late complications which usually are the ones the diagnostic radiologist is concerned with. There is a loose correlation between the intensity of the reactions during treatment, such as skin reaction or mucosal reaction, diarrhea or cystitis, with late complications. The acute complications result from the damage to the active proliferative systems, epithelium of the skin, of mucosa, of the bladder, the bowel, and the late complications which are essentially due to fibrosis resulting from damage to the nonproliferative tissues. The mechanism of these late complications is poorly understood. Late complications can stabilize or they may increase through the years. For instance, if one is comparing a radiograph taken 5 years after radiotherapy for breast cancer with one taken after 10 years, an increase in severity of rib osteitis and pathologic fractures does not mean that the patient has active disease.

The important irradiation parameters are as follows.

Total Dose

As the dose increases, the incidence and severity of complications increases. For instance, more complications will be produced with 7,000 rad given in 7 weeks than with 4,000 rad given in 4 weeks.

Overall Treatment Time

Four thousand rad given in 2 weeks will produce more complications than 4,000 rad given in 4 weeks.

Fraction Size

The same total dose in the same overall time results in considerably more damage if given with fewer large fractions. The importance of fraction size in the development of complications was underscored in the following example. To shorten the treatment time in the palliation of very advanced breast cancer, four fractions of 500 rad were used instead of the 200-rad fraction used in the long protracted technique. Despite a much higher total dose in the protracted technique (nominal standard dose (NSD) of 1,743), there were less complications than with 4×500 rad (NSD of 1,271). When complications are unusually severe, the diagnostic radiologist should inquire about the details of treatment.

Volume of Tissue Irradiated

In the kilovoltage days, because it was a daily observation that the dose the skin can tolerate diminishes sharply as the area irradiated increases, the radiotherapists were reminded of the relationship of volume irradiated to tolerance. Because of the absence of skin reaction with megavoltage, the relationship of complications with volume irradiated is no longer as strongly appreciated.

In patients treated for an early vocal cord cancer with a small volume of larynx irradiated (20–25 cm^2 portal size) complications are extremely rare,

whereas in patients with a supraglottic cancer the field size is at least 50 cm^2 and various degrees of edema, chronic laryngitis, or even necrosis can develop.

Necrosis of the mandible is more frequent and more severe when a long segment of the mandible has been irradiated. Sigmoiditis after irradiation of pelvic malignancies is more common and more severe when the field sizes are more than the usual 15 × 15 cm. This has been well documented with the use of extended fields to irradiate the common iliac and/or para-aortic nodes.

For irradiation of peripheral lymphatics after radical mastectomy, one can give safely 5,000 rad in 5 weeks, 200 rad per fraction, to an L-shaped field, 6 cm wide over the parasternal area and 8 × 10 cm over the apical lung. A streak of asymptomatic pulmonary fibrosis is the only sequela. For irradiation of both whole lungs for bilateral pulmonary metastases, the total dose can only be 1,500 rad, 750 rad per week, 150 rad a day, if one wants to avoid crippling, at times fatal, diffuse pneumonitis.

Associated Therapies, Either Surgery or Anticancer Drugs

Bowel complications increase with celiotomy, more so if a lymphadenectomy is performed. Bleomycin and irradiation are synergistic in producing pneumonitis.

Dose Response Curves

Complications increase with the radicalism of the treatment, either in terms of total dose, fraction size, increased irradiated volume, and associated therapies. With a particular treatment regimen there may be either no or only minor complications and with what seems to be a small increase in the radicalism of the treatment, complications appear. The curve of increase in incidence and severity of complications is sigmoid shaped with a steep slope (Fig. 1.1). This sudden increase was experienced at M. D. Anderson Hospital by changing the irradiation for breast cancer to 3 days a week instead of 5 days a week (1). In the 5 day a week technique, the complications were quite acceptable. With the larger size fractions, multiple rib fractures, frozen shoulder, pneumonitis, etc., develop in a significant percentage of the patients.

DISCUSSION

Following irradiation of early tumors of the vocal cords or of the oral cavity there is practically no damage observable either by clinical or radiologic examination. For more advanced lesions, sequelae are an unavoidable consequence of treatment and should not be considered negligence on the part of the radiotherapist. It is the price that the patient has to pay to be cured of the cancer. The surgical equivalents would leave even larger deficits. For instance, laryngectomy eliminates normal speech. Cystectomy and prostatectomy for cancer of the urinary bladder and abdominoperitoneal resection for tumors of the sigmoid and rectum leaves the patient with considerable deficits. However, surgeons do not consider the loss of a useful organ a complication, but part of the treatment.

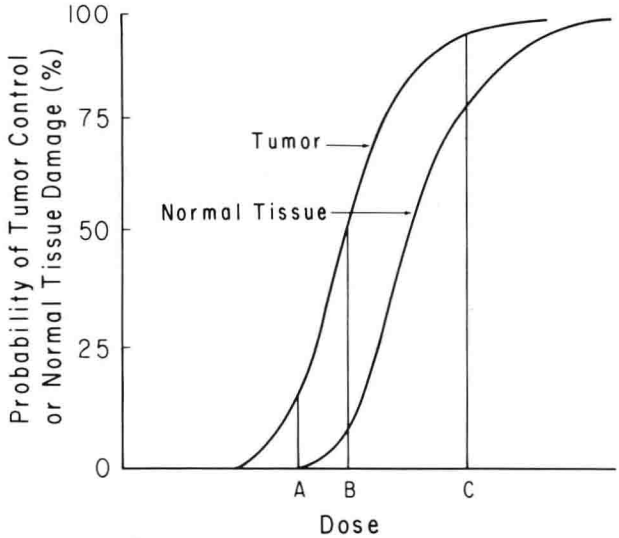

Figure 1.1. The curves, both for control and complications, have a steep slope.
(Courtesy of G. H. Fletcher, M.D., Houston, Texas. Reproduced with permission from G. H. Fletcher, H. R. Withers, and L. J. Peters: *Textbook of Radiotherapy*, Ed. 3. Lea & Febiger Publishing Company, Philadelphia, in press, 1978.)

Severe complications must be evaluated in a proper frame. For instance, there is no way to cure a high percentage of patients with extensive lesions of the tonsillar area without some patients experiencing osteonecrosis. With tumor doses less than 6,000 rad there are no complications but the control rates for the T_2 and T_3 lesions are low. There is a choice between low control rates and no complications versus high control rates and an incidence of complications.

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chapter 2

Head and Neck

BAO-SHAN JING, M.D., and MARVIN M. LINDELL, JR., M.D.

Radiation therapy plays a vital role in the treatment of malignant tumors of the head and neck. The early effects and late sequelae of irradiation upon both tumorous and normal tissues of the irradiated area depend upon the structure involved and its radiosensitivity, the time-dose-volume relationship of irradiation and presence or absence of complicating factors such as trauma, infections, and vascular compromise. The radiation change can be arbitrarily divided into acute, chronic, and late stages. In the acute stage of radiation changes, the parenchymal tissue may be lifted and sloughed as a result of acute edema secondary to acute vascular damage. The ability of the parenchymal tissue to regenerate is determined not only by the survival of the parenchymal cells and their capacity to proliferate, but also by the integrity of the supporting stroma and vasculature. Under favorable conditions, the damaged parenchyma may regenerate and the acute edema subsides. During the chronic stage when there is permanent tissue damage, progressive vascular and interstitial fibrosis may produce radionecrosis. In the late period, in addition to the slow progression of permanent residual tissue damage, radiation-induced sarcomatous degeneration may be manifested, usually preceded by chronic radiation damage. Among the radiation effects and sequelae, the most serious complications are severe soft tissue edema with fibrosis and necrosis, osteonecrosis, and sarcomatous degeneration.

LARYNX

POSTIRRADIATION EDEMA

Edema of the laryngeal structures is often encountered following external irradiation despite the best of techniques. It occurs most frequently during the latter stage or at the completion of treatment. The severity of edema is dependent upon the time, dose, and volume of the irradiated tissues. Edema of laryngeal structures usually recedes in the majority of cases within 6 months following proper treatment. Persistence of severe edema, with or without necrosis, may cause seriously impaired function of laryngeal structures.

Roentgen Findings

Postirradiation edema is usually manifested by generalized swelling of the laryngeal soft tissues, with or without significant distortion. It is greatly dependent upon the stage and extent of the lesion. Soft tissue roentgenograms of the neck usually suffice to confirm the diagnosis [Fig. 2.1]. In differentiating postirradiation edema of the larynx from tumor mass, the laryngogram is most diagnostic [Fig. 2.2]. A useful guide for differential diagnosis is as follows:

PARAMETER	*EDEMA*	*TUMOR*
1. Appearance	Generalized thickening	Localized thickening
2. Mucosal surface	Smooth	Irregular
3. Mobility	Normal	Impaired
4. Distensibility	Normal	Impaired

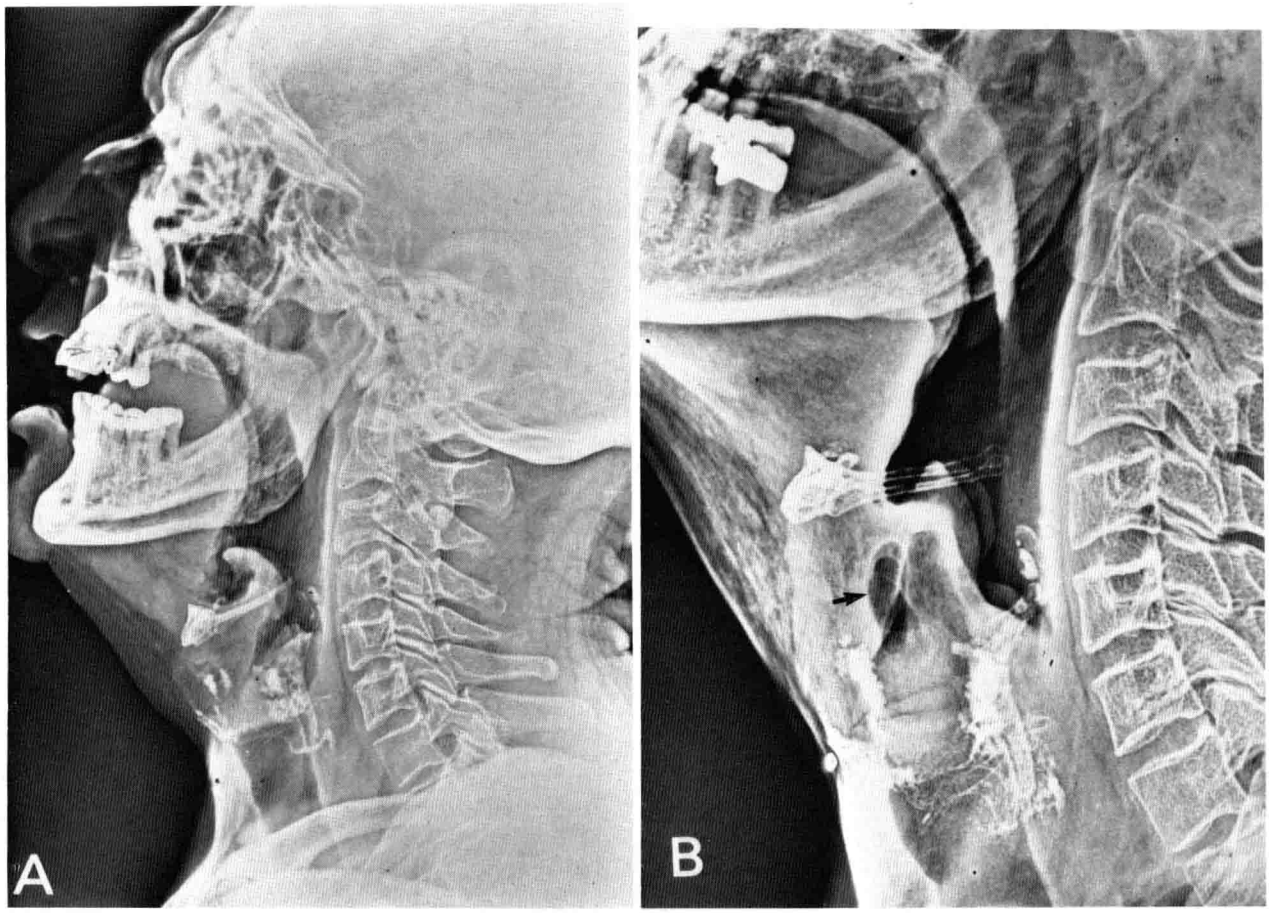

Figure 2.1. Postirradiation edema of larynx.
This 50-year-old man was treated for squamous cell carcinoma of the suprahyoid epiglottis over a 51-day period. Treatment was 7,000 rad tumor dose, 5,000 rad by ^{60}Co and 2,000 rad boost by 18 MeV photons. Postirradiation edema was still demonstrable 1 year following radiation therapy. **(A)** Lateral soft tissue xeroradiograph of neck prior to therapy shows extensive tumor of suprahyoid epiglottis. **(B)** Lateral soft tissue xeroradiograph of neck 1 year postirradiation therapy still shows postirradiation edema of infrahyoid soft tissues. Note presence of bilateral laryngoceles (*arrow*).

POSTIRRADIATION NECROSIS

Severe postirradiation edema of the larynx may progress to radiation necrosis. This may involve both soft tissues of the neck and the thyroid cartilage. It occurs more frequently with tumors that infiltrate the thyroid cartilage, particularly when the cartilage is exposed and infection is present. The basic cause of this necrotic process is the adverse effect of ionizing radiation upon the blood supply to the treated area. Contributing factors in the development of necrosis of the larynx include: short treatment time, large treatment portals, chronic upper respiratory disease, generalized arteriosclerosis, and chemical and mechanical irritants.

Most instances of laryngeal edema with subsequent necrosis appear within a year, half of them within 6 months and usually in patients whose treatment field utilized large portals. The incidence of laryngeal radiation necrosis is 7–10% (19, 41). Early cases may respond to medical treatment, but most often when thyroid cartilage necrosis has occurred, laryngectomy is necessary. Excision of the affected soft tissue and/or wound closure at a later date are advocated to limit the spread of infection.

Roentgen Findings [Fig. 2.3]

The pertinent manifestations are:

1. Generalized laryngeal edema.
2. Localized irregular soft tissue defects indicating ulcerative change.
3. Sclerosis in association with lytic defects of the thyroid cartilage.

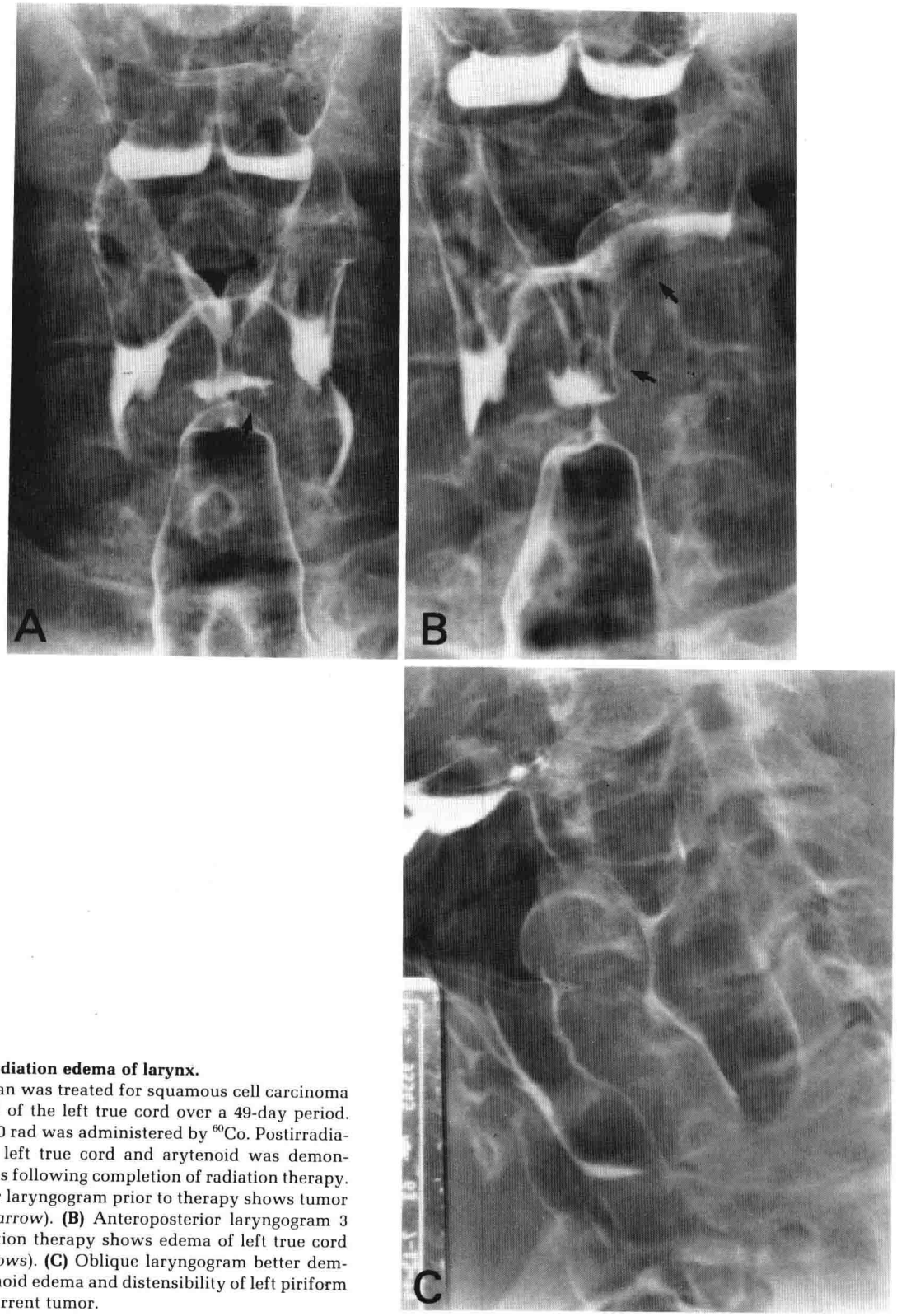

Figure 2.2. Postirradiation edema of larynx.
This 64-year-old man was treated for squamous cell carcinoma of the middle third of the left true cord over a 49-day period. Tumor dose of 7,000 rad was administered by ^{60}Co. Postirradiation edema of the left true cord and arytenoid was demonstrated three months following completion of radiation therapy. **(A)** Anteroposterior laryngogram prior to therapy shows tumor of left true cord (*arrow*). **(B)** Anteroposterior laryngogram 3 months after radiation therapy shows edema of left true cord and arytenoid (*arrows*). **(C)** Oblique laryngogram better demonstrates left arytenoid edema and distensibility of left piriform sinus rules out recurrent tumor.

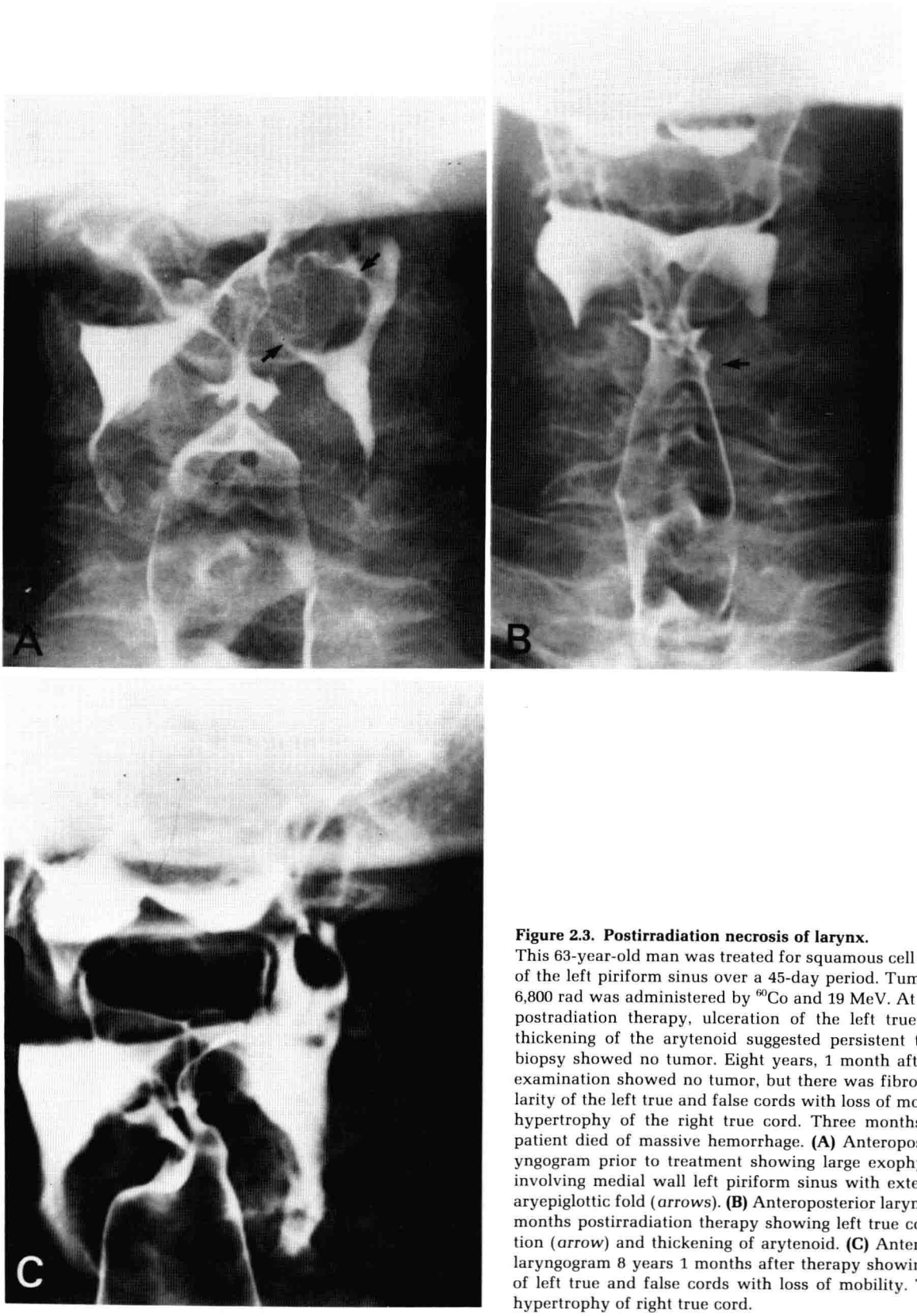

Figure 2.3. Postirradiation necrosis of larynx.
This 63-year-old man was treated for squamous cell carcinoma of the left piriform sinus over a 45-day period. Tumor dose of 6,800 rad was administered by ^{60}Co and 19 MeV. At 10 months postradiation therapy, ulceration of the left true cord and thickening of the arytenoid suggested persistent tumor, but biopsy showed no tumor. Eight years, 1 month after therapy examination showed no tumor, but there was fibrosis, irregularity of the left true and false cords with loss of mobility, and hypertrophy of the right true cord. Three months later the patient died of massive hemorrhage. **(A)** Anteroposterior laryngogram prior to treatment showing large exophytic tumor involving medial wall left piriform sinus with extension into aryepiglottic fold (*arrows*). **(B)** Anteroposterior laryngogram 10 months postirradiation therapy showing left true cord ulceration (*arrow*) and thickening of arytenoid. **(C)** Anteroposterior laryngogram 8 years 1 months after therapy showing fixation of left true and false cords with loss of mobility. There was hypertrophy of right true cord.