A Case of Oropharyngeal Fistulae in Post-Transplant Lymphoproliferative Disorder

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Abstract

Objectives: At the conclusion of this presentation, the participants should be able to demonstrate understanding of the clinical presentation of post-transplant lymphoproliferative disorder (PTLD) and appreciate populations at risk, cytopathologically distinguish PTLD from other etiologies of adenotonsillar hypertrophy, and discuss management of patients with PTLD of the head and neck.

Methods: We report a unique manifestation of PTLD as severe oropharyngeal ulcers and fistulae in an immunocompromised renal transplant patient with EBV recipient-donor mismatch. Chart review and pathologic analysis were performed. Literature review compares and contrasts this unique case with other presentations of PTLD in the head and neck in an immunocompromised host.

Results: A 67 year-old immunocompromised post-renal transplant patient presented with severe oropharyngeal ulcers that ultimately resolved with reduction in immunosuppression and rituximab. The patient was known EBV-negative prior to transplant and the donor was known EBV seropositive, a phenomenon known as EBV-donor mismatch.

Conclusions: PTLD frequently presents with head and neck manifestations. Treatment of PTLD aims at lowering the immunosuppressive medication to allow for adequate immunity, use of anti-B cell antibody rituximab, chemotherapy, and interferon-alpha. Surgical intervention is indicated in airway obstruction (tonsillectomy) or local control (incision and drainage of deep neck space infections unresponsive to intravenous antibiotics).

Introduction

PTLD represents a spectrum of Epstein-Barr virus (EBV)-induced B-cell lymphoid expansion in the setting of pharmacologically suppressed host T-cells.

The incidence of PTLD in adult recipients of solid-organ transplant is 2-3% and higher in children.1 PTLD remains the second most common malignancy in the transplant population behind cutaneous malignancy.2 Because of its high incidence, otolaryngologists should be aware of its manifestations as forty percent of PTLD manifests in the head and neck, commonly in Waldeyer’s ring.3 Severe oropharyngeal ulceration, adenotonsillar hypertrophy, cervical adenopathy, sleep apnea, and airway obstruction may also be observed. Symptoms may mimic mononucleosis with fever, night sweats, weight loss, pharyngitis, and malaise.

Risk factors for development of PTLD include exposure to EBV, patient age, degree of immunosuppression, and type of solid organ transplant received.3

Case

A 67 year old patient post-renal transplant from a related donor presented with a one month history of fatigue, night sweats, odynophagia, halitosis and weight loss.

Direct visualization of the oropharynx revealed severe ulceration of the right tonsillar fossa and lateral pharyngeal wall with deep necrotic abscess that fistulated into the neck and right level II lymphadenopathy.

Biopsy revealed an infiltrate of EBV+ B-cells, confirming a diagnosis of PTLD. Immunosuppression was reduced and treatment with rituximab was initiated. The patient’s clinical condition improved and kidney function is normal despite the reduction in tacrolimus.

Figure 1. A. Multiple sites of oropharyngeal ulceration at initial presentation with severe erythema, with primary lesion on the right posterolateral oropharyngeal wall and other satellite lesions bilaterally. B. Erosion of both anterior and posterior right tonsillar pillars with a deep, necrotic ulceration extending into the neck space. C. One month post-initiation of rituximab and reduction in immunosuppressive agents. Broad localized erythema remains however the ulcers show evidence of granulation and diminished necrosis.

Figure 2. The oropharynx biopsy shows patchy necrosis and morphologically polymorphous proliferation of small, intermediate and large lymphocytes, immunoblasts and plasma cells. A. Hematoxylin & eosin stain. B. Hematoxylin & eosin stain 50X. C. CD20 immunostain demonstrating a B-cell rich infiltrate. D. EBER in situ hybridization demonstrates positivity for EBV in many of the lymphoid cells. The EBER is a dark blue nuclear stain, an in situ hybridization reaction with an EBV-specific probe. E. In situ hybridization with probes to lambda and F. kappa immunoglobulin light chain RNA, respectively. We can see that the vast majority of cells are lambda, with only a few kappa positive cells, indicating a lambda monotypic population. These findings are consistent with a post-transplant lymphoproliferative disorder, polymorphic type with lambda monotypic B-cells. Positive for EBV by EBER.

Figure 3. Pre-operative transnasal laryngoscopy reveals multiple smooth, cystic structures in the submucosal of the left ventricle, the right aryepiglottic fold. A lesion on the anterior surface of the epiglottis was visualized but is not shown in this image.

Discussion

Initial treatment of PTLD is reduction of immunosuppression, with success rate of this therapy alone ranging from 23-50%.4,5 and with the addition of rituximab, an anti-B cell antibody, increased to 64%.5

Chemotherapy directed against similar lymphomas, such as CHOP, has been shown to achieve remission rates of 75% with but high morbidity and mortality. Antiviral thymidine kinase inhibitors such as ganciclovir and acyclovir have no therapeutic role, as the tumor cells lack this enzyme, but may play a crucial role in prophylaxis in an EBV-negative patient.1 Interferon-alpha is used as an adjunctive treatment.

Surgical management is reserved for treatments of local complications of PTLD, including mass effect, pain, bleeding, and airway obstruction.

Conclusions

Recipients of solid-organ transplant are at an increased risk to develop PTLD. Commonly this disease can be treated with a reduction in immunosuppression and rituximab, where surgical intervention is indicated in airway obstruction.

References