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Extramedullary plasmacytoma of larynx manifesting as chronic hypertrophic laryngitis

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Introduction

Extramedullary plasmacytoma (EMP) is a rare variant of plasma cell myeloma (PCM) that is localized to soft tissues in the absence of any detectable signs of systemic disease including marrow plasma cell infiltration, osteolysis or monoclonal protein. EMPs have a strong predilection towards the head and neck region, and more than 80% of cases are located in the upper aerodigestive tract (UADT) [1, 2]. Most UADT EMPs occur in the nasal cavity, paranasal sinuses, oropharynx and nasopharynx, while the larynx is rarely involved (6–18% of cases) [1, 3–5]. Importantly, EMP constitutes less than 0.2% of laryngeal malignancies [1].

A biological basis for EMP's affinity to the UADT has not yet been elucidated. Interestingly, chronic laryngitis, a nonspecific prolonged laryngeal inflammation, is a clinical precancerous condition [6, 7]. However, to the best of our knowledge, any association between chronic laryngitis and EMP of the larynx has yet to be postulated.

Case description

A 70-year-old male patient with a history of gastroesophageal reflux disease (GERD), smoking and asbestos exposure was referred to our Department of Otorhinolaryngology in August 2017 due to recurrent hypertrophic lesions within the larynx causing hoarse voice, cough and mild dyspnea. In the preceding year, the patient had been hospitalized in another Department of Otorhinolaryngology due to hoarseness, and histopathological examination of the larynx had revealed paraepidermal epithelium with strong p16 expression, indicative for human papilloma virus (HPV) infection.

During the first stay, directoscopy with subsequent histopathological examination of laryngeal specimens showed severe inflammatory infiltrates. Endoscopic examinations performed during outpatient follow-up visits revealed periodic recurrence of hypertrophic lesions, primarily affecting the epiglottis, aryepiglottic folds, arytenoids and ventricular folds bilaterally (Figure 1A, B). Moreover, generalized thickening of supralaryngeal structures was found in a computed tomography (CT) scan (Figure 1C, D). Four subsequent diagnostic hospitalizations with microsurgical laser procedures of the larynx provided inconsistent histopathological findings. Proposed differential diagnoses included plasma cell dyscrasia and IgG4-related disease, but the diagnostic criteria of these conditions were not met. No consensus was reached until the last histopathological finding in October 2019 revealed lambda light chains secreting infiltration of plasma cell with aberrant CD19-negative immunophenotype (Figure 1E, F).

The patient was referred to the Department of Hematology for further evaluation. No anemia, hypercalcemia or increased creatin level were found. Electrophoresis and immunofixation of serum and urine were negative for monoclonal component, and the serum concentrations of kappa and lambda free light chains were normal. Bone marrow aspiration, flow cytometry and biopsy did not reveal clonal

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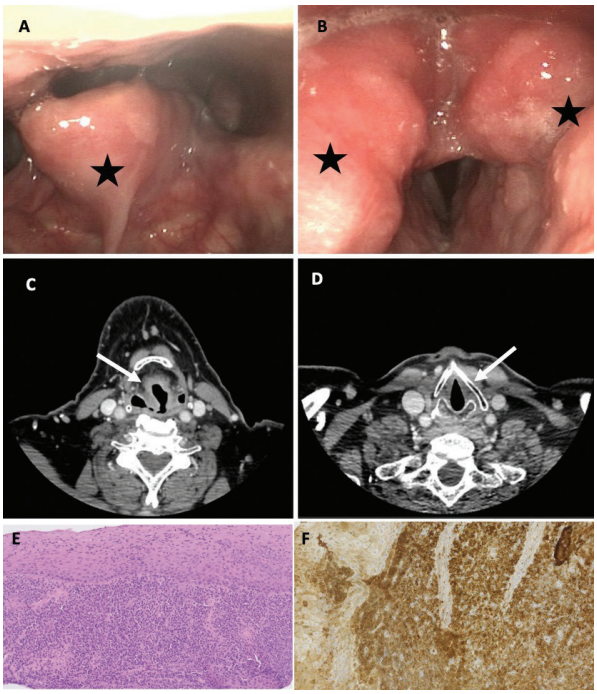

Figure 1. Endoscopic view of edematous epiglottis (black asterisk) (**A**) and hypertrophic aryepiglottic folds, arytenoids and ventricular folds bilaterally (black asterisk) (**B**) and of patient's larynx infiltrated with extramedullary plasmacytoma. Neck computed tomography (CT) scan with enlarged, edematous supralaryngeal structures (white arrow) without increased tissue enhancement (**C**) and without features of thyroid cartilage (white arrow) infiltration (**D**). Histological view of hematoxylin and eosin staining of laryngeal specimen with diffused plasma cell infiltration beneath squamous epithelium layer (**E**), and strong cytoplasmic lambda light chain positivity (**F**)

plasma cells. Low-dose CT body scan revealed no osteolitic lesions.

Based on these results, systemic involvement of PCM was excluded, and the diagnosis of laryngeal EMP was established. The patient was successfully treated with radiotherapy of the larynx area with a cumulative dose of 50 Gy. At the last follow up visit, 18 months following treatment completion, the patient remained in complete remission.

Discussion

EMP of the larynx primarily affects patients aged over 50 years with a strong male predominance (male: female ratio 3:1) [3–5]. The most common symptoms are dysphonia, dysphagia, cough, and dyspnea. In examination, it often presents as a polypoid or sessile mass and occasionally appears to be a diffuse submucosal swelling [3].

Chronic laryngitis is a nonspecific condition of prolonged laryngeal inflammation manifesting mainly with hoarseness and cough resulting from voice overuse, irritation or infection. Chronic hypertrophic laryngitis, leukoplakia and erythroplakia are macroscopically considered to be premalignant lesions [8]. There is a known association between chronic laryngitis and neoplastic transformation. About 90% of malignant tumors of the larynx are carcinomas developing from premalignant lesions [6, 7].

In the presented case, EMP may be the underlying cause and the medium for the development of chronic laryngitis.

However, another, more intriguing, scenario is possible. It could be hypothesized that chronic inflammation, resulting from known chronic irritation in the patient's history (GERD, smoking, asbestos, HPV viral infection), had played a crucial role in the development of EMP. This theory could be supported by the observation by DiStadio et al. [9] who described the development of EMP of the nasal cavity stimulated by chronic inflammation. It is evident that more data needs to be accumulated to prove any causal relationship between these two entities.

Current treatment options for EMP of the larynx include local radiotherapy or surgical excision of the tumor with subsequent local radiotherapy. Potential treatment side effects of radiotherapy are skin reactions, sore throat, dry throat, and voice changes. Based on previous anecdotal reports, both short-term and long-term efficacy seem satisfactory [1, 10].

From the clinical point of view, our case highlights the crucial role of laryngeal biopsy in identifying the cause of chronic laryngitis, and illustrates the difficulties in the diagnostic process of EMP localized in the UADT (e.g. multiple biopsies, ambiguous histopathological findings). Furthermore, it underscores the efficacy of standard treatment

of EMP with radiotherapy [3]. Nevertheless, based on the literature, the risk of transformation to systemic PCM is 11–30% [11]. Such systemic progression of EMP should be treated with standard chemotherapy or immunochemotherapy for PCM, and response needs to be consolidated by a high-dose melphalan with autologous stem cell transplantation in younger patients. Despite the impressive advances in the treatment of plasma cell neoplasms that have been made over the last two decades, evolution to PCM appears to be the main cause of death among patients with EMP.

Authors' contributions

ES — clinical analysis, writing manuscript. AR — clinical analysis, writing manuscript. AK — writing manuscript, critical revision. KN — clinical analysis, critical revision, writing manuscript. IH — clinical analysis, critical revision. JG — histopathological revision, microscopic images, critical revision. KJ — clinical analysis, critical revision, writing manuscript.

Conflict of interest

None.

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None.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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