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Case report

The asymmetry of the laryngeal ventricle – the very rare cases and review of the literature

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ABSTRACT

Introduction: The most common neoplastic lesion found in the larynx is squamous cell carcinoma. In this study, we report the set of cases of unexpected neoplastic lesions found in the laryngeal ventricle. These are extranodal lymphoma and two cases of Warthin's tumors.

Aim: To report these extremely rare lesions, as they require special diagnostic, therapeutic attention and collaboration with the pathologist.

Case study: The case records of two patients with the diagnosis of Warthin's tumor and one with lymphoma limited to the laryngeal ventricle were retrospectively reviewed.

Results and discussion: The histopathologic diagnosis revealed one case of diffuse large B-cell lymphoma – centroblastic variant, non GCB type and two cases of papillary cystadenoma lymphomatosum (Warthin's tumor). Details of the presentation, diagnostic procedures, treatment, and outcome of these patients were presented. In the differential diagnosis of laryngeal asymmetry laryngocele, benign and malignant lesions need to be taken into consideration. Warthin's tumor and primary lymphoma located in the larynx require special diagnostic, therapeutic attention and collaboration with the pathologist.

Conclusions: (1) This case series serves to highlight the rich and varied pathology which can affect the larynx. (2) In addition to the more commonly encountered conditions, the otolaryngologists should always be aware of the varied pathology of the larynx with conditions such as Warthin's tumor and extranodal lymphoma.

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1. INTRODUCTION

The asymmetry of the laryngeal ventricle in most cases does not represent pathology. In several studies, an asymmetry to greater or lesser extent was shown in all examined larynges.[1,2] However, in some cases, the asymmetry is a result of benign or malignant neoplastic growth within the laryngeal ventricle. Some of the lesions, which may be present in this particular anatomical site are laryngocele, schwannoma, rhabdomyoma, amyloidosis, squamous cell carcinoma (SCC), adenoid cystic carcinoma (ACC) or rhabdomyosarcoma. Warthin's tumor and primary laryngeal lymphoma are also extremely rare causes of laryngeal asymmetry with fewer than 20 and 100 cases, respectively reported in the English literature.[3,4]

2. AIM

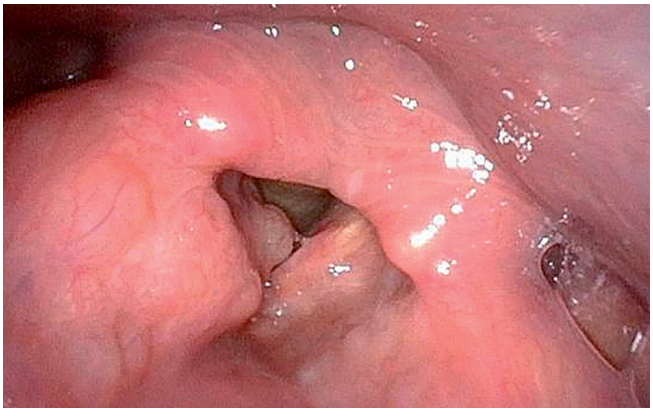
In this article, we describe two cases of Warthin's tumor and one case of diffuse large B-cell lymphoma located in the laryngeal ventricle that remained undiagnosed in the preoperative period owing to the difficult differential and lack of specific symptoms. The aim of the study was to report these extremely rare lesions, as they require special diagnostic, therapeutic attention and collaboration with the pathologist.

3. CASE STUDY

A 58-year-old woman was admitted to the hospital (07/2016) presenting persistent hoarseness for about 2 years accompanied by progressive dyspnea since October 2015. She denied any other symptoms. The patients had a long-term cigarette smoking history. In the physical examination no changes of head and neck region lymph nodes were palpable. The direct laryngoscopy revealed bilateral well-defined, smooth masses originating from laryngeal ventricles and vestibular folds (Figure 1 and 2). However, there was no severe deterioration of her airway tract. The changes noted in the direct laryngoscopy were later confirmed in the ultrasound examination of the neck, which also revealed multinodular goiter. The primary diagnosis was laryngocele. Therapeutic excision in Kleinsasser microlaryngoscopy using CO2 laser was performed. Histological examination showed a cystadenolymphoma (Warthin's tumor). The patient is on frequent follow-up scheme in the outpatient setting, which after one year remains uneventful.

An 81-year-old man was admitted to our department (07/2016) due to persistent mild hoarseness for about 12 months. His past medical record included hypertension, brain stroke, heart infarct and asthma. He was an active smoker for many years. The direct laryngoscopy was performed and showed unilateral smooth mass located in the left laryngeal ventricle and comprising the left vestibular fold. The patient was qualified for transoral surgery in Kleinsasser microlaryngoscopy. During the procedure, a specimen samples for intraoperative histopathological examination were taken. The result showed a variable amount of salivary gland tissue with histological features of Warthin's tumor. The final histology confirmed the diagnosis. The patient is on frequent follow-up scheme in the outpatient setting with no sign of recurrence.

The third patient was a 74-year-old woman admitted to ENT department (07/2016) due to progressive mild hoarseness and dyspnea for about 3 months without any other specific symptoms. The physical examination revealed no palpable lymph nodes. In the direct laryngoscopy a smooth, round mass in the right laryngeal ventricle was observed, covering the right vocal fold. There were no signs of airway obstruction. Based on laryngoscopy and ultrasound laryngocele was suspected and as a result the patient was qualified for microlaryngoscopy with the use of the CO_2 laser. During the surgery, an intraoperative histopathological examination was performed. It revealed neoplastic malignant cells in the specimen. Consequently, the lesion was fully excised and the final histopathology indicated diffuse B-cell lymphoma centroblastic variant. Further immunohistopathological examination revealed a set of unfavorable prognostic factors: expression of Bcl-2 and MUM-1, non GCB subtype and high Ki67 score (60-70%). A hematology consultation was carried out and as a result the patient was planned to



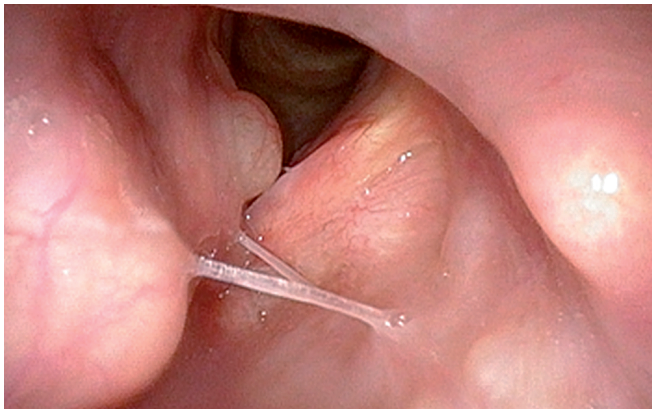


Figure 1 and 2. The direct laryngoscopy revealing bilateral well-defined, smooth masses originating from laryngeal ventricles and vestibular folds.

Table 1. Clinical data of presented patients.

Year	Age/Sex	Presentation	Location	Surgical approach	Pathology
2016	58/F	Hoarseness Dyspnea	Supraglottic	Microlaryngoscopy (CO_2 laser)	Cystadenoma papillary lymphomatosum (Warthin's tumor)
2016	81/M	Hoarseness	Supraglottic	Microlaryngoscopy (CO_2 laser)	Cystadenoma papillary lymphomatosum (Warthin's tumor)
2016	74/F	Hoarseness Dyspnea	Supraglottic	Microlaryngoscopy (CO_2 laser)	Lymphoma malignum diffusum centroblasticum (Diffuse B-cell lymphoma centroblastic variant, non GCB-type)

be admitted to the ward. However, due to a sudden deterioration of her clinical condition, the patient passed away shortly afterwards, before appropriate hematological treatment could have been implemented.

4. RESULTS

Clinical data of the presented patients were summarized in Table 1. Diagnostic and therapeutic approach implemented in our patients are discussed in this part of the article based on the available literature.

Cystadenolymphoma (CAL) also known as Warthin's tumor is a benign tumor of the salivary glands, consisting of oncocytic epithelial cells and lymphoid stroma containing lymphoid follicles with reactive germinal centers.[5] It was first described in 1895 by Hildebrand and is named after an American pathologist Aldred Warthin who contributed the most to its description.[6] Warthin's tumor is reported most often in smokers.[6–8] The highest prevalence occurs in the sixth or seventh decades of life and a male predominance was noted.[6] However, there are also reports of the increasing incidence in females and even those of equal predilection in both sexes since 1970 which is explained by changing patterns of tobacco use.[6–8] A correlation of the Warthin's tumor's occurrence with Epstein–Barr virus (EBV) infection has also been observed, but the relationship is so far unclear.[8]

It is found most often in the parotid gland and represents about 10 % of all salivary gland tumors which makes it the second most frequent benign tumor of salivary glands, with 10% of these being bilateral.[6]

CALs are believed to originate from the excretory ductules of salivary glands and since the occurrence of the salivary gland tissue in ectopic locations within the head and neck has been reported also cases of Warthin's tumors outside the salivary glands have been noted.[9,10]

However, other locations are rare (about 8%) and most often include the lymph nodes of the cervical region.[7,8] They were also reported in the nasopharynx, the minor salivary gland in the buccal mucosa or in the larynx.[6,10,11] Approximately 6% of CALs are discovered incidentally as part of a specimen after neck dissections for malignancies of the head and neck and a case of multiple unilateral Warthin's tumors demonstrating the complete transition from salivary ductal inclusions to the CAL was published which may suggest a continuum resulting ultimately in grossly detectable lesions.[12,13]

Until now, only few cases of a Warthin's tumor in the larynx were reported often with the coexistence within one or both parotid glands. These involved the location of the tumor in the region of the aryepiglottic fold, the lateral thyroarytenoid muscle or the left Morgagni sinus.[11]

It's pathogenetic mechanism still remains unclear and the most common theories explaining the origin of the CAL include a delayed hypersensitivity reaction of the parotid parenchyma to a ductual metaplasia; an abnormal blending of salivary and lymphoid tissues during embryogenesis or a holdover of the branchial cleft apparatus.[11]

Clinically the Warthin's tumor is mostly asymptomatic,[14] however depending on its localization, which may range from the middle ear to the larynx, such symptoms as pain (varying from mild discomfort and tenderness to very severe pain), earache, tinnitus, deafness, facial weakness and swelling may occur.[15] CALs usually grow very slowly and have a shape of a well-circumscribed, egg-shaped swelling of 1–3 cm in diameter.[15,16] Whenever a CAL is suspected the differential diagnosis should be performed and include cysts, lymph nodes, pleomorphic adenoma, papillary cystadenoma or squamous cell carcinoma among others.

Ultrasonography has been found helpful not only in detecting Warthin's tumors but also in describing the structure and even the vascularity of the lesions.[17] In ultrasonography the Warthin's tumor has been described as echogenic, strikingly hypoechoic or sonolucent with few internal focal echoes.[18] In PET/CT they show hypermetabolism and it is believed that the increasing use of these techniques could increase a number of its incidental findings at unusual locations including the larynx.[6]

The data concerning the management of Warthin's tumors are limited and suggest that it should be resected fully with an adequate margin to avoid local recurrence and the conservative treatment seems to be less favorable.[19] Of the resection methods the transoral approach seems to be appropriate for most of the cases as it has little side effects and is most often curative.[6] Larger or invasive neoplasms which are more difficult to excise these way may require an external approach.

The risk of recurrence following excision in the parotid gland is high, estimated 5%–25%.[7] In the larynx they are not well-known and the recurrence seems to be an exception there, however its possibility always has to be kept in

mind as few have been reported.[6] As a result it is important to obtain a fully excised specimen and patients should be under a longer follow-up period in case of the need for further surgery.

Moving to the next entity, diffuse large B-cell lymphoma (DLBCL) is a lymphoid malignancy with neoplastic transformation of mature peripheral B lymphocytes arising in germinal centers. It is the most prevalent type of non-Hodgkin lymphoma among adults with the average age at diagnosis of 70 years with a male predominance.[20] The etiology of the disease still remains unclear.

Different environmental, immunological, infectious and iatrogenic factors are taken into consideration. EBV infection contributes to the occurrence of some subgroups of DLBCLs. The researches show EBV positive DLBCLs are associated with unfavorable prognostic features, poor treatment response and worse survival than EBV negative.[21]

Patients usually present lymphadenopathy, however, in up to 40% of them the location of a lymphoma is extranodal. The Waldeyer's ring is the most common extranodal area involved in the head and neck region.[22] Primary lymphomas restricted to larynx are extremely rare lesions. The occurrence of them is reported to be less than 1% of laryngeal neoplasm. Moreover, there are fewer than 100 histologically confirmed cases reported in the global literature.[22–24] DLBCL and extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) are predominant recognitions and represent approximately 75% of laryngeal NHLs.[22,23] Extremely rare cases are also described in the literature such as NK/T-cell lymphoma, peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS), Burkitt lymphoma.[25,26] Moreover, a case of an 8-year-old boy suffering from primary laryngeal lymphoma is also reported.[28]

The majority of the lesions is located in the supraglottic region as a result of follicular lymphoid tissue presence in this site.[22,23] They can expand locally, affecting surrounding structures as thyroid, tonsils, salivary glands and nasopharynx.[24] Clinically the patient may present various symptoms including dysphagia, dysphonia, hoarseness, cough, dyspnea, cervical lymphadenopathy and systemic signs like fever, weight loss and night sweats.[22,29]

As the presentation is usually nonspecific, the diagnosis may be challenging. The case of our patient with only one symptom (progressive mild hoarseness) confirms it. However, rarely the course of illness may be rapid with acute airway obstruction.[24] Based on currently available data, the laryngoscopy usually reveals discrete, unilateral lesions described as smooth submucosal masses, rarely ulcerated.[22] Histopathological examination is necessary for the definite diagnosis.

The review of the literature reveals chemotherapy, radiotherapy, immunotherapy and combination of them as effective methods of treatment. The choice of therapy depends on staging (Ann Arbor), the extent of expansion and immunohistopathological results. Surgery is not recommended as the first line of treatment in these lesions, however, it can be necessary when the mass of the tumor obstructs the airways and the patient suffers from difficulties in breathing.[23] Some data indicate that excision of the tumor by the Carbon dioxide laser before other therapies may be beneficial for the patient and may allow avoiding tracheostomy or laryngectomy.[22]

6. CONCLUSIONS

(1) This case series serves to highlight the rich and varied pathology which can affect the larynx.
(2) In the differential diagnosis of laryngeal asymmetry laryngocele, benign and malignant lesions need to be taken into consideration.
(3) In addition to the more commonly encountered conditions, the otolaryngologists should always be aware of the varied pathology of the larynx.

Conflict of interest

None declared.

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