

Chondroradionecrosis of the larynx: still a diagnostic dilemma

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Abstract

Following radiation treatment for carcinoma of the larynx it may be very difficult to differentiate between persistent or recurrent tumour and severe radiation effects particularly chondroradionecrosis. Despite repeated negative biopsy it may be necessary to perform total laryngectomy where the concern about persistent cancer remains and the larynx is non-functioning. We report nine cases presenting as chondroradionecrosis over a five-year period. Two patients settled on medical treatment. Of seven patients treated with laryngectomy the histology on two revealed residual or recurrent carcinoma.

We outline the dilemmas in diagnosis and propose management strategies to deal with this condition including recommendations for prevention and treatment.

Key words: Laryngeal neoplasms; Radiotherapy, complications

Introduction

In 1972 Lederman outlined the four main complications of radiation in cancer of the larynx. These were (1) laryngeal oedema, (2) radiation damage to skin, (3) perichondritis, (4) cartilage necrosis (Lederman, 1972). Despite improvements in radiotherapeutic technique and the use of steroids and antibiotics these complications still occur albeit less commonly than before. The incidence has fallen from five per cent of patients undergoing radiotherapy for laryngeal cancer in 1970 to less than one per cent in the 1990s (Stell and Morrison, 1973; Oppenheimer *et al.*, 1989).

According to Stell and Morrison (1973) the worst possible complication that can befall a patient undergoing radiotherapy for cancer of the larynx is chondronecrosis. The patient frequently presents with persistent hoarseness and soreness long after the accepted radiation reaction should have settled. Indeed this complication can occur as late as 20 years after radiotherapy (Berger *et al.*, 1984). The main problems are pain, fetor and aspiration. On examination there is laryngeal oedema and there may even be ulceration and cartilage exposure (Chandler, 1979). There is often a high suspicion of residual or recurrent tumour and the patient undergoes numerous laryngoscopy procedures. Despite multiple biopsies histological confirmation is not obtained and yet the suspicion lingers. CT scan has done little to help resolve the diagnostic dilemma (Flood and Brightwell, 1984).

In such cases it may be decided that the best and safest option is to perform a total laryngectomy (Stell and Morrison, 1973; Oppenheimer *et al.*, 1989). The main indications for total laryngectomy are firstly, the presence of a painful functionless larynx and secondly, the suspicion of

the presence of tumour which may only be confirmed on histological examination of the entire larynx (Flood and Brightwell, 1984).

The problem does not end here since healing after a laryngectomy in these circumstances is not without its complications and infection and pharyngocutaneous fistulae are relatively frequent (Stell and Morrison, 1973).

Materials and methods

Over a five-year period 1988–1993 nine patients presented to Otolaryngology/Head and Neck units in Dublin with a diagnosis of chondroradionecrosis. All had been treated in one central radiotherapy unit. There were eight males and one female whose ages ranged from 42–70 years with a mean age of 56 years.

Their clinical notes were reviewed for details of clinical presentation and treatment. Initial tumour stage for each patient was as shown in Table I. We reviewed the radiotherapeutic data, the operative notes and the histological records on all patients.

Results

All patients had external beam treatment using cobalt 60. The exact dose, number of fractions and duration of therapy for each patient is shown in Table II. It is immediately obvious that there are variations in the total dose, the number of fractions and the duration of treatment in the case of each patient. No two patients received the same regime even for the same stage tumour. In the group of T₁ tumours total dose varied from 4400 to 6250 cGy. The number of fractions in this group varied from 16 to 27 and

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Accepted for publication: 27 October 1994.

TABLE I

Tumour stage	Number of patients
T ₁ N ₀ M ₀	5
T ₂ N ₀ M ₀	3
T ₃ N ₂ M ₀	1

the duration of therapy from first to last day of treatment varied from 28 to 61 days. Similar variations were noted for T₂ and T₃ tumours. Suspicion of chondroradionecrosis was aroused when patients presented with varying degrees of pain, hoarseness, fetor and symptoms of upper airway obstruction (Table III). The time interval between cessation of radiotherapy and time of presentation varied from three and six months.

All patients had direct laryngoscopy as part of their initial assessment and all had repeated biopsy because of the grave suspicion of residual or recurrent tumour. At post-treatment laryngoscopy all patients were found to have marked redness and gross laryngeal oedema. Six patients had cartilage exposure and in five there was additional marked mucosal ulceration. On assessment of vocal fold mobility seven patients were found to have reduced vocal fold mobility including three who had a fixed unilateral fold. Four patients were described as having a 'fibrotic fixed larynx' and three had significant problems with aspiration. Seven patients required tracheostomy as an emergency procedure for acute onset of stridor and the other two had tracheostomy as a planned procedure for increasing airway difficulties.

All patients were initially managed conservatively using humidification, steroids and an antibiotic regime which included metronidazole. All patients had repeated direct laryngoscopy on at least three separate occasions to monitor progress and to facilitate further biopsy because of suspicion of tumour. There was an initial improvement in all patients but a sustained result was seen in only one case. One other patient responded to medical treatment following debridement.

In the remaining seven patients despite a negative biopsy it was decided after much deliberation and multiple biopsies that the most appropriate treatment was total laryngectomy. These patients had failed to improve over a six-week period with intensive medical treatment. All were in severe pain and three had significant problems with aspiration. In two cases in particular there was suspicion of tumour but we were unable to confirm our suspicions from a pre-operative biopsy.

TABLE II

Patient no.	T stage	Total dose (cGy)	Number of fractions	Duration of treatment in days
1	T ₂ N ₀ M ₀	6000	25	35
2	T ₁ N ₀ M ₀	6000	27	42
3	T ₂ N ₀ M ₀	6000	25	35
4	T ₃ N ₀ M ₀	5980	42	42
5	T ₁ N ₀ M ₀	5000	16	20
6	T ₂ N ₀ M ₀	6000	30	28
7	T ₁ N ₀ M ₀	6250	26	54
8	T ₁ N ₀ M ₀	4625	25	32
9	T ₁ N ₀ M ₀	4400	26	61

Following total laryngectomy the histology results revealed tumour in two larynges. We had suspected recurrence in one of these patients and chondroradionecrosis in the other. The remaining five patients showed chondroradionecrosis with no evidence of residual or recurrent tumour.

Not surprisingly the post-operative course for these patients was prolonged and fraught with problems. Four patients developed cutaneous fistulae all of which subsequently healed. One patient had a cerebrovascular accident from which he made a complete recovery. One patient died of tumour invasion of a major vessel. There are eight surviving patients in the group at the present time with a mean follow-up time of four years.

Discussion

The expected incidence of chondroradionecrosis is nowadays taken as less than one per cent (Oppenheimer *et al.*, 1989). There are a number of possible precipitating factors, the most important of which are considered to be radiotherapeutic factors (McGovern *et al.*, 1973; Chandler, 1979). The incidence of this complication is directly related to the total dose, the number of fractions, the field size and the duration of therapy (Chandler, 1979).

A number of other factors are felt to increase the tissue susceptibility to radiotherapy. These include respiratory tract infections (McGovern *et al.*, 1973; Flood and Brightwell, 1984). It was interesting to note that almost all of our patients suffered from chronic obstructive airways disease. All had a previous history of smoking and in fact one third of our patients continued to smoke following commencement of radiotherapy. There is felt to be increased individual susceptibility in patients who suffer from diabetes mellitus, arteriosclerosis, peripheral vascular disease or in those who continue to smoke after the commencement of treatment (Rugg *et al.*, 1990; DesRochers *et al.*, 1992).

Regarding the possible increased risk of developing radionecrosis following combined radiotherapy-chemotherapy treatment for head and neck tumours, it appears that when known risk factors are avoided the incidence of this complication is not increased (Schratter *et al.*, 1991). Mechanical injury in the form of repeated direct laryngoscopy and biopsy, while essential for diagnosis on the one hand, may be felt to be contributory in a small number of cases in converting perichondritis into frank necrosis (Chandler, 1979).

The changes secondary to chondroradionecrosis are very similar to those of carcinoma and this presents a major diagnostic dilemma to the practising otolaryngologist and pathologist. When a patient presents with this condition the appropriate initial management is medical. A trial of treatment of humidification, steroids and anti-

TABLE III

Presenting complaint	Number of patients
Hoarseness	9
Pain	7
Dysphagia	9
Fetor	3
Stridor	7

biotic therapy should be given for up to six weeks if necessary. Virtually all patients require a tracheostomy and this is probably best done sooner rather than later (Oppenheimer *et al.*, 1989). The changes due to radiation fibrosis may obscure residual or recurrent carcinoma and this presents a great diagnostic dilemma. CT scan unfortunately is not of great benefit in helping to differentiate between the two (Flood and Brightwell, 1984). Repeated laryngoscopy and biopsy are essential to help resolve this dilemma. Even then the answer is not always forthcoming. Sometimes there is no other option but total laryngectomy (Stell and Morrison, 1973; Oppenheimer *et al.*, 1989).

We would advocate total laryngectomy in the following instances, firstly in the case of a patient with a painful, functionless larynx particularly where aspiration is a significant problem and secondly in the patient where there is a strong clinical suspicion of tumour despite repeated negative biopsy. Clearly this latter case presents a potential medicolegal problem but these indications are in keeping with those suggested by leading authorities who have written about this condition in the past and unfortunately nothing has helped to resolve this dilemma since that time (Stell and Morrison, 1973; Flood and Brightwell, 1984).

Like many conditions the emphasis nowadays is probably better placed on prevention. We would like to make a number of recommendations in order to decrease further the incidence of this condition. It is important to aggressively treat respiratory tract sepsis and in particular patients should stop smoking prior to commencement of radiotherapy. Unfortunately as we found this does not always happen.

While radiotherapeutic techniques have shown vast improvement in the past 20 years it cannot be stressed too much that further improvements are necessary in standardization of radiotherapy regimes. There are still wide variations in total dose, fraction size, field size and duration of therapy. It is not always easy to prevent movement of a patient during treatment even with a cast. It is important to note that radiation beams directed even a little off the intended site may have serious consequences particularly in a susceptible patient. As with all other types of apparatus, despite the utmost attention to calibration, it is often difficult to ensure that the number of cGy intended is the number put out by the machine and consequently the number received by the patient.

It may be quite difficult to distinguish between the so-called 'normal' or acceptable radiation reaction and the more severe reaction of chondroradionecrosis; hence, a high index of suspicion is required particularly now that the incidence is not as high as it was. With so many potential factors involved it is surprising, and to the credit of the high standards of modern radiotherapy, that this complication does not occur more frequently than it does.

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