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CASE REPORT

SYNCHRONOUS MANTLE CELL LYMPHOMA OF LARYNX AND NASOPHARYNX

Abstract

Mantle cell lymphoma is a variant of non-Hodgkin's lymphoma and is known as a mature peripheral B-cell lymphoid neoplasm. Lymphomas of the larynx and nasopharynx are rare; mantle cell lymphoma is exceedingly rare. In most mantle cell lymphoma cases, the tumoral lymphoid cells express nuclear cyclin D1 due to a t(11;14) chromosomal translocation between an IGH gene and CCND1. This is considered to be an important genetic event in mantle cell lymphoma. There are case reports in the literature on various histologic types of non-Hodgkin's lymphomas which affect the nasopharynx and larynx simultaneously. However, to the best of our knowledge, mantle cell lymphoma involvement of the nasopharynx and larynx simultaneously has not been reported. In this case report, the detailed clinical manifestations and pathological findings of a mantle cell lymphoma patient have been presented along with a literature review of mantle cell lymphoma.

Keywords: Mantle Cell Lymphoma; Lymphoma; Larynx; Nasopharynx.

OLGU SUNUMU

LARENKS VE NAZOFARENKSTE SENKRON MANTLE HÜCRELİ LENFOMA

Öz

Mantle hücreli lenfoma, Non-Hodgkin lenfomanın bir çeşididir ve matür periferik B hücreli bir lenfoid neoplazi olarak bilinir. Larenks ve nazofarenks lenfoması nadirdir; mantle hücreli lenfoma aşırı derecede nadirdir. Çoğu mantle hücreli lenfoma vakasında; tümör lenfoid hücreleri, IGH geni ve CCND1 arasındaki t (11; 14) kromozomal translokasyonu nedeniyle nükleer siklin D 1'i eksprese eder. Bunun mantle hücreli lenfomada önemli bir genetik olay olduğu düşünülmektedir. Literatürde nazofarenks ve larenksi eş zamanlı etkileyen Non-Hodgkin lenfomanın çeşitli histolojik tipleri hakkında olgu sunumları bulunmaktadır. Bununla birlikte, bildiğimiz kadarıyla, nazofarenks ve larenkste eşzamanlı olarak mantle hücreli lenfoma tutulumu bildirilmemiştir. Bu olgu sunumunda, bir mantle hücreli lenfoma hastasının ayrıntılı klinik belirtileri ve patolojik bulguları, mantle hücreli lenfomanın literatür taraması ile birlikte sunulmuştur.

Anahtar: Sözcükler: Mantle Hücreli Lenfoma; Lenfoma; Larenks; Nazofarenks.

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INTRODUCTION

Non-Hodgkin's lymphomas (NHLs) are known by ear, nose, and throat (ENT) physicians to affect lymphoid tissues in Waldeyer's ring (1). Lymphoma of the nasopharynx represents about 8% of the head and neck lymphomas (2). Mantle cell lymphoma (MCL) is a variant of NHL and is known as a mature peripheral B-cell lymphoid neoplasm (3). MCL is among the most common lymphomas involving the nasopharynx, after diffuse large B-cell lymphoma. MCL is an aggressive subtype of NHL and only comprises 3–4% of all Waldeyer's ring lymphomas and 5% of all NHLs (4). The median age of MCL patients is about 70 years and more males are diagnosed with MCL than females (1).

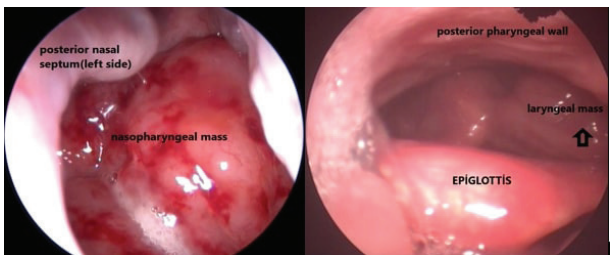
Squamous cell carcinoma is the most common malignant tumor of the larynx. Primary hematopoietic neoplasms constitute less than 1% of the malignant laryngeal tumors. Among these hematopoietic neoplasms, lymphoma ranks as the second most common primary laryngeal tumor, after plasmacytomas. Lymphoma of the larynx is rare; MCL is exceedingly rare (5).

There are case reports in the literature on various histologic types of NHLs which affect the nasopharynx and larynx simultaneously. However, to the best of our knowledge, MCL involvement of the nasopharynx and larynx simultaneously has not been reported. In this case report, the detailed clinical manifestations and pathological findings of an MCL patient have been presented along with a literature review of MCL.

CASE

A 76-year-old male patient was admitted to our outpatient clinic with complaints of a nasal obstruction that particularly increased over the last month. Due to existing hypothyroidism, the patient was taking 100 mg/day levothyroxine. Though he quit smoking 20 years earlier, he had a history of smoking one pack a day for 24 years. Examination with a flexible fiberoptic endoscopy revealed not only a midline nasopharyngeal mass but also a mass originating from the left aryepiglottic fold (Figure 1).

Figure 1. Endoscopic images of nasopharynx and larynx.



Apart from those findings, the ENT examination was normal. Biopsies were obtained from both masses in the nasopharynx and the larynx under general anesthesia. The specimens were examined in the Pathology Department. Histopathological examination of the hematoxylin and eosin-stained slides of the nasopharynx and larynx biopsies showed similar appearances. Diffuse monomorphic lymphoid cell infiltration was seen under the squamous epithelium in the larynx and pseudostratified epithelium in the nasopharynx biopsies. The lymphoid cells were small-to-medium-sized with slightly irregular nuclear contours and inconspicuous nucleoli (Figure 2 and Figure 3). In the immunohistochemical examination, these lymphoid cells stained intensely with CD20, CD5, and bcl2 antibodies, and nuclear cyclin D1 positivity was detected in both biopsies (Figure 2 and Figure 3).

Figure 2. Larynx stained with hematoxylin and eosin (A), anti-CD5 (B), anti-CD20 (C), and anti-cyclin D1 (D).

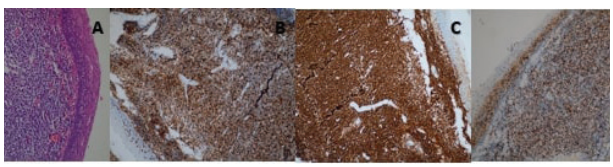
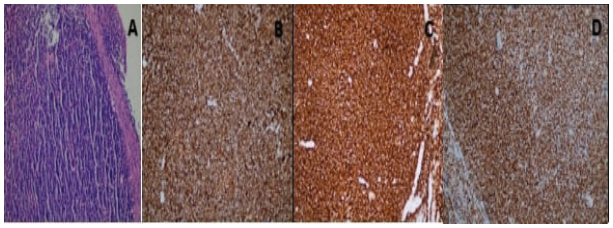


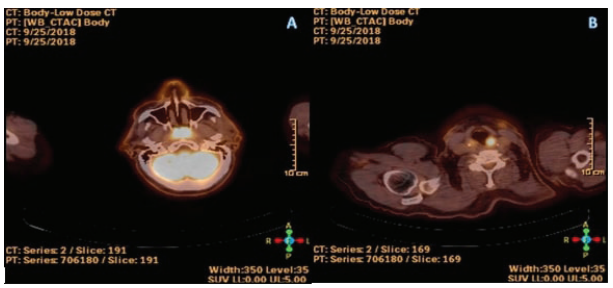
Figure 3. Nasopharynx stained with hematoxylin and eosin (A), anti-CD5 (B), anti-CD20 (C), and anti-cyclin D1 (D).



The cells were negative for CD10 and CD23 and Pankeratin was positive on the surface of the epithelial cells but not in the tumor cells. The morphological and immunohistochemical findings in both biopsies were consistent with MCL.

The Positron emission tomography–computed tomography (PET-CT) screening examination showed a 4 × 4 cm nasopharyngeal hypermetabolic mass (SUV max 9.3) and a 2-cm left lateral laryngeal mass (SUV max 6.6). Moreover, a 4-cm hypermetabolic lesion (SUV max 7.5) over the base of the tongue and 2-cm cervical lymph nodes (SUV MAX 5.0) in both jugular lymphatic sequences were seen (Figure 4).

Figure 4. PET-CT axial image of the



The patient was sent to the Hematology Department for consultation. The R-COP chemotherapy protocol was administered to the patient in eight sessions, and simultaneous radiotherapy was applied. There were no pathological findings in PET-CTs taken three and five months after treatment. Flexible fiberoptic examinations of the larynx and nasopharynx were also normal. The patient was in remission at his 6-month follow-up examination.

DISCUSSION

Lymphoid lesions of the head and neck mainly affect the nasopharynx, nasal and paranasal sinuses, and the salivary glands. These three structures are involved with different forms of lymphoid malignancies and can serve as models for the mechanisms of lymphomagenesis (3).

The nasopharynx and Waldeyer's ring functionally mimic the mucosal-associated lymphoid tissue (MALT) of the gastrointestinal tract and are most commonly involved in B-cell lymphomas, of which MCL is a relatively frequent subtype. As Waldeyer's ring is the site of copious lymphoid tissue, both lymphoid hyperplasia and lymphoma can arise from nasopharyngeal lymphoid tissues (3) From many perspectives, the lymphoid tissue of the nasopharynx is similar to the lymphoid tissues of the gastrointestinal tract and is considered a part of the MALT system (3). Follicular hyperplasia is the most commonly seen lymphoid reaction. Lymphocytes commonly infiltrate the overlying epithelium, leading to lymphoepithelial lesions (3). The nasopharynx is the second most common site of lymphomas, after the tonsils (6). Although malignancies of the hematopoietic system are less common than malignant epithelial tumors of the nasopharynx, NHL should be kept in mind in the differential diagnosis because the treatment modalities for these two nasopharyngeal malignancies are completely different. In our case, we decided that a punch biopsy should be performed for the new nasal complaints under endoscopic examination.

Laryngeal lymphomas are rare and constitute less than 1% of all laryngeal neoplasms. The most common site of involvement of primary laryngeal lymphomas is the supraglottic region because

it contains lymphoid collections in the lamina propria and ventricles. This should be kept in mind in the differential diagnosis of a non-ulcerate polypoid mass in the neck region, especially in the supraglottic area, including the epiglottis and aryepiglottic fold (5, 7). The MCL in our case involved the supraglottic region of the larynx and appeared non-ulcerated, which is consistent with the literature.

In 2012, Naciri et al. claimed to have reported the first case of MCL of the larynx. However, a literature review revealed that Kelly et al. reported MCL presenting as a saccular cyst of the larynx in 2011 (8). Lymphoma of the larynx tends to influence other sites as well, including the salivary glands, thyroid, nasopharynx, and tonsils (7). Different kinds of histological subtypes of laryngeal lymphomas have been reported. The great majority of laryngeal NHLs are of B-cell lineage, frequently presenting as diffuse large cell lymphoma. Very few T-cell lineage NHLs and only one MCL have been reported (9, 10). We found no case of coexistent MCL of the larynx and nasopharynx in the literature. Our case is the first reported MCL involving larynx and nasopharynx simultaneously and the second report of laryngeal MCL after Naciri. Though it was shown by PET-CT but not proven histologically, a third mass lesion on the base of the tongue might also be considered a lymphoma.

The age of onset for laryngeal lymphomas varies between 4 and 81 years, with the mean age of occurrence in the seventh decade of life (11). Our patient was 76-years-old, consistent with previously reported patients.

It is difficult to diagnose nasopharyngeal lymphoma since it manifests few clinical symptoms that mimic benign entities, such as adenoid vegetation and rhinitis. Laryngeal malignancies usually display symptoms, such as dysphonia, dysphagia, dyspnea, and swollen cervical lymph nodes. Our case presented with only a nasal obstruction but no laryngeal symptoms. We detected a coexistent mass lesion in the nasopharynx and supraglottic region of the larynx by a complete fiberoptic endoscopic examination.

MCL is a mature B-cell lymphoma and the classical type is composed of small-to-medium-sized lymphocytes with irregular nuclei (12, 13). The nuclei have dispersed chromatin but inconspicuous nucleoli (12), as seen in our case. However, a broad spectrum of morphologic features, ranging from small-cell to blastoid types also exists and these may reflect distinct biologic characteristics (13). The histopathological variants, including blastoid and pleomorphic types, can cause diagnostic confusion (12). The variants are derived from peripheral B-cells of the inner mantle zone and most cases are pre-germinal center B-cells (12). As detected in our case, the tumoral lymphoid cells in most MCL cases express nuclear cyclin D1 due to a t(11;14) chromosomal translocation between an IGH gene and CCND1. This is considered to be an important genetic event in MCL (12, 14, 15).

There is no consensus on the treatment of MCL. Early-stage patients (stages I–II) are usually treated with chemotherapy and radiotherapy, but those with advanced forms (stages III and IV) are treated with chemotherapy only. MCL is an aggressive lymphoma with the poorest long-term survival among the many subtypes (13). Similar to the laryngeal version, MCL of the nasopharynx has an aggressive clinical course with frequent relapses after conventional chemotherapy (16). We managed our patient with chemotherapy and radiotherapy modalities simultaneously.

In conclusion, the diagnosis of masses in the nasal cavity, nasopharynx, oral cavity, oropharynx, and endolarynx is very important in otorhinolaryngology practice because the treatment modality (surgery, chemotherapy, or radiotherapy) is determined according to the pathological diagnosis of the mass. Here, we emphasize that a simultaneous mass in the nasopharynx and larynx may be MCL and that MCL can also be observed in the head and neck areas.

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