Case Report / Olgu Sunumu

Nasal type natural killer T-cell lymphoma involving nasooropharynx and larynx

Nazoorofarenks ve larenksi tutan nazal tip doğal katil T hücreli lenfoma

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Lymphoma is one of the malignant non-squamous tumors involving the head and neck. Lymphomas in this region are mostly B-cell type in origin and usually seen in Waldeyer's ring. In this article, we report a 45-year-old female case of primary natural killer T cell lymphoma-nasal type involving the nasooropharynx and larynx. This is a very rare entity with poor prognosis.

Keywords: Larynx; lymphoma; nasopharynx; natural killer/T-cell type; oropharynx.

Lenfoma, baş boyun bölgesini tutan yassı hücreli olmayan malign tümörlerden biridir. Bu bölgedeki lenfomalar çoğunlukla B hücre tipi kaynaklıdır ve genellikle Waldeyer halkasında görülür. Bu yazıda, nazo-orofarenksten larenkse uzanan primer nazal tip doğal katil T hücreli lenfoma tanılı 45 yaşında bir kadın olgu sunuldu. Nadir görülen bu olgu, kötü prognoza sahiptir.

Anahtar Sözcükler: Larenks; lenfoma; nazofarenks; doğal katil T hücre tipi; orofarenks.

The most common malignancy encountered in the larynx is squamous cell carcinoma. However, some other rare neoplastic transformations must be included in the differential diagnosis since there are fundamental differences with respect to treatment. Primary hematopoietic neoplasms are among these rare tumors, occurring in less than 1% of all malignant laryngeal tumors.[1] Among these, lymphoma is the second most common primary laryngeal tumor after plasmacytoma. Cervical lymph nodes are common sites of involvement in the head and neck region but in about one fourth of cases extranodal extralymphatic sites may be involved. These include Waldeyer's ring (the tonsils being the most common region), the paranasal sinuses, nasal and oral cavities, thyroid gland and orbita as well as the larynx. Primary laryngeal lymphomas are almost always non Hodgkin lymphomas (NHL) and usually occupy the supraglottic region attributed to its follicular lymphoid content.[2]

Concerning subtypes, primary NHL of the larynx is presumed to arise from aggregates of submucosal lymphoid tissue in which the B cell line is predominant, that is, diffuse large B cell lymphoma. The others are mucosa associated lymphoid tissue-MALT-type and marginal

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zone B cell lymphoma primarily arising from aryepiglottic folds and epiglottis. T cell or natural killer (NK) cell lymphomas are very rarely encountered as a primary laryngeal NHL.[3]

Nasopharyngeal lymphomas usually arise from Waldeyer's ring and are B cell type- Burkitt lymphomas. Their relation to Ebstein Barr virus (EBV) is very well documented. Nasal type NK/T cell lymphoma of the nasopharynx is also rare and more prevalent in Asia and in some areas of South and Central America.

In this report, we aimed to present a very rare case of primary extranodal NK/T-cell lymphoma, nasal type starting in the nasopharynx going down to the hypopharynx and larynx. The distinct diagnosis is very important in terms of patient care, dissemination and control of the disease.

CASE REPORT

A forty-five-year-old female patient was admitted to our clinic with complaints of hoarseness, dysphagia and cervical lumps existing for three months. Additionally, she had considerable weight loss due to dysphagia. From her medical history, we learned that she had been treated for tularemia the year before and had a diagnosis of Crohn disease. She was under treatment with azothioprin and 5-ASA which she stopped by herself a few months ago.

Endoscopic evaluation of the patient revealed a lymphoid hypertrophy beginning in the nasopharynx, lateral pharyngeal band and going down to the hypopharynx with scarce small necrotic regions that were dirty white in color. Laryngoscopy revealed a granulomatous lesion invading the entire supraglottic region starting from the epiglottis, aryepiglottic folds and ventricular bands destroying the mucosal integrity covered by whitish membranous lesions (Figure 1). There were lumps in the neck bilaterally; 3x2 cm on the left level 2 and 4x3 cm on the right level 2, firm and hard to mobilize on both sides.

Computed tomography (CT) revealed a diffuse submucosal nodular thickening at nasopharyngeal and oropharyngeal levels causing asymmetrical narrowing of the airway. Mucosal enhancement and nodular thickening were also observed at the supraglottic region. In the neck, bilateral lymphadenopathies were noted at levels 2a and 3, the biggest being 30x31x60 mm in diameter showing heterogeneous enhancement (Figure 2).

Hematological tests were unremarkable. Elisa test was normal for toxoplasma. Tests for cytomegalovirus (CMV), EBV, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and *Brucella* were normal. Acid-resistant bacilli (ARB) was also

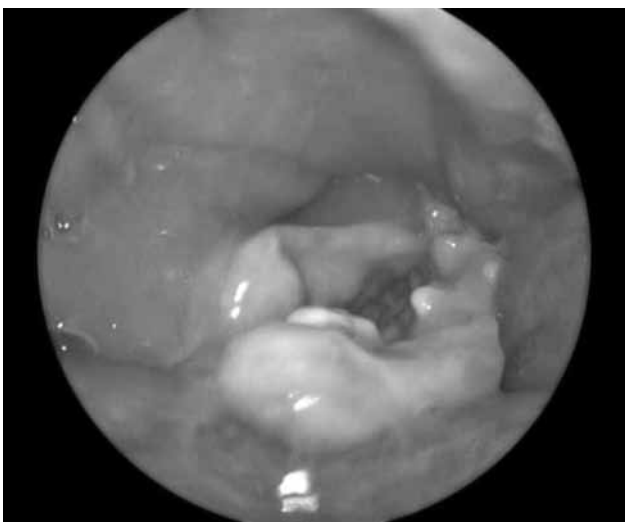

Figure 1. *Endoscopic view of the lesions in the larynx.*

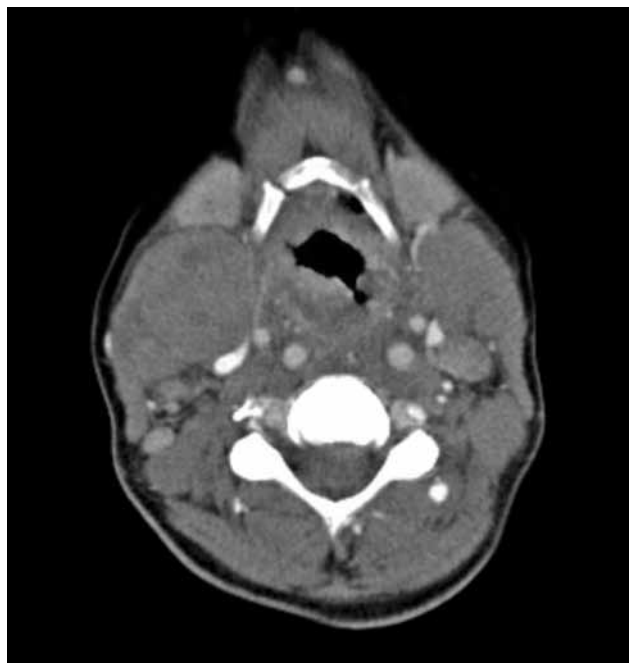

Figure 2. *Computed tomography revealed diffuse submucosal nodular thickening narrowing the airway together with bilateral cervical lymphadenopathies.*

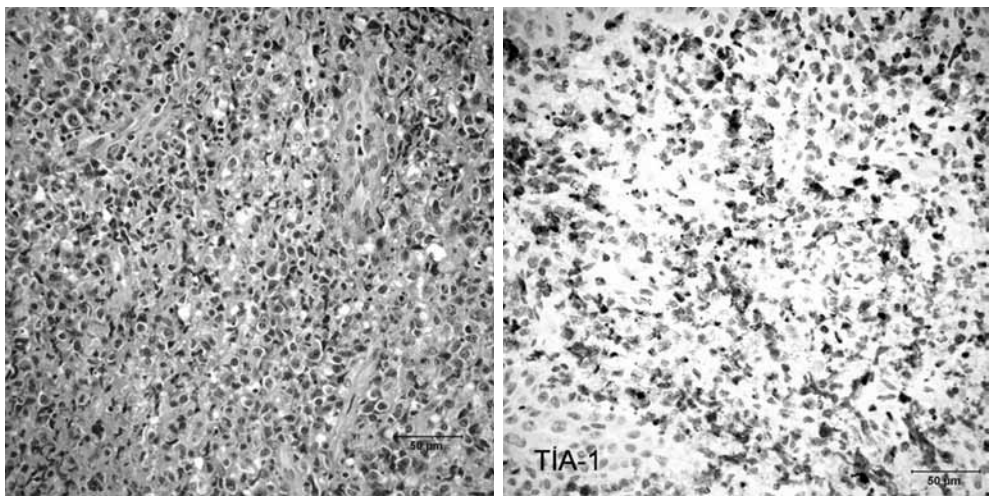

Figure 3. *Histologic examination; a diffuse lymphoid infiltration with atypical lymphocytes was observed (left) (H-E x 400). Atypical lymphocytes positive for T cell-restricted intracellular antigen T cell-restricted intracellular antigen were seen on the right. (TIA-1 x 400).*

negative. Serological test for tularemia was within normal limits. For histopathological examination, biopsies from various regions of the lesion were taken during endoscopy.

Histologic examination of the punch biopsies from the arytenoid and left nasopharynx revealed a lymphoid neoplasm (Figure 3). The lymphoid infiltration was diffuse and composed of medium sized atypical lymphocytes. The atypical lymphoid cells exhibited pale-to-clear cytoplasm with irregular, indented or cleaved nuclei and hyperchromasia. The chromatin was granular, except in the large cells, which had blastic chromatin. Nucleoli were generally inconspicuous or small. Mitotic figures were easily found. The background was rich in foci of necrosis and focal groups of plasma cells. On immunohistochemical analysis, the neoplastic cells were diffusely positive for CD2, CD30, and leukocyte common antigen (LCA), focally positive for T cell-restricted intracellular antigen (TIA-1), but negative for CD20, CD56, CD3, epithelial membrane antigen (EMA), creatine kinase (CK), CK5/6, EBV latent membrane protein-1 (LMP1), granzyme B, anaplastic large cell lymphoma kinase (ALK) and cyclin D1. Immunostaining for CD138 demonstrated numerous plasma cells accompanying the infiltrate. Stains for kappa and lambda light chains showed a polyclonal pattern. The histological features were consistent with a diagnosis of extranodal NK/T cell lymphoma, nasal type.[4]

Upon diagnosis, the patient was referred to Medical Oncology. Unfortunately, she died before starting any treatment.

DISCUSSION

Primary laryngeal lymphoma is a very rare entity with less than 100 cases reported in the literature so far.[1] Although mostly nodal, 25% of NHL present in extranodal sites, and in most of these, the disease is seen in locations containing lymphoid tissue.[5] However, it may be seen also in nonlymphoid organs such as the thyroid. In the head and neck region, extranodal lymphomas are NHL and mostly seen in Waldeyer's ring.

Laryngeal lymphoma may be seen together with lymphomas of other head and neck regions. In our case, lymphoma was histopathologically diagnosed concurrently in the nasopharynx and larynx. It would have been better had we confirmed the diagnosis also with the biopsy taken from the oropharynx. Endoscopic view made us consider the lesion to continue from the nasopharynx down to the larynx. Although it was in the submucosal region in the nasopharynx, it was mucosal and ulcerative in the larynx. Supraglottic and primarily submucosal locations were noted in the literature.[6] Nevertheless, laryngeal lymphoma may show mucosal invasion, and if so, the histopathological type is asserted to be T cell phenotype lymphoma. Histopathologically, most reported cases of laryngeal lymphomas have been of B-cell type.[1]

The ratio of B cell phenotype to NK/T cell phenotype of lymphoma in the head and neck was reported to be 6/1.[7]

Siddiqui et al.[7] reported imaging findings of 18 primary laryngeal lymphoma cases and concluded that a large uniformly enhancing supraglottic submucosal tumor without central necrosis and without cervical lymphadenopathy to be characteristic for laryngeal lymphoma. In our case, CT revealed a prominent submucosal nodular thickening with uniform enhancement in the upper airway from the nasopharynx down to the larynx. There was also mucosal enhancement in the supraglottic larynx and the epiglottis was deformed by the nodular thickening. In this respect, our case was similar regarding the naso and oropharyngeal location but not the laryngeal involvement as it was mucosal at this site and had cervical metastasis although this could not be differentiated in origin.

Laryngeal lymphoma may present with the usual laryngeal symptoms like dysphagia, hoarseness, dyspnea and cervical lump like our patient. This type of lymphoma is known to be very aggressive as in our case, where our patient died just after the diagnosis. Because the patient has had tularemia history and the laryngeal findings reminded us of granulomatous diseases primarily, a wide diagnostic work-up was performed. Moreover, she has had Crohn disease and was under treatment with Azothioprin which is an immunomodulatory agent. The lesion was in the spectrum of possible diagnosis as a manifestation of Crohn disease. Head and neck manifestations of Crohn disease may be observed in 0.5% to 15% of the patients. Although the oral cavity is the mostly involved site, the larynx was also reported to be involved.[8] The argument about the cancer risk in patients with a diagnosis of inflammatory bowel disease (IBD) continues. In their population-based study, Bernstein et al.[9] reported a higher risk developing lymphoma among males with Crohn disease regardless of the immunomodulatory therapy. Nevertheless, in a later meta-analysis, Kandiel et al.[10] reported a four-fold increased risk of lymphoma in IBD treated with azathioprine and or 6-mercaptopurine. In light of these data, our patient already had an increased risk of lymphoma.

Conclusion

Differential diagnosis is of great value with respect to morbidity and mortality. Histopathological examination is the best way to diagnose lymphoma. The disease is treated primarily with chemoradiotherapy and surgery is avoided. This is such a big contrast from squamous cell carcinoma which is the most commonly encountered cancer in head and neck, where surgery remains the primary treatment modality together with chemoradiotherapy.

Declaration of conflicting interests

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