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Distant Metastasis of Locally Controlled Supraglottic Laryngeal Carcinoma: A report of two cases

Charles N. Ford, MD,* William W. Finch, MD,** and Roger W. Kwong, MD***

Two cases of supraglottic laryngeal carcinoma are presented in which distant metastasis occurred after adequate local control had been established. The metastasizing tendency of this lesion is discussed, and the efficacy of combined therapeutic approaches in treating these cases is questioned.

Introduction

TUMORS of the larynx are generally predictable, and the head and neck surgeon relies on therapeutic measures aimed at control of the primary cancer and regional metastases. Distant metastasis occurs infrequently and is usually associated with advanced, uncontrolled, or recurrent disease locally. This report describes the finding of unsuspected distant metastases in two patients with supraglottic laryngeal cancer who appeared to have adequate primary and regional control.

Supraglottic cancer of the larynx differs significantly from other laryngeal tumors because it can achieve significant growth before becoming symptomatic and, unlike glottic cancer, the patient typically presents with advanced disease. The rich lymphatic system of the supraglottis predisposes to early metastasis. Multiple small foramina in the epiglottic cartilage can be invaded by tumor cells which replace minor salivary gland tissue.¹ This facilitates early metastatic spread into the pre-epiglottic space, which is clinically a silent area.

In our experience, the nonsmoker may be more likely to present with supraglottic cancer than the smoker. From our review of 159 patients with laryngeal carcinoma, 3% were nonsmokers; but within the subgroup of supraglottic laryngeal carcinoma, 7% (3 of 43) were nonsmokers. We also found that 26% in this subgroup (11 of 43) had poorly differentiated tumors versus only 8% in the total group of 159. These patterns tend to distinguish the supraglottic lesion from other laryngeal cancers.

Case Reports

Case 1

A 57-year-old man presented with a minimally symptomatic right neck mass that had grown progressively for three months. During that time he lost 10 pounds. His only complaint was pain in the right ear. Physical examination revealed an exophytic tumor of the

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epiglottis, right aryepiglottic fold, false vocal cord, and tip of arytenoid with a mobile, grossly uninvolved vocal cord. Two large, relatively fixed nodes were present in the upper and mid-deep jugular chain measuring 8 and 5 cm, respectively. After biopsy had confirmed the diagnosis of squamous cell carcinoma, the patient underwent preoperative Cobalt 60 radiation therapy (5000 rads to the neck and 4500 rads to the primary) and supraglottic laryngectomy with right radical neck dissection. The pathological report revealed residual carcinoma in the epiglottis. There was histologic evidence of breakthrough of tumor from the cervical lymph nodes into surrounding fibrofatty tissue. Specimen margins as well as superior and inferior-most nodes were negative. The patient was followed carefully every month for one year, then every other month without evidence of residual and recurrent disease. Eighteen months postoperatively, he complained of general poor health, decreased appetite, and a tendency to vomit. Although the entire head and neck examination was negative, he had a large mid-epigastric mass, decreased breath sounds, and a chest x-ray showing widespread pulmonary metastatic disease. A liver biopsy showed grade IV squamous cell carcinoma similar to the primary cancer but with greater indications of anaplasia. He died after failing to respond to chemotherapy, and the autopsy revealed generalized metastasis to all systems.

Case 2

A 35-year-old woman presented with an asymptomatic left neck mass of one year's duration and increasing hoarseness of five month's duration. This patient had never smoked. Examination revealed an exophytic tumor involving the epiglottis, left aryepiglottic fold, and false cord without involvement of the true vocal cord. Biopsy showed infiltrating squamous cell carcinoma which was poorly differentiated. Treatment consisted of a supraglottic laryngectomy with left radical neck dissection, followed in four weeks by a planned postoperative course of 5000 rads megavoltage radiation therapy. The specimen showed poorly differentiated squamous cell carcinoma with penetration to the thyroid cartilage and positive mid-jugular nodes. Five months postoperatively, the patient developed an asymptomatic firm mass in the right forearm. When it was excised, it was found to be poorly differentiated grade IV carcinoma with an histology identical to that seen in the primary lesion. She was evaluated by a medical oncologist and found to have no evidence of disease elsewhere. She refused chemotherapy. Instead, she chose to use vitamins and health foods and became a strict vegetarian. After one year of careful follow-up, there is still no further evidence of metastatic disease, and the residual larynx and neck examinations remain negative for local recurrence.

Discussion

Three factors generally determine the likelihood of metastasis in head and neck cancers: 1) the location of the primary lesion; 2) its size and pervasiveness; and 3) the degree of cellular differentiation. The most important factor seems to be the location of the primary lesion. The propensity of supraglottic lesions to show early metastasis to

cervical nodes is well documented^{2,3} and sets them apart from glottic carcinoma.

The occurrence of distant metastasis in supraglottic cancer is well recognized. In reviewing 55 patients with supraglottic laryngeal carcinoma treated with conservative surgery, De Santo⁴ found that 9% died of distant metastasis. Two of these patients apparently had no evidence of local or regional nodal disease. Our two patients also reflect this pattern of distant metastasis in the presence of adequate local control. This capricious tendency in supraglottic laryngeal carcinoma raises the questions of whether such behavior can be predicted and whether current modes of treatment are appropriate.

From these two cases, it would seem that the pathogenesis and eventual occurrence of distant metastasis may be predictable. Given their parameters of primary site, size, and histological grade, both patients would be expected to have metastatic disease, and did, in fact, present with cervical node involvement.

There appears to be a qualitative difference between lesions arising in response to known irritative carcinogens and those arising apparently *de novo*, as the former tend to be better differentiated. Both patients in our report were non-smokers, and nothing in their history suggested ongoing, respiratory tract irritation. In such a setting, the chances are greater that a laryngeal cancer would be poorly differentiated.

In our first case, there was a premonitory finding of cervical node fixation. After 18 months the patient showed no evidence of disease in the neck, but there was widespread blood borne metastasis. The histologic finding of extranodal spread into cervical fibrofatty tissue, as noted in the initial surgical specimen, signals his predisposition to vascular dissemination.

On the basis of the clinical histories presented, it is possible to speculate that a major role is played by the impaired integrity of the immunological system. The magnitude and extent of metastatic disease in Case 1 reflects a loss of immunocompetence reminiscent of the familiar case of the head and neck cancer patient who is overwhelmed by multiple primary carcinomas.

It has been conclusively shown that immunodeficiency states are associated with an increased incidence of malignancy.^{5,6,7} Immunosuppression is also a factor in the increased incidence of recurrence and metastases in cancer patients lacking delayed cutaneous hypersensitivity to 2,4-dinitrochlorobenzene.⁸ In the patients we have presented, there are at least four factors which have been independently demonstrated to suppress immunocompetence: 1) the presence of a malignancy in the head and neck;⁹ 2)

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administration of anesthesia;^{10,11} 3) a major surgical procedure;¹² 4) radiation therapy.¹³

It is important to consider the possible effects of therapy on the immunological integrity of the patient. The anticipated efficacy of a combined therapeutic approach must be carefully reassessed with each individual patient. In reviewing the results of radiation and surgical treatment in laryngeal cancer, DeSanto found that, in most instances, one or the other was as effective as the combination.⁴ Furthermore, the decreased morbidity and increased cost effectiveness of a single mode of therapy should also be considered. We suggest that combined therapy may have a greater immunosuppressive effect than either modality alone. In the patients presented in this report, the tumor cells tended to thrive, even with adequate local control, in an apparently immunosuppressed substrate.

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