

# Chronic Lymphocytic Leukemia as an Incidental Finding in a Laryngectomized Patient

## Larenjektomi Yapılan Bir Hastada İnsidental Bir Bulgu Olarak Kronik Lenfositik Lösemi

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### ABSTRACT

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Chronic lymphocytic leukemia (CLL) is the most common type of leukemia which has a variable clinical course. The patients with CLL have increased risk of developing secondary malignancies including the skin, lung and gastrointestinal system. However, the coexistence of laryngeal carcinoma and CLL has only very rarely been reported in the literature. We presented a 73 year old male patient who admitted to the department of otolaryngology with the complaints of dysphonia and stridor. The patient underwent total laryngectomy and bilateral neck dissection for squamous cell carcinoma of larynx but incidentally all cervical lymph nodes indicated chronic lymphocytic leukemia/small lymphocytic lymphoma. There was also small lymphocytic infiltration surrounding carcinomatous laryngeal tissues. The simultaneous coexistence of different malignancies as in this case, emphasizes the importance of careful histopathological examination of the surgical specimen.

#### Keywords

*Laryngeal carcinoma, chronic lymphocytic leukemia,  
secondary malignancy*

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### ÖZET

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Kronik lenfositik lösemi (KLL) en sık görülen lösemi tipi olup, oldukça farklı klinik seyir gösterebilir. KLL tanısı olan hastalar deri, akciğer ve gastrointestinal sistem kanserleri gibi pek çok sekonder malignite gelişiminde yüksek riske sahiptirler. Ancak literatürde larenks karsinomu ve KLL birlikteliği çok nadiren bildirilmiştir. Olgumuzda otolaringoloji kliniğine disfoni ve nefes darlığı şikayetleri ile başvuran 73 yaşında erkek hasta sunulmuştur. Hastaya larenks skuamöz hücreli karsinomu tanısı ile total larenjektomi ve bilateral boyun disseksiyonu uygulanmıştır. Hastanın rezekt edilen tüm boyun lenf nodlarında insidental olarak kronik lenfositik lösemi/küçük lenfositik lenfoma tespit edilmiş ve ayrıca larenksin karsinomlu dokularını saran küçük lenfositik hücre infiltrasyonu izlenmiştir. Bu vakada olduğu gibi, farklı malignitelerin simültane birlikteliği cerrahi spesmenin histopatolojik değerlendirilmesinin çok dikkatli yapılması gerekliliğini göstermesi açısından önemlidir.

#### Anahtar Sözcükler

*Larinks kanseri, kronik lenfositik lösemi,  
sekonder malignensi*

Çalışmanın Dergiye Ulaştığı Tarih: **22.03.2013**

Çalışmanın Basıma Kabul Edildiği Tarih: **04.12.2013**



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## INTRODUCTION

Chronic lymphocytic leukemia (CLL) is the most common lymphoid malignancy which accounts for nearly 25 % of all adult leukemias.<sup>1</sup> The disease has a variable clinical course and unpredictable prognosis. Some patients may be asymptomatic with a silent course and normal life expectancy while in others the disease may be in a late stage which necessitate immediate radiochemotherapy.<sup>2,3</sup>

In recent studies, the authors reported that in patients with CLL there was an increased risk of developing secondary malignancies such as skin, GIS and lung.<sup>3-7</sup> This association was supposed to be related to alterations in immune responses in CLL patients or to presence of common etiological risk factors.<sup>3,8</sup> However, the coexistence of laryngeal carcinoma and CLL has only very rarely been reported in the literature.<sup>9-11</sup>

Herein we presented a patient who underwent total laryngectomy with bilateral neck dissection and incidentally cervical lymph nodes were diagnosed as CLL in the absence of any preceding symptom or sign.

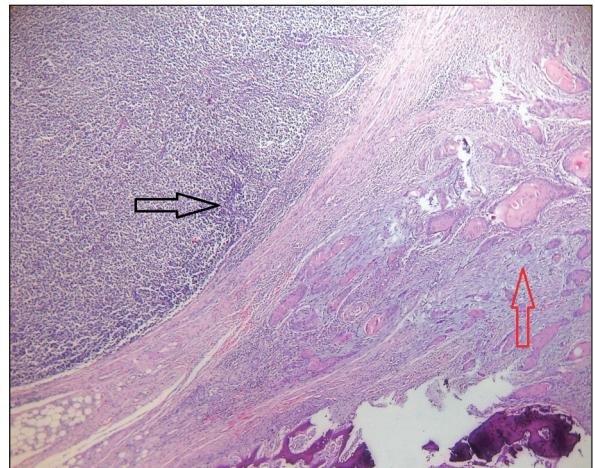
## CASE REPORT

A 73 year old male patient was admitted to the department of otolaryngology with the complaints of persistent dysphonia for almost eight months and recently evolved stridor. There was a history of surgical intervention for primary rectosigmoid carcinoma and his recent colonoscopic examination was completely normal. The patient smoked 20 cigarettes a day for more than 40 years. On endoscopic examination, there was a tumor of the right hemilarynx which involved vocal cord and ventricular band with subglottic extension. The preoperative biopsy demonstrated squamous cell carcinoma. There were also multiple lymph nodes located bilaterally at the jugular chain.

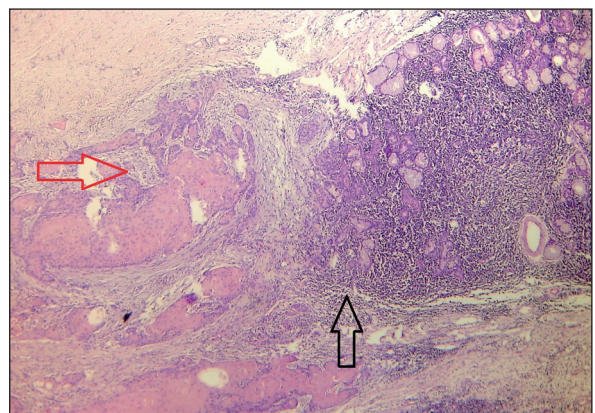
The complete blood count revealed mild anemia (Hct: 35.60 %, Hgb: 12.10g/DL), elevated white blood cells (wbc: 14.70K/ $\mu$ L) with lymphocyte predominance (52.3%) and normal thrombocyte count. The computed tomography of the neck revealed bilateral multiple cervical lymph nodes at all zones and an infiltrative mass lesion invading right paraglottic region with extension inferiorly to subglottis. The tumor was classified as T2 N2c M0. Eventually, we performed total laryngectomy

with bilateral modified radical neck dissection and paratracheal node dissection including total thyroidectomy. The postoperative period was uneventful except mild tracheal tissue necrosis which healed by sterile dressing and the patient was discharged at the 10<sup>th</sup> day after surgery. An informed consent form was taken from the patient in order to use his medical data for scientific purposes.

The macroscopic examination of the operative specimen showed anterior commissure invasion and subglottic extension of more than 15 mm. There was diffuse involvement of enlarged and smooth surfaced lymph nodes at all zones. The pathological examination of the total laryngectomy material was consistent with



**Figure 1.** The figure represents the coexistence of squamous cell carcinoma and malignant lymphoid cell infiltration in the laryngeal specimen (H.E.x40); black arrow shows lymphoid infiltration and red arrow shows squamous carcinoma.



**Figure 2.** This figure shows carcinomatous laryngeal specimen by red arrow and coexisting malignant lymphoid cell infiltration in the same specimen by black arrow (H.E.x40).

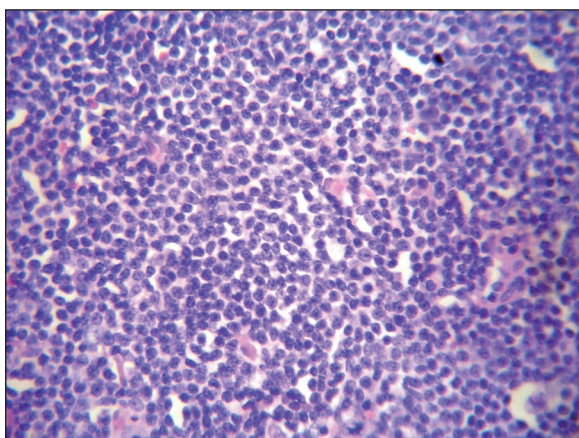


squamous cell carcinoma and small lymphocytic infiltration in surrounding laryngeal tissues (Figure 1 and 2). There were 248 lymph nodes dissected from left and right neck; 152 and 96 respectively. None of the lymph nodes showed metastasis of carcinoma, however they were all infiltrated with neoplastic lymphoid cells which were morphologically identical to chronic lymphocytic leukemia/small lymphocytic lymphoma. The immunophenotype of neoplastic cells was CD20<sup>+</sup>, CD5<sup>+</sup>, CD43<sup>+</sup>, CD23<sup>+</sup>, IgM<sup>+</sup>, Bcl2<sup>+</sup>, CD21<sup>+</sup> and IgD<sup>-</sup>, Kappa<sup>-</sup>, Lambda<sup>-</sup>, CD10<sup>-</sup>, CD3<sup>-</sup>, CD138<sup>-</sup>, Siklin D1<sup>-</sup> and BCL-6 negative (Figure 3, 4 and 5). Subsequently, the patient was consulted to the department of hematology and oncology for further systemic assessment, staging and to define the treatment strategy.

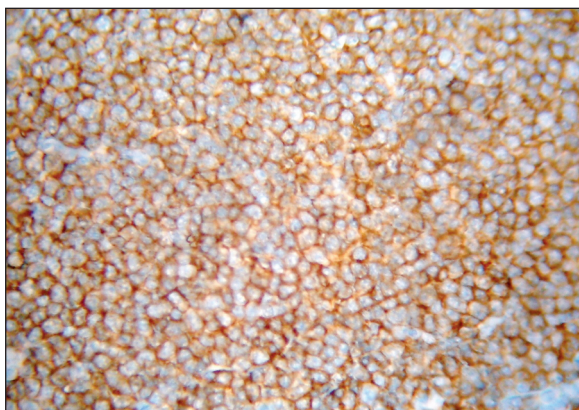
## DISCUSSION

The risk of developing a second malignancy was found higher in patients with CLL compared to general population. Travis et al. reported that the observed to expected ratio of a second malignancy was significant in patients with CLL especially for cancers of lung, brain and malignant melanoma.<sup>5</sup> In another study, 27.2% of 2028 CLL patients were indicated to develop another malignancy and among these malignancies, skin, prostate, breast, melanoma, GIS and lung carcinoma were encountered most commonly.<sup>4</sup> Similarly, in the study of Schöllkopf et al. which evaluated 12,373 patients who were diagnosed with CLL, the observed number of second malignancy was 1105 although the expected number was 695, with a standardized incidence ratio of 1.59.<sup>3</sup> Even though all these recent studies reported a higher ratio of secondary malignancy in CLL patients, there were only few cases which revealed the association of CLL with laryngeal carcinoma.<sup>9-11</sup>

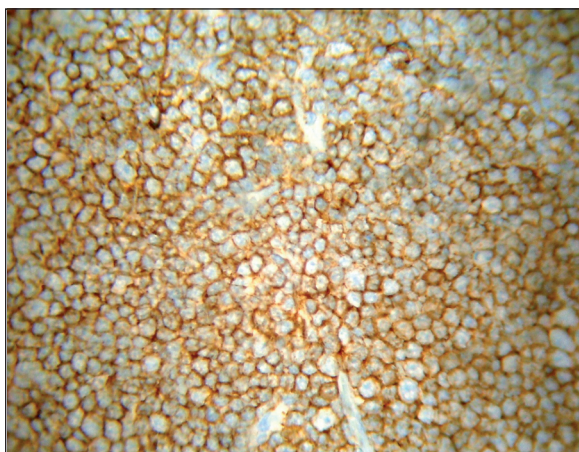
Ferlito et al. indicated that in the cervical lymph nodes there was coexistence of both the squamous carcinoma metastasis and diffuse infiltration by small lymphocytes but the laryngeal specimen only revealed poorly differentiated squamous cell carcinoma.<sup>10</sup> In addition, two other articles reported a simultaneous infiltration of laryngeal tissues by lymphoid proliferation and squamous cell carcinoma.<sup>9,11</sup> Hammai et al. also reported that other than two lymph nodes which showed carcinomatous invasion with capsular rupture, all others were the seat of diffuse lymphomatous proliferation.<sup>9</sup> (Table 1) On the contrary, in our case the pathological



**Figure 3.** Lymph node diffusely infiltrated by homogenous small lymphocytic neoplastic cells (H.E. x400)



**Figure 4.** CD20 expression of the neoplastic lymphoid cells (CD20 x 400).



**Figure 5.** CD23 expression of the neoplastic lymphoid cells (CD23 x 400).

examination of cervical lymph nodes were only consistent with the diagnoses of chronic lymphocytic leukemia/small lymphocytic lymphoma but not the seat

**Table 1.** The table which shows the clinical features of patients who had coexistent chronic lymphocytic leukemia and squamous cell carcinoma of the larynx and presented in previous case reports.

Case reports	Age	Gender	Larynx pathology	Lymph nodes	TNM	Leukemia type
Hamami et al. <sup>9</sup>	75y	m	SCC+B cell CLL	SCC+CLL (n=2), CLL (n=74)	T3N2bM0	B cell CLL
Ferlito et al. <sup>10</sup>	57y	m	SCC only	SCC+CLL (n=4), CLL (n=70)	T2N2bM0	B cell CLL
Stering et al. <sup>11</sup>	82y	m	SCC+CLL/SLL	-	-	CLL/SLL
Our case	73y	m	SCC+CLL/SLL	CLL only (n=248)	T2N2cM0	CLL/SLL

CLL/SLL: Chronic lymphocytic leukemia/small lymphocytic lymphoma; CLL: Chronic lymphocytic leukemia; SCC: Squamous cell carcinoma; m: male; n: number.

of the metastasis of squamous cell carcinoma. However, examination of laryngectomy specimen revealed the features of squamous cell carcinoma in contact with diffuse lymphomatous proliferation.

There are few hypotheses which discuss the association between CLL and synchronous or metachronous secondary malignancy. CLL is characterized by various defects in cellular immunity with low gammaglobulin levels and T-cell defects which eventually deteriorate the immune system, so that the patients are vulnerable to both secondary infections and malignancies.<sup>5,8</sup> In addition, exposure to carcinogenic environmental risk factors such as cigarette smoking, asbestos and UV light was suggested to induce the development of a secondary malignancy in these patients. Especially smoking, a well-known etiological factor for laryngeal cancer was also considered to play role in the pathogenesis of CLL.<sup>3,9</sup> Another possible mechanism may be the genetic

factors that increase the risk of both CLL and other malignancies such as lung, larynx or oropharyngeal carcinoma.<sup>12-16</sup>

## CONCLUSION

Although the risk of secondary malignancy in patients with CLL was reported higher compared to the general population, this association was very rarely reported regarding laryngeal carcinoma. According to our knowledge, we have presented the fourth case in literature which reported a patient who underwent laryngectomy with bilateral neck dissection and incidentally all cervical lymph nodes were found positive for preexisting CLL. The simultaneous coexistence of different malignancies as in this case, emphasizes the importance of careful histopathological examination of the surgical specimen.

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