The Journal of Laryngology & Otology
April 2001, Vol. **115,** pp. 324–326

Isolated primary non-Hodgkin's malignant lymphoma of the larynx

Andrea Luigi Cavalot, Giuliana Preti, Nicola Vione, Giuseppe Nazionale, Francesca Palonta, Gian Luca Fadda

Abstract

We report a case of glottic primary laryngeal lymphoma. Although the head and neck region is a frequent site of origin of extranodal non-Hodgkin's lymphomas, laryngeal involvement is exceptional. Including this case, about 90 primary laryngeal lymphomas have been reported in the literature. Microscopic study showed a diffuse malignant lymphoma of high-grade malignancy (WF sub-division H). A diffuse, large, B-cell-type NHL was diagnosed histopathologically.

The patient was treated with combination chemotherapy, including cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP), which resulted in complete clinical remission after two courses. Four courses of combination chemotherapy were subsequently performed, making a total of six courses of combination chemotherapy. No recurrence has been observed during the 16-month follow-up period.

Key words: Lymphoma; Larynx

Introduction

The incidence of non-Hodgkin's lymphoma (NHL) originating in extranodal sites ranges from 10 to 35 per cent and is more commonly seen in lymphomas with diffuse histology.[1]

Non-Hodgkin's lymphoma localized exclusively to the larynx at the time of diagnosis is even rarer and is uncommon as a primary neoplasm, accounting for less than one per cent of all laryngeal neoplasms.[2] It is an example of an extranodal NHL arising from mucosa-associated lymphoid tissue (MALT).[3,4] Recommendations about treatment for these patients is anecdotal, and radiotherapy has been thought to be curative and is recommended as the treatment of choice.[5,6] Radiation has also been given in combination with chemotherapy[7] with similar results.

In this work the authors describe a case of primary non-Hodgkin's lymphoma localized in the glottic region of the larynx (Stage IEA), in a patient who presented with a small mass in the posterior commissure.

No case of the non-Hodgkin's lymphoma of the glottic larynx has been reported in the literature to date.

Case report

A 79-year-old man was admitted to the hospital in April 1997 for progressive foreign body sensation in his throat and change in the quality of his voice for about three months; also some associated difficulty in swallowing. There was no history of smoking, fever, night sweats, or weight loss. The patient suffered from essential hypertension and he was cardiopathic. During the hospitalization the patient had some episodes of dyspnoea, caused by his illness.

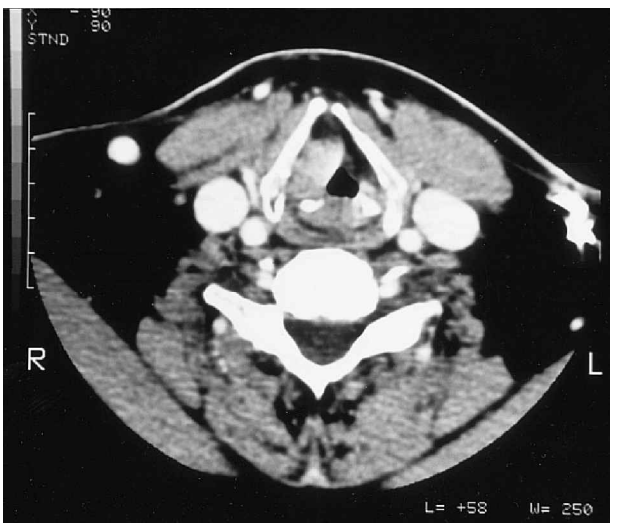

Fig. 1

Axial computed tomography scan demonstrating thickening of right vocal fold and posterior commissure.

Indirect laryngoscopy revealed a small mass in the posterior commissure. The findings on physical examination were normal: no cervical or other peripheral lymphadenopathy, and no hepatosplenomegaly. Laryngeal tomography and computed tomography demonstrated thickening of the right true vocal fold and posterior commissure, with a partial obliteration of the ipsilateral perilaryngeal space, but without infiltration of the thyroid cartilage (Figure 1). On admission, direct laryngoscopy and excisional biopsy were performed under inhalation anaes-

From the Department of Physiology, Second Chair of ENT, University of Turin, Italy.
Accepted for publication: 16 November 2000.

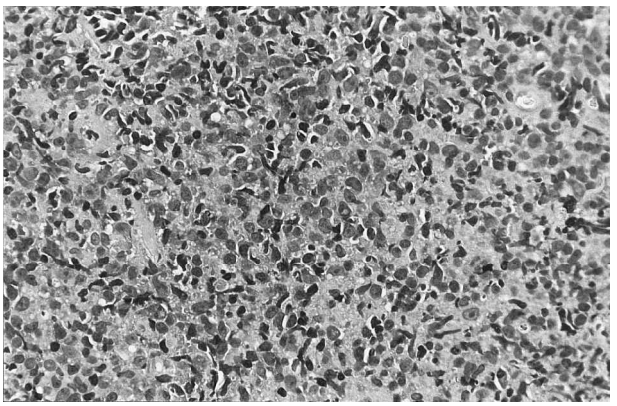

FIG. 2

Laryngeal biopsy specimen showing a diffuse, large-cell lymphoma. Minute plasma cells, neutrophils, and eosinophils are dispersed in a diffuse infiltrate of large atypical lymphoid cells (H & E; ×400).

thesia by fibre-optic-guided endotracheal intubation. The endoscopic findings of the nasopharynx, oropharynx and epiglottis were within normal limits, and the true vocal folds moved normally.

Microscopically the biopsy specimen showed a diffuse infiltrate of large atypical lymphoid cells with pleomorphic and round nuclei, and scattered minute plasma cells, neutrophils, and eosinophils (Figure 2). The lesion was therefore histopathologically diagnosed as a diffuse, large-cell and B-cell-type NHL, according to the proposed classification with the working formulation (WF subdivision H). No other tumour was found in the oral cavity or in the Waldeyer's ring lymphoid tissue.

A chest X-ray revealed no evidence of lung infiltration or intrathoracic involvement. Computed tomography of the chest, abdomen and pelvis revealed no lymphadenopathy. The results of a bone marrow biopsy were also normal. All these investigations failed to reveal the presence of other tumour sites. The clinical stage of this patient was evaluated as stage IE according to the Ann Arbor staging system.[8]

The patient was treated with chemotherapy only because radiotherapists considered radiation therapy dangerous for the fits of dyspnoea.

The patient was treated with combination chemotherapy, including cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP), which results in complete clinical remission after two courses. Four courses of combination chemotherapy were subsequently performed, making a total of six courses of combination chemotherapy. No recurrence has been observed during the 16-month follow-up period.

Discussion

Although non-Hodgkin's lymphoma usually presents in lymph nodes, approximately 25 per cent of cases originate in extranodal sites. The condition usually occurs in late adult life and occasionally in childhood. The male to female ratio is about 1.5:1. In the head and neck region, most NHLs are of B-cell origin.[5]

These tumours tend to remain localized for a long period of time and then to disseminate to other extranodal and unusual sites, as other extranodal lymphomas arising from mucosa-associated lymphoid tissue.[6]

There have been some reported cases of NHL limited to the larynx at time of presentation.[4,5,6,9,10] Two thirds of primary laryngeal lymphomas are on the left side, and most of the tumours are located in the supraglottic area, in particular the epiglottis and aryepiglottic folds.[11]

B-cell primary laryngeal lymphomas appear to be much more common than T-cell lymphomas.[4] In 1998 Marianowski *et al.* reported the first case of primary laryngeal gamma-delta T-cell lymphoma related to Epstein-Barr virus infection.[12]

The first malignant primary lymphoma of the larynx was described by MacKenty in 1934,[13] as reported by Remacle *et al.*, 1987, in their review.[14] These authors also mentioned two earlier cases briefly cited in the literature, one seen by Stoerck in 1895, another by Tanturri in 1932. Diebold *et al.* in 1990, documents 84 previously reported primary NHLs of the larynx.[15]

In previous reports of primary NHL of the larynx, the median age of patients is 62 years, with ages ranging from four to 81 years. These lymphomas are predominantly found in the male population. Symptoms at presentation include: dysphonia, hoarseness, dysphagia and cervical lymphadenopathy[16] with a duration of two to 60 months. Stridor, cough, and weight loss were also reported.

The lymphoma is often localized to one side of the larynx, with a predominantly supraglottic localization with, or without, glottic or subglottic involvement. In general, the macroscopic appearances were those of a smooth submucosal swelling or polypoid mass, without ulceration.[15]

There have been common clinical features in the previously described cases of laryngeal NHLs: 1) this lymphoma tends to remain localized for a long period of time, without progress of symptoms, and many of the cases present with a localized stage IE or IIE disease; 2) dissemination occurs often to other extranodal sites such as the upper respiratory tract, stomach, orbit, or skin, with a long disease-free interval; 3) local therapy such as radiotherapy and/or surgery is effective for both primary and disseminated tumours, and long-term survival can be achieved.[6]

The majority of laryngeal lymphomas reported in the literature have been of the B-cell lineage, with only a small minority possessing the T-cell immunophenotype. Diffuse large B-cell lymphoma is generally considered to be potentially curable with aggressive therapy.[17]

In the majority of published cases it has not been possible to determine the exact histological type of the lymphoma. Only a few of the cases can be interpreted in terms of either the Kiel classification[18] or the Working Formulation. Swerdlow *et al.*, 1984 reported one case classified as diffuse small cleaved lymphomas.[16] Ferlito *et al.*, 1981, reported three cases of diffuse lymphomas classified respectively as large cleaved, small cleaved, and large non-cleaved follicular centre cells.[19] Ten other cases of low-grade lymphoma can be identified: one malignant lymphoma of low differentiation,[20] one low-grade malignant lymphosarcoma,[21] three lymphocytic lymphosarcomas,[22] one diffuse mixed lymphoma,[22] and four lymphocytic lymphomas.[23] Only one case of high-grade lymphoma can be identified as centroblastic or large non-cleaved lymphoma.[14] In all the other cases, information, description, and denomination are not precise enough to allow correct classification.

It has been reported that radiotherapy is the best initial treatment for isolated NHL, since this tumour is thought to be highly radiosensitive. Chemotherapy is the treatment of choice in patients with disseminated NHL.[19]

https://doi.org/10.1258/0022215011907325 Published online by Cambridge University Press

Most previously reported cases have been treated with radiation therapy alone.[6] A few recent studies have also reported cases treated with combined modality treatment[7] or chemotherapy alone.[24] Many articles have recommended radiation therapy as the treatment of choice in primary laryngeal lymphoma with, or without, local node involvement.[4–6,10] Extranodal recurrences are also radioresponsive and a long disease-free survival may be anticipated.

In patients with limited-stage intermediate and high-grade lymphoma, the literature suggests that combination chemotherapy plus radiotherapy is the treatment of choice for many sites of presentation. Although CHOP is the standard treatment regimen for diffuse large-cell non-Hodgkin's lymphoma,[25] two recent randomized trials have reported that chemotherapy followed by radiation was superior to chemotherapy alone in patients with clinical stage I and II disease. Patients with multiple sites of extranodal disease were included in these trials.[26,27]

Wang in 1972 described that a dose ranging between 40 and 50 Gy was required to ensure a permanent cure of the local disease, and the portals should have been sufficiently large to include the primary tumour and its lymphatic drainage areas, because regional lymph-node involvement was not infrequent.[28]

References

1 Rudders RA, Ross ME, DeLellis RA. Primary extranodal lymphoma: response to treatment and factors influencing prognosis. *Cancer* 1978;**42**:406–16

2 Anderson HA, Maisell RH, Cantrell RW. Isolated laryngeal lymphoma. *Laryngoscope* 1976;**86**:1251–7

3 Isaacson PG, Spencer JO. Malignant lymphoma of mucosae-associated lymphoid tissue. *Histopathology* 1987;**11**:445–62

4 Cheng CJ, Chen PR, Liu MC, Kuo MS, Hsu YH. Primary malignant lymphoma of mucosa-associated lymphoid tissue of larynx. *Otolaryngol Head Neck Surg* 1999;**121**:661–2

5 Pak MV, Woo JKS, van Hasselt CA. T-cell non-Hodgkin's lymphoma of the larynx and hypopharynx. *Otolaryngol Head Neck Surg* 1999;**121**:335–6

6 Morgan K, Mac Lennan KA, Narula A, Bradley PJ, Morgan DA. Non-Hodgkin's lymphoma of the larynx (stage IE). *Cancer* 1989;**64**:1123–7

7 Cohen SR, Thompson JW, Siegel SE. Non-Hodgkin's lymphoma of the larynx in children. *Ann Otol Rhinol and Laryngol* 1987;**96**:357–61

8 Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M. Report of the committee on Hodgkin's disease staging classification. *Cancer Res* 1971;**31**:1860–1

9 Chen KTK. Localized laryngeal lymphoma. *J Surg Oncol* 1984;**26**:208–9

10 De Bree R, Mahieu HF, Ossenkoppele GJ, Van Der Valk P. Malignant lymphoma of mucosa-associated lymphoid tissue in the larynx. *Eur Arch Oto-Rhino-Laryngol* 1998;**255**:368–70

11 Horny H-P, Kaiserling E. Involvement of the larynx by hemopoietic neoplasms – An investigation of autopsy cases and review of the literature. *Pathol, Res Prac* 1995;**191**:130–8

12 Marianowski R, Wassef M, Amanou L, Herman P, Tran-Ba-Huy P. Primary T-cell non-Hodgkin lymphoma of the larynx with subsequent cutaneous involvement. *Arch Otolaryngol & Head Neck Surg* 1998;**124**:1037–40

13 MacKenty JE. Malignant disease of the larynx. *Arch Otolaryngol* 1934;**20**:297–328

14 Remacle M, Deggouj N, Noel H, Bertrand B. Les lymphomes non hodgkieniens du larynx. A propos d'un cas. *Acta Otorhinolaryngol Belgica* 1987;**41**:49–65

15 Diebold J, Audouin J, Viry B, Ghandour C, Betti P, D'Omano G. Primary lymphoplasmacytic lymphoma of the larynx. A rare localization of MALT-type lymphoma. *Ann Otol Rhinol Laryngol* 1990;**99**:577–80

16 Swerdlow JB, Merl SA, Davey FR, Gacek RR, Gottlieb AJ. Non-Hodgkin's lymphoma limited to the larynx. *Cancer* 1984;**53**:2546–9

17 Harris NL, Jaffe ES, Stein H, Banks PM, Chan JKC, Cleary ML, *et al.* A revised European-American classification of lymphoid neoplasms: A proposal from the international lymphoma study group. *Blood* 1994;**84**:1361–2

18 Stansfeld A, Diebold J, Kapanci Y. Updated Kiel classification of lymphomas. *Lancet* 1988;**1**:292–3

19 Ferlito A, Carbone A, Volpe R. Diagnosis and assessment of non-Hodgkin's malignant lymphomas of the larynx. *ORL* 1981;**43**:61–78

20 Podoshin L, Fradis M, Schalit M. Lymphosarcoma of the larynx. *J Laryngol Otol* 1971;**85**:1063–8

21 Droga TS. Lymphosarcoma of the larynx. *J Laryngol Otol* 1972;**86**:535–41

22 DeSanto LW, Weiland LH. Malignant lymphoma of the larynx. *Laryngoscope* 1970;**80**:966–78

23 Gregor RT. Laryngeal malignant lymphoma: an entity? *J Laryngol Otol* 1981;**95**:81–93

24 Kawaida M, Fukuda H, Shiotani A. Isolated non-Hodgkin's malignant lymphoma of the larynx presenting as a large pedunculated tumor. *ORL* 1996;**58**:171–4

25 Fisher RI, Gaynor ER, Dahlberg S. Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in patients with intermediate or high-grade non-Hodgkin's lymphoma. *New Engl J Med* 1993;**328**:1002–6

26 Glick J, Kim J, Earle JD, O'Connell MJ. An ECOG phase III trial of CHOP *vs.* CHOP + radiotherapy for intermediate grade early stage non-Hodgkin's lymphoma (NHL). *Proc Am Soc Clin Oncol* 1995;**14**:1221a

27 Miller TP, Dahlberg S, Cassady JR. Three cycles of CHOP plus radiotherapy is superior to eight cycles of CHOP alone for localised intermediate and high grade non-Hodgkin's lymphoma (NHL): a Southwest Oncology Group study. *Proc Am Soc Clin Oncol* 1996;**15**:411

28 Wang CC. Malignant lymphoma of the larynx. *Laryngoscope* 1972;**82**:97–100

Address for correspondence:
Dr Palonta Francesca,
Via Monginevro 21 bis,
10044 Pianezza (Torino),
Italy.

E-mail: fpalonta@libero.it

Dr P. Francesca takes responsibility for the integrity of the content of the paper.
Competing interests: None declared