

Post-transplant Lymphoproliferative Disease (PTLD) of The Larynx in an Adult With Kidney Transplant; A Case Report

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Summary: Post-transplant lymphoproliferative disease (PTLD) is a clinicopathologic entity characterized by an abnormal lymphocytic proliferation that occurs in immunosuppressed patients following organ transplantation. Several sites in the head and neck may be affected by PTLD with rare involvement of the larynx. Affected patients often present with symptoms and signs suggestive of a malignant lesion. Early diagnosis using histopathologic examination is paramount to prevent life-threatening airway compromise. The authors of this manuscript report a 52-year-old woman, diagnosed case of renal failure for which she had undergone kidney transplant, who presented with symptoms of laryngeal PTLD. The clinical work-up and management of these cases is reviewed.

Key Words: Post-transplant lymphoproliferative disease—Dysphagia—Kidney transplant—Upper airway—Larynx.

INTRODUCTION

Post-transplant lymphoproliferative disease (PTLD) is a clinicopathologic entity characterized by an abnormal lymphocytic proliferation that occurs in patients following organ transplantation. Since its initial description by *Hanto DW* in 1968 as a late complication of immunosuppressive therapy,¹ numerous reports have been described in the literature predominantly in children with an estimated prevalence of 0.8%–4%.^{2–7} In a large retrospective review of 292 heart-transplant patients, PTLD accounted for 50% of de-novo malignancies in patients who survived more than 1 month.⁸ Similarly, in another review of 1675 patients who underwent orthotopic liver transplantation, *Ettore et al* reported 22 cases of PTLD out of 98 cases of de novo tumors. The authors emphasized the need for active surveillance to detect these malignancies in view of their high morbidity and mortality.⁹

Several sites in the head and neck may be affected by PTLD. These include the Waldeyer's ring, tonsils, sinuses, salivary glands, gingiva, and cervical lymph nodes among others. Otolaryngologic manifestations include ear infection, sinus infection, tonsillar hypertrophy, and/or cervical lymphadenopathy. Systemic complaints such as febrile illness and flu-like syndrome may also be present. Involvement of the upper airway and particularly the larynx has rarely been described, with only 14 pediatric cases being reported in the literature till 2016.⁶ The authors of this manuscript describe a rare case of laryngeal PTLD in an adult patient who had undergone kidney transplant, with emphasis on the clinical presentation.

CASE REPORT

A 52-year-old woman presented with history of dysphagia, sore throat, and mild change in voice quality of few

month duration. The patient is a diagnosed case of lupus nephritis and renal failure for which she underwent a kidney transplant 1 year prior to her presentation. The patient was on immunosuppression therapy, namely Advagraf and Cellcept. Fiberoptic laryngeal examination revealed a fungating ulcerative epiglottic lesion that extended to the aryepiglottic folds bilaterally with narrowing to the upper airway (Figure 1). Computed tomography of the neck showed an epiglottic mass with irregular edges, invading the epiglottic cartilage, and suggestive of a malignant process. The patient underwent suspension microlaryngoscopy and partial excision of the epiglottis using cold steel instruments. The pathology revealed atypical lymphocytic infiltration that stained negative for CD 56 and ALK, and positive for CD3/CD5. The atypical cells expressed CD30, CD20, and PAX 5. *In situ* hybridization for EBV-encoded RNA was positive in numerous cells (Figure 2). Given the history of renal transplant and immunosuppression, the findings were consistent with polymorphic lymphoproliferative disorder. Patient was treated with Mabthera in addition to a reduction in her immunosuppressive therapy. On follow-up, the patient had complete regression of her lesion.

DISCUSSION

PTLD of the upper airway is a rare entity. Its clinical presentation can be misleading in view of the large variation in the median time between the transplantation and the clinical onset of the disease (7–98 months).⁶ Affected patients can present with symptoms and signs suggestive of infectious mononucleosis, or with a more aggressive course similar to that observed in patients with laryngeal lymphoma. The symptoms vary in intensity depending on the site of the lesion, its extent, and the severity of the disease. These include dyspnea, obstructive sleep apnea, dysphagia, dysphonia, odynophagia, cough, and stridor.^{2,4,6} On laryngeal examination, the supraglottis is most commonly affected with edema and narrowing of the laryngeal lumen. Based on a review by *A. F. O'Neill et al*, the epiglottis and aryepiglottic folds are the sites mostly involved with signs of ulceration and necrosis often noted. The subglottis and trachea

Accepted for publication January 16, 2020.

There is no conflict of interest or financial support in relation to this paper.

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Journal of Voice, Vol. 35, No. 5, pp. 810.e7–810.e8

0892-1997

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<https://doi.org/10.1016/j.jvoice.2020.01.014>

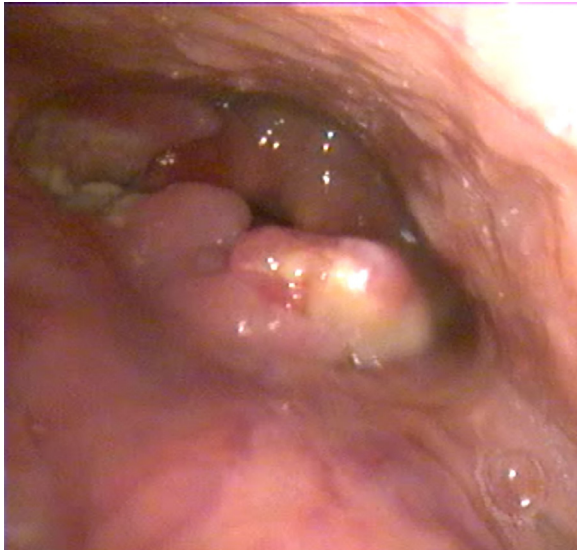


FIGURE 1. Laryngeal fiberoptic endoscopy showing a fungating lesion of the epiglottis with narrowing of the airway.

may also be involved with evidence of intratracheal masses, or para-tracheal compression.^{2,4,5} Proper work-up of suspected cases using computed tomography, magnetic resonance images, and or positron emission tomography is helpful in detecting suspicious lesion seen on laryngeal examination and in delineating the extent of involvement. Immunohistochemistry of a tissue biopsy shows evidence of cellular hyperplasia, and/or monoclonal proliferation of lymphocytes with or without malignant features similar to those seen in patients with non-Hodgkin's lymphoma.¹⁰ It is important to note the strong association between lymphocytic proliferation post-transplant and Epstein-Barr virus (EBV) infection. *Ho et al* reported 21 cases of EBV-associated lympho-proliferative syndrome among 1,467 patients with organ transplantation, and highlighted the role of EBV in promoting LPS.²

A review of the literature till 2016 revealed only 14 cases of PTLD of the upper airway, pediatric patients who had liver transplant. The first case of laryngeal PTLD following kidney transplantation was reported by *Banks et al* in 2012.⁷ The authors of this manuscript report the second case of laryngeal PTLD in a patient on immune-suppressive therapy following kidney transplantation. The first reported patient was an 11-year-old boy, known case of kidney transplant at the age

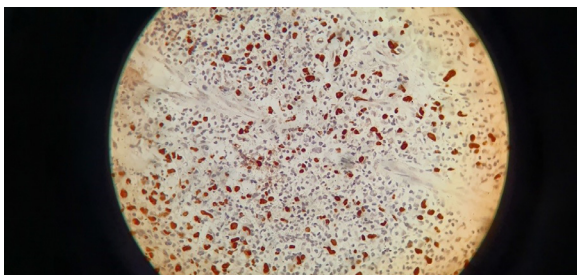


FIGURE 2. Epiglottic mass 400x: Numerous nuclei positive for EBV-encoded RNA (EBER).

of 10 months, who presented with cough and airway obstructive symptoms. The patient had been diagnosed with PTLD at the age of 9 years, for which he was treated with multiple cycles of chemotherapy. Laryngeal examination and bronchoscopy showed swelling and obliteration of the laryngeal ventricle with an obstructive lesion at the trachea. Biopsy taken confirmed the diagnosis of recurrent PTLD with B-cell proliferation.⁷ The clinical presentation of this second case is similar to previously reported PTLD of the upper airway. The patient had symptoms and signs of the upper aerodigestive tract very suggestive of a malignant process. Computed tomography of the neck has helped in delineating the extent of the lesion and its spread to contiguous structures. The histopathologic examination showed PTLD consistent with T cell lymphocytic background and positive EBV-encoding present in numerous cells. These findings are in accordance with numerous reports substantiating the strong link between EBV infection and PTLD.^{2,6,10}

CONCLUSION

The diagnosis of PTLD requires a high index of suspicion. In case of laryngeal involvement, the clinical presentation may mimic that of a primary laryngeal neoplasm. Early diagnosis using histopathologic examination is paramount to prevent airway compromise and life-threatening conditions. Cessation of immunosuppression and initiation of systemic therapy can lead to regression of the disease. Surgical resection should be limited.

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