Sequential Combination Chemotherapy and Radiotherapy of an Isolated Non-Hodgkin's Lymphoma of the Larynx

– Report of A Case –

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INTRODUCTION

Approximately 10-25 per cent of non-Hodgkin's lymphomas arise in extranodal sites(Friedmann and Ferlito, 1988), and most arise in the gastrointestinal tract, but other mucosal organs may be involved, especially upper aerodigestive tract(Horny et al., 1996). Primary localized laryngeal lymphoma is rare (Anderson et al., 1976). It is an example of an extranodal non-Hodgkin's lymphoma arising from mucosa-associated lymphoid tissue and accounting for less than one per cent of all laryngeal neoplasm(Friedmann and Ferlito, 1988). Most cases are supraglottic, non-ulcerated, pale laryngeal masses(Gregor, 1981; Remacle et al., 1987). A significant number of cases remain localized to the larynx, and radiation therapy is the best initial treatment(Alraham et al., 1989). If the tumor does not respond to radiation, then operation to remove the lesion is required as occasion demands(Anderson et al., 1976). In the case of extralaryngeal lymphomatous involvement, management is based on radiotherapy to the affected area, associated with chemotherapy( Remacle et al., 1987). The present paper reports a case of stage IE laryngeal non-Hodgkin's lymphoma which was treated by six cycles of combination chemotherapy and subsequent external beam radiotherapy.
CASE REPORT

A 41-year-old male presented to the Department of Ear, Nose and Throat of the Yeungnam University Hospital with hoarseness for four months and abrupt aggravation of dyspnea recently. Before this admission, he has experienced sore throat, odynophagia and progressing dyspnea. Indirect laryngoscopic examination showed diffuse swelling of both false cords and aryepiglottic folds with poor mobility of both true vocal cords. Computerized tomogram of the larynx(Fig. 1) showed diffuse encircling thickening of subglottic region without no demonstrable mass lesion. Initial clinical impression was nonspecific inflammatory condition rather than true neoplasm. So he was treated with conservative medical cares, including wide spectrum antibiotic and antiinflammatory drug. But his symptoms revealed no improvement, the physician performed suspension laryngoscopic examination with biopsy of true vocal cord lesion. Diagnostic Staging investigation revealed no evidence of disease outside the larynx.

The microscopic examination (Fig. 2) revealed proliferation of atypical lymphoid cells, which have large hyperchromatic noncleaved nuclei with distinct nucleoli and moderate to scanty amount of cytoplasm. Mitotic figures are frequently seen and extensive necrosis is also noted.

The Immunohistochemical study showed positive reaction to leukocyte common antigen and T-cell antigen receptors, and negative reaction to B-cell antigen receptors. The pathological diagnosis was malignant lymphoma, diffuse large cell type by Working formulation.

To alleviate airway obstruction dyspnea, emergency tracheostomy was performed. After careful clinical staging medical oncologist recommended combined modalities treatment. Initially six cycles of "CHOP" chemotherapy (Table 1), cycles were repeated every 21 days. Intercycle follow up computerized tomogram (Fig. 3) of the larynx after 3 cycles of chemotherapy showed slight diminution of thickening of the true vocal cords and diffuse thickening of subglottic laryngeal wall. So further 3 cycles of chemotherapy were given. After completion of 6 cycles of chemotherapy the patient was referred to radiation oncologist and preradiotherapy follow up computerized tomogram showed partial response and he received 45 Gy radiotherapy in the form of external beam radiation for 5 weeks to the larynx and whole neck lymph node chains from skull base to supraclavicular area. Afterthen the patient complained oral and throat soreness and medical cares for mucositis were given for 2 weeks. Follow up computerized tomogram (Fig. 4) at 4 weeks after completion of radiation therapy revealed no evidence of residual lesion in the larynx or enlarged lymph nodes in the neck, and he was symptom-free 10 months after diagnosis.
Fig. 1. Prechemotherapy computerized tomogram of the larynx showed diffuse encircled swelling of the laryngeal wall with severe air way narrowing.

Fig. 2. Microscopic finding of biopsy specimen revealed diffuse proliferation of atypical large lymphoid cells of cleaved and noncleaved type in a necrotic background (H&E X100).
Fig. 3. Postchemotherapy computerized tomogram of the larynx showed diminution of diffuse swelling of the laryngeal wall with persistent airway narrowing.

Fig. 4. Postradiotherapy computerized tomogram of the larynx showed marked improvement of diffuse laryngeal wall swelling.
Table 1. CHOP Chemotherapy regimen

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<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Administration</th>
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<tr>
<td>Cyclophosphamide</td>
<td>750 mg/m²</td>
<td>intravenously on day 1</td>
</tr>
<tr>
<td>Hydroxydaunorubicin</td>
<td>50 mg/m²</td>
<td>intravenously on day 1</td>
</tr>
<tr>
<td>Vincristine</td>
<td>1.4 mg/m²</td>
<td>intravenously on day 1</td>
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<tr>
<td>Prednisolone</td>
<td>100 mg/m²</td>
<td>orally every day for 5 days</td>
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**DISCUSSION**

Extranodal lymphomas are common, and usually arise in the gastrointestinal tract, but mucosal organs of the upper aerodigestive tract are frequently affected (Horny et al., 1996). According to the literatures, primary laryngeal lymphoma is a rare occurrence (Anderson et al., 1976; Remacle et al., 1987; Friedmann and Ferlito, 1988; Abraham et al., 1989; Paya et al., 1994).

The presenting symptoms are hoarseness of long duration and slowly progressing dyspnea with unilateral otalgia (Abraham et al., 1989). There is no sex or age preference (Gregor, 1981), but most patients are male subjects over fifty years of age. This patient complained hoarseness and progressing dyspnea without otalgia. Laryngoscopic examination shows a smooth-surfaced tumor mass, regular in shape and pinkish grey in colour, generally located at the supraglottic larynx (Gregor, 1981; Remacle et al., 1987; Paya et al., 1994), but in this case the lesion uncommonly located in glottic and subglottic larynx. Clinically there are no specific diagnostic clue suggesting isolated laryngeal lymphoma. Occasionally histological diagnosis is difficult and in some cases repeated biopsies are necessary for diagnosis (Abraham et al., 1989).

It is likely that isolated laryngeal lymphomas arising from lymphoid nodules present in the lamina propria of the supraglottic area and epiglottis, presumably similar to the bronchus-associated lymphoid tissue. The nodules are composed mostly of B-lymphocytes and are overlayed by specialized epithelium which is infiltrated by lymphocytes (Friedmann and Ferlito, 1988). The tumors displayed a diffuse pattern (Friedmann and Ferlito, 1988; Ferlito et al., 1981).

Sometimes histologic classification and clinical staging of lymphomas have limited value in the treatment of this disease, because the tumor can change cell type during the course of the disease process (Anderson et al., 1976). But therapeutic strategy is closely linked with histologic investigation and the stage of the disease. Although computerized tomographic findings such as diffuse laryngeal wall thickening as in this case is a nonspecific finding which can be seen in other disease processes such as a variety of inflammations or lymphoid reactive
hyperplasia, computerized tomographic examination is very important diagnostic tool in initial presentation (Abraham et al., 1989) as well as in follow up study after radiotherapy and chemotherapy. In selecting treatment modalities, a careful histopathologic diagnosis is most important, which may separate other pathological conditions, and an appropriate clinical staging, which may exclude dissemination of the disease, are stressed as representing the basis for effective treatment (Ferlito et al., 1981).

For an isolated laryngeal lymphoma as this case, the treatment of the choice is moderate dose local radiotherapy and the prognosis is usually good (Chen, 1984), whereas the prognosis of the laryngeal location of advanced disease is rather poor (Stemmelen et al., 1992). If the tumor is unresponsive to radiation therapy, then operation to remove the lesion is required (Anderson et al., 1976). But in the case of poor prognosis and extralymphatic lymphomatous involvement, treatment is based on radiotherapy to the larynx, which is associated with combination chemotherapy (Remacle et al., 1987). Unusually, combination chemotherapy was given due to abrupt progression of dyspnea as in this case. After 6 cycles of chemotherapy, he complained no remarkable dyspnea, and follow up computerized tomogram showed slightly decreased thickening of subglottic laryngeal wall. So 45 Gy of external beam radiotherapy was given.

However a significant number of cases remain localized to the larynx, and consequently have a good prognosis only with radiation therapy, it is very important that this tumor has a tendency to recur at distant sites many years later, careful evaluation by experts and lifelong long-term follow up is very important (Anderson et al., 1976; Gregor, 1981; Abraham et al., 1989).

REFERENCES


병합 항암 요법 및 방사선 치료를 이용한 원발성 후두 림프종 치험 1례보고

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전신적인 침범없이 후두에만 국한되는 악성 림프종은 매우 드문 예로서 일반적으로 두경부에만 국한된 방사선 치료로 근치 가능하다. 그러나 반대로 급성 호흡곤란을 초래하여 응급 기관 절개와 병합 항암제를 투여해야 되는 경우를 간혹 경험하게 된다. 본 증례는 수 개월간 지속되어온 악성과 최근에 갑자기 심해진 호흡곤란으로 급성 후두염이란 임상 진단명으로 보존적인 치료를 하였으나 증상이 호전되지 않아서 후두 조직 검사 결과에서 비 호즈킨 림프종으로 확진되어 6회의 복합 항암제를 투여한 다음 남아있는 병변에 대한 45 Gy의 외부 방사선 치료후 병원환자 단층 활영에서 완전 관해를 보였으며 진단후 10개월이 지난 현재 무병 상태를 보이는 환자를 경험하였기에 간단한 문헌 고찰과 함께 보고한다.

중심 단어: 후두, 비 호즈킨 림프종, 항암 방사선 병합 치료