Results and Prognostic of pNO Laryngeal Cancer Treated by Post-Operative Irradiation

Introduction

Worldwide, there are approximately 130,000 new laryngeal cancer cases and 70,000 deaths annually. In the United States, laryngeal cancer accounts for about 25 percent of the 53,000 cases of head and neck cancer diagnosed annually [1]. Glottic, supraglottic, and subglottic cancers represent approximately two-thirds, one-third, and two percent of laryngeal cancers respectively. Survival rates of laryngeal cancer patients range from 73% to 92% for early disease stage (I and II) and from 50% to 64% for advanced stage (III and IV) [2]. Many prognostic factors have been studied and linked to the locoregional control and survival of laryngeal cancer. They include: resection margin, treatment modality, site of origin, disease stage, extracapsular spread, tumor volume, tumor grade, perineural invasion, lymphatic vessel density and nodal status [3-11].

The aim of our study is to investigate the survival and to determine prognostic factors of the larynx cancer in patients with pathological stage pN0.

Case Presentation

Between January 2011 and December 2012, a total of 102 patients were retrospectively analyzed. Subgroups of pN0 patients with laryngeal cancer included 38 patients. Primary surgical treatment consisted of total laryngectomy and neck dissection. The type of lymphadenectomy was selective neck dissection. The total dose of adjuvant radiotherapy was between 46 and 66 Gy in 2 Gy per fraction on the tumor bed. Concurrent chemotherapy with cisplatin 40 mg/m\(^2\)/week was used in 5 cases which 4 with positive margins and one with close margin.

They were retrospectively analyzed. Local control rate, Overall survival (OS) and Disease-free survival (DFS) were calculated using SPSS 20. For the univariate analysis, we study prognostic variables: margin status, T stage and subglottic extension.

Results

Most of patients were males (97.4%). Median age was 58 years (range: 44-78). Subglottic extension was observed in 23 patients (60.5%). Stages I, II, III and IV patients accounted for 2.6%, 15.8%, 36.8% and 44.8% respectively. In this study, the median follow-up time was 29.5 months (6-58). In Table 1, the characteristics of the patients were summarized. The main characteristics were the predominance (81.5%) of advanced stage and the tumor extension.

After a median follow-up of 29.5 months (6-58), we found one local relapse in the tumor bed which had positive margins, 3 distant relapses in the lung (7.9%) which had stage IV, and one death. No patient presented a nodal relapse. 2 patients (5.3%) were lost to follow-up. Local control rate was 89.5%. The 4-year overall survival (OS) and disease-free survival (DFS) rates were 96.4%, 80.9% respectively (Figures 1 and 2). The main long-term complications of therapy were xerostomia (28.9%), neck fibrosis (21%), dysphagia (7.8%) and hoarseness (16.7%). Univariate analysis demonstrated an insignificant influence on survival (p=0.21, p=0.50 and p=0.64) for subglottic extension, margin status, and T stage respectively (Figure 3).

Discussion

Postoperative radiotherapy is generally restricted to patients thought to be at elevated risk of locoregional recurrence. It should be used with caution and only in those at risk because of the morbidity of postoperative radiotherapy and uncertainty regarding a survival benefit. Factors associated with an increased risk of locoregional recurrence after surgery include: Advanced tumor (T) stage (T3/T4), positive resection margins or tumor close

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The prognosis of laryngeal carcinoma is related to a variety of clinical and histological factors, including nodal status. The presence of cervical positive lymph nodes is a significant predictor of poor survival outcomes in patients with laryngeal squamous cell carcinoma [9,21,22]. N stage decreases the disease-related survival by approximately 50% and is considered as the only significant factor for distant metastasis [6,9]. Published series node-negative cases were scarce. They were characterized by the extensively locally advanced tumor [23-25]. In our material, there was no significant effect of prognostic factors (margin status, T stage and subglottic extension) on the treatment results, but we found a good result for this sub group of pN0 laryngeal cancer (The local control rate, the 4-year overall survival (OS) and disease-free survival (DFS) rates were 89.5%, 96.4% and 80.9% respectively). Clinical trials have demonstrated that postoperative concurrent chemoradiation therapy with cisplatin is more likely than to the resection margin, tumor extension through the lymph node capsule (extracapsular extension), two or more positive lymph nodes (N2/N3), perineural invasion and lymphovascular space invasion [12-20].

Table 1 Patient characteristics.

| Characteristics                        | N (%) or range |
|----------------------------------------|----------------|
| Gender                                 |                |
| Male                                   | 37 (97.4 %)    |
| Female                                 | 1 (2.6 %)      |
| Age, Years (Median)                    | 58 (44-78)     |
| Tobacco use                            | 31 (81.6%)     |
| Alcohol use                            | 6 (15.8%)      |
| Presenting symptom                     |                |
| Neck mass                              | 0              |
| Hoarseness                             | 34 (89.5%)     |
| Dysphagia                              | 6 (15.8%)      |
| Dyspnea                                | 28 (73.7%)     |
| Anatomic regions                       |                |
| Supraglottis                           | 1 (2.7%)       |
| Glottis                                | 5 (13.2%)      |
| Subglottis                             | 2 (5.3%)       |
| Supraglottis+Glottis                   | 9 (23.6%)      |
| Subglottis+Glottis                     | 9 (23.6%)      |
| Three anatomic regions                 | 12 (31.6%)     |
| Pathologic type: Squamous cell carcinoma | 38 (100%)    |
| T stage                                |                |
| T1                                     | 1 (2.6%)       |
| T2                                     | 6 (15.8%)      |
| T3                                     | 14 (36.8%)     |
| T4                                     | 17 (44.7%)     |
| N stage                                |                |
| N0                                     | 38 (100%)      |
| M stage                                |                |
| M0                                     | 38 (100%)      |
| M1                                     | 0              |
| Surgery                                |                |
| Larynx preservation surgery            | 36 (94.7%)     |
| Total laryngectomy                     | 2 (5.3%)       |
| Positive margins                       | 4 (10.5%)      |
| Close margins                          | 1 (2.6%)       |
| Negative margins                       | 33 (86.8%)     |
| Lymphovascular space invasion          |                |
| Yes                                    | 1 (2.6%)       |
| No                                     | 37 (97.4%)     |
| Perineural invasion                    |                |
| Yes                                    | 2 (5.3%)       |
| No                                     | 36 (94.7%)     |
| Radiation therapy                      |                |
| Postop chemo radiation therapy         | 5 (13.1%)      |
| Postop radiation therapy               | 33 (86.9%)     |
| Late toxicity                          |                |
| Dysphagia                              | 2 (8.3%)       |
| Xerostomia                             | 7 (28%)        |
| Neck fibrosis                          | 5 (20.8%)      |
postoperative radiation therapy (RT) alone to locoregional control disease and improve disease-free survival for patients with positive surgical margins and extracapsular extension [12,26,27].

Data supporting the use of postoperative RT without concurrent chemotherapy to improve locoregional control and survival is limited to two small randomized trials and retrospective observational data: One trial in 51 patients with advanced head and neck cancer found that the addition of RT to surgery decreased the overall recurrence rate [28]. However, no difference in overall survival was observed. A second trial, limited to 140 patients, all with squamous cell carcinoma of the oral cavity, did observe a statistically significant increase in disease-free survival at three years with postoperative RT compared to surgery alone [29]. In this study, the main cause of failure was distant metastases in the lung which were reported in 3 patients (7.9%). The main long-term complications of therapy were xerostomia (28%), neck fibrosis (20.8%) and dysphagia (8.3%).

According to the study by Nguyen-Tan et al. assessed a group of 223 laryngeal cancers postoperatively irradiated. They reported three tracheocutaneous fistula (1.3%) and three esophageal strictures (1.3%) [4].

Another study by Maillard et al. [30], including 166 patients with laryngeal cancer, fibrosis was noticed in 11 patients (7%) and tracheoesophageal fistula in two patients (1%).

The prognostic of larynx cancer stage N0, pN0 remains good. The main cause of failure was distant metastases in our study despite a small sample size.

Conclusion

Subgroups of patients with pathologically negative regional lymph nodes, despite the extensively locally advanced tumor, have a good local control and survival.

Declaration

KM, AS and LR were the major contributors in writing the manuscript. HE, TK, SM and NB cared for the patient during her time in the hospital and assisted in the data collection and the preparation of the manuscript. All authors read and approved the final manuscript.

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Availability of Data and Materials

The dataset supporting the conclusion of this article is presented in this manuscript.

Competing Interests

The authors declare that they have no competing interests.

Ethics, Approval and Consent

The research of this case report was conducted in accordance with the National Institute of Oncology of Rabat.

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