



Autopsy Findings in Patients with Head and Neck Squamous Cell Cancer and Their Therapeutic Relevance

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A series of 63 autopsied patients with a history of head and neck squamous cell cancer (HNSCC) is reported with emphasis on the importance of locoregional disease (LRD) versus distant metastasis (DM) in the terminal course of the disease. There were 49 males and 14 females; mean age 64.9 years (range 35–94 years). Locoregional disease was present in 39 patients (62%), in 25 (40%) without tumour at other body sites outside the head and neck region. Distant metastasis was observed in 15 patients (24%); in 12 (19%), it occurred with concomitant LRD. Second primary tumours (SPT) were observed in 20 patients (32%). They occurred in the head and neck region ($n = 7$; 11%), the lung ($n = 9$; 14%) and at miscellaneous other sites ($n = 4$; 6%). Of the 13 patients with SPT outside the head and neck region, 2 had concomitant LRD. 11 patients (17%) died due to other causes, no tumour being found at autopsy. These figures indicate that still a major part of HNSCC patients die with LRD as the single tumour manifestation, which means that improvement of local tumour control will result in a significant therapeutic gain. Copyright © 1996 Elsevier Science Ltd

Key words: head and neck tumours, squamous cell cancer, autopsy, metastasis, second primary tumour

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INTRODUCTION

Recent studies that increased effectiveness of treatment of patients with head and neck squamous cancer (HNSCC) resulted in a substantial decrease of persistent or recurrent locoregional disease (LRD) defined as tumour above the clavicle [1–3]. In comparative studies with historical controls, LRD as cause of death in HNSCC patients is reported to have diminished from 30 to 15% [1]; from 96 to 44% [2] or from 70 to 15% [3]. However, this reported improvement of locoregional cure rates has not resulted in a substantial increase in survival figures in patients with HNSCC, which suggests that more patients die due to distant metastasis or second primary tumours [1–3].

In the present paper, we report the autopsy findings of a group of HNSCC patients with the aim of analysing the relative importance of LRD in comparison with distant metastasis (DM) and second primary tumour (SPT) as causes of treatment failure, thus assessing the potential increase in survival figures that is attainable by improved local tumour control and the adverse influence on survival of DM and SPT.

MATERIALS AND METHODS

Between January 1983 and December 1995, autopsies were performed on 63 patients with a clinical history of HNSCC. Of the 63 patients, 49 were male and 14 female. The mean age was 64.9 years (range 35–94 years).

During the same time span, approximately 3000 patients had been treated for HNSCC at the University Hospital of the Utrecht University. As in The Netherlands the death rate from head and neck cancer is 40% [4], these 63 patients can be considered to represent a sample from the 1200 HNSCC patients who died during the same time interval. How far this sample is representative of all deaths cannot be assessed beyond doubt.

We decided only to study autopsy cases, as clinical data including imaging techniques have been shown to be unreliable in yielding data on tumour spread outside of the head and neck area [5], the incidence of distant metastasis found at autopsy being twice as great as that determined by clinical studies [6, 7].

Cases were evaluated for the following findings at autopsy: LRD defined as tumour in the head and neck area; SPT outside the head and neck area; DM defined as metastatic tumour from HNSCC occurring below the clavicle, and death from other causes (DOC). Secondary primary HNSCC was classified in the category LRD. Part of the

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Table 1. Autopsy findings in 63 patients suffering from HNSCC* during life

No tumour at autopsy	11	(17%)
Death with LRD† only	25‡	(40%)
Death with LRD† + DM§	12	(19%)
Death with DM§	3¶	(5%)
Death with SPT**	10	(16%)
Death with LRD† + SPT¶	2	(3%)

* HNSCC, head and neck squamous cell cancer.

† LRD, locoregional disease.

‡ Including 4 patients with LRD due to second primary HNSCC tumour.

§ DM, distant metastasis.

|| Including 3 patients with LRD due to second primary HNSCC.

¶ Including 1 patient with second primary tumour in the bladder.

** SPT, second primary tumour.

material has been published previously, but has been included to expand the data available for analysis [8].

RESULTS

The findings at autopsy are listed in Table 1. From this table, it appears that 39 (62%) patients had tumour in the head and neck region at the time of death. In 7 of these patients, the local tumour was due to a second HNSCC.

In 15 patients (24%), DM was observed. In 2 of them, DM was the only tumour found at death; in 1 DM occurred together with transitional carcinoma of the urinary bladder. In the other 12 patients, DM occurred together with persistent local disease. All patients with DM had, with 2 exceptions, neck node metastasis either being manifest during their clinical course or found at autopsy.

In 20 patients (32%), SPT was observed. In 7 of them, as mentioned above, this second tumour was another HNSCC; in 7, it was a squamous cell carcinoma of the lung. 2 patients died with an adenocarcinoma of the lung and the other 3 had an adenocarcinoma of the gall bladder, an adenocarcinoma of the caecum and a hepatocellular carcinoma, respectively. In 1 patient, as already mentioned above, a urinary bladder carcinoma was present together with DM from HNSCC.

24 patients (38%) died without local tumour; however, 13 of them had either a SPT below the clavicle or DM or both and only 11 (17%) had no tumour at all; these 11 died due to bronchopneumonia and/or myocardial infarction.

DISCUSSION

The aim of the present study was to analyse, by means of autopsy data, the importance of locoregional disease versus distant metastasis as a cause of treatment failure in HNSCC

patients. Moreover, the significance of SPT above or below the clavicle as a cause of the patient's demise was registered. Such data form basic knowledge when discussing whether therapeutic strategies aimed at increasing survival figures should be focused on improving locoregional therapy, or that prevention of DM or SPT will be more fruitful.

For such an analysis, data have to be tabulated as patients dying with LRD with and without DM separately. Such data are relatively scarce, as most of the older reports only mention the incidence of DM without LRD data, or used the presence of LRD as a criterion for inclusion in their study.

In fact, only four studies are detailed sufficiently to allow comparison with our data [9–12]. These are tabulated in Table 2 together with the present data. To obtain comparable data, patients with SPT outside of the head and neck region have been omitted from this table.

It appears that, in all series, the majority of deceased patients have LRD. Distant metastasis as single tumour manifestation plays a minor role. As a substantial proportion of patients succumb with LRD as well as DM, increased effectiveness of locoregional treatment will, indeed, result in a shift from LRD to DM as a more important cause of death as outlined before [1–3].

However, there is still a significant number of patients with LRD as the single tumour manifestation at the time of death for which category improvement of local control could have been life-saving.

Another aspect jeopardizing the survival of patients with HNSCC is the occurrence of SPTs. In previous autopsy-based data, they are reported to occur in approximately 20% [3, 11, 13]. We observed a percentage of 32% second primaries; most of them occurring in the lung; if one excludes SPT in the head and neck area, the incidence is 21%. As the lung is also the most common site of DM; the classification of a lung lesion as a primary tumour or metastatic lesion is not always unequivocal and additional diagnostic criteria other than morphological ones are needed urgently. We made an attempt in this direction by applying DNA flow cytometry, but this approach did not yield useful data due to DNA heterogeneity within individual lesions [14].

It is tempting to use our results to calculate the influence of further improved local control on survival. If we assume that the survival rate for patients with HNSCC is approximately 60% [15], the influence of improved local control on survival rate can be calculated as follows; the 63 patients in the present series have all died. However, 11 of them were without tumour; therefore, tumour-related deaths are 52.

Table 2. Occurrence of LRD* in comparison with DM* in autopsied HNSCC* patients

Reference	LRD ⁺ /DM ⁻	LRD ⁺ /DM ⁺	LRD ⁻ /DM ⁺	LRD ⁻ /DM ⁻
[9]	33%	52%	2%	12%
[10]	—	42%	4%	—
[11]	40%	35%	5%	21%
[12]	38%	27%	10%	25%
Present study†	51% (27)	23% (12)	6% (3)	21% (11)

* See footnote to Table 1.

† In these data, 10 patients with only second primary tumour below the clavicle are excluded, whereas cases dying to secondary HNSCC are included as LRD⁺.

These 52 cases could be considered to represent the 40% of deaths from a population that thus, theoretically, consists of 130 patients. Successful treatment of LRD would have resulted in only 13 deaths (patients dying with SPT or DM) instead of 52 deaths, which theoretically would improve the survival rate from 60 to 90% (13 deaths out of a population of 130 patients makes a survival rate of 90%). However, 14 of the 39 patients with LRD also suffered from either DM or SPT and, as these patients would have died notwithstanding successful local treatment, the survival rate improves not to 90% but only to 80% (25 patients dying with only LRD from the theoretical population of 130 cases). Thus, it is shown that successful local treatment will reduce the tumour-related mortality in HNSCC patients, from 40 to 20%; the remaining 20% mortality being due to either SPT, DM or both together. How far this optimal result will be compromised by the development of additional SPT and/or DM in this 80% of patients initially treated successfully cannot be foreseen.

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