Case Report

Supraglottic laryngeal lymphomatoid granulomatosis in an immunocompetent patient: a case report

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Received: 07 November 2020
Revised: 13 December 2020
Accepted: 14 December 2020

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ABSTRACT

Lymphomatoid granulomatosis is a rare lymphoproliferative disease caused by Epstein-Barr virus described in 1972 by Liebow. The most common primary localization is the lungs. Other systems are affected occasionally such as the skin, central nervous system, renal and gastrointestinal system. Some cases have been described at the laryngeal level in immunosuppressed patients. This is a case report of supraglottic lymphomatoid granulomatosis in an immunocompetent patient. A literature review on lymphomatoid granulomatosis will be detailed and the clinical case will be described including investigations, treatment and follow-up. The differential diagnosis of this pathology as well as the importance of histopathology will also be discussed. Several radiological imaging and histopathology slides will be presented. Emphasis will be placed on the difficulty of diagnosis given the frequent multisystem involvement and on the importance of the multidisciplinary team approach including otolaryngology, haematology- oncology, nephrology, pathology and radiology. We will end with a discussion about the case with reference to the current literature on the subject.

Keywords: Lymphomatoid granulomatosis, Supraglottic, Lymphoproliferative, Larynx

INTRODUCTION

Primary laryngeal lymphomatoid granulomatosis (LG) is very uncommon. A few cases in immunosuppressed patients have been described in the literature. We report the first case of laryngeal lymphomatoid granulomatosis in an immunocompetent patient.

Lymphomatoid granulomatosis has been described in 1972 by Liebow. It is a rare, Epstein-Barr virus (EBV)- associated lymphoproliferative disorder, which mainly affects the lungs and occasionally the skin, the central nervous system and the kidney. This condition is frequent in immunosuppressed patients. However, some studies have identified age as a factor of relative immunosuppression in patients with EBV-associated lymphoproliferative disease.1 Laryngeal localization of non-Hodgkin's lymphomas or other lympho-proliferative processes are very rare, accounting for less than 1% of laryngeal tumours.2 In the literature, a case of primary laryngeal LG has been described in an HIV-positive patient.3 A few cases of laryngeal EBV-associated lymphoma have been described mainly in immunosuppressed patients.2,3 A few cases of lymphomatoid granulomatosis have also been described in the oral cavity.4,5 The diagnosis of LG can be challenging. Differential diagnosis includes for example Wegener's granulomatosis, tuberculosis, and another non-Hodgkin's lymphoma.6,7 Accurate diagnosis relies on pathological analysis of the affected organ. Histopathology of LG typically demonstrates angiocentric and Angio destructive accumulation of T cells with varying numbers of atypical clonal EBV-positive large B-Cell CD20-positive. Necrosis along with a population of small reactive CD3-positive T cells are common findings.8-11 No consensus has been established for the treatment of this disease. Some authors suggest a conservative treatment for patients with mild impairment.
Some treatments are established for high-grade disease or in cases of severe organ dysfunction. The main treatment is standard chemotherapy, consisting of R-CHOP, as used for type B lymphomas.10

**CASE REPORT**

A 68-year-old man was referred to a tertiary center for a supraglottic lesion with multiple pulmonary nodules. A biopsy initially done in a regional center demonstrated moderate dysplasia without evidence of squamous cell carcinoma. A CT scan of the neck and chest demonstrated a significant 4.9 cm supraglottic mass involving the vocal cords, the epiglottis and the aryepiglottic folds along with multiple pulmonary nodules, the largest was 2.3 cm in the left upper lobe.

In our institution, evaluation revealed a significant lesion on flexible endoscopy (Figure 1). An emergency PET scan and biopsies under general anaesthesia were organized. The PET scan demonstrated significant metabolic activity of the supraglottic lesion with extension to the hypopharynx and the oropharynx (Figure 2). Suspicious lymphadenopathy has also been demonstrated in the cervical region. The lung lesions had slightly increased metabolic activity. The first biopsies done in our center failed to reveal a final diagnosis. The differential diagnosis included lymphoma, EBV mucocutaneous ulcer, vasculitis, or infection. The patient underwent investigations for vasculitis, which was ultimately negative. On follow-up, the lesion was progressing both clinically and radiographically. More investigation was warranted by the impeding airway obstruction.

**Figure 1: Endoscopy of the supraglottic and glottic lesion.**

**Figure 2: PET scan and CT-scan of the supraglottic and glottic lesion.**

The CT scan (Figure 2) demonstrated the progression of the supraglottic lesion and stability of the lung lesions. The urine workup demonstrated significant proteinuria. Renal biopsy demonstrated proliferative focal crescentic-type glomerulonephritis of pauci immune type. A transthoracic lung biopsy has also been done not being contributory. In an ultimate attempt to get a diagnosis, another biopsy of the laryngeal lesion along with an excisional cervical lymph node biopsy has been done. The pathology of the lymph node was not contributory. Interestingly, the biopsy of the supraglottic lesion demonstrated atypical EBV-positive B cells on an inflammatory background with angiocentric and Angio destruction. However, CD20 immunochemistry was only partially positive (Figure 3).

**Figure 3: Pathology of the biopsy of the supraglottic lesion (A) HE 40X, (B) CD-20 40X, (C) LMP-1 20X (D) Ki-67 20X.**
Based on histopathology result, differential diagnosis narrowed to lymphomatoid granulomatosis, EBV-associated mucocutaneous ulcers or EBV-positive lymphoproliferation in the context of age-related immunodeficiency. Given the renal and pulmonary involvement, we concluded to lymphomatoid granulomatosis. A high dose prednisone treatment has been initiated considering the potential airway obstruction. A multidisciplinary decision was made to initiate a 6-cycle R-CHOP chemotherapy treatment. The patient was therefore discharged home having demonstrated a significant reduction in symptoms with prednisone. Further chemotherapy treatments were planned on an outpatient basis.

The patient had been followed by medical oncology during the chemotherapy treatments. The patient had been seen in ENT mid-treatment and at the end of treatment. Endoscopy demonstrated complete resolution of the lesion with an almost normal larynx (Figure 4). A PET scan after 6 cycles of R-CHOP demonstrated a complete metabolic response (Figure 4). On CT scans, there was a complete resolution of the supraglottic lesion and disappearance of the pulmonary lesions. At follow-up, the patient had a complete resolution of his proteinuria and thus, we concluded to a paraneoplastic glomerulonephritis. Patient’s follow-up is still ongoing, and he showed no evidence of recurrence to date.

CONCLUSION
We have detailed the investigation and treatment of what we believe to be the first case of supraglottic laryngeal lymphomatoid granulomatosis described in the literature. We hope that this article will be useful for reference for all clinicians when investigating a lesion of the larynx with suspected lymphoproliferative disease associated with EBV.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Harvey-Bolduc SP, Guay B. Supraglottic laryngeal lymphomatoid granulomatosis in an immunocompetent patient: a case report. Int J Otorhinolaryngol Head Neck Surg 2021;7:375-8.