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Review Article

Post-transplant lymphoproliferative disorder of the pediatric airway: Presentation and management

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ABSTRACT

Objective: Post-transplant lymphoproliferative disorder (PTLD) is a rare complication of immunosuppression with little consensus on its evaluation and management. The purpose of this contemporary review is to describe a pediatric patient with PTLD of the airway and review the literature to provide multidisciplinary recommendations regarding management.
Data Sources: Retrospective chart and literature review.
Review Methods: A pediatric patient with PTLD of the airway is described. An extensive literature search to review the existing data on pediatric PTLD of the upper airway was also performed.
Results: A pediatric patient with mixed fetal/embryonal hepatoblastoma developed laryngo-tracheal PTLD following liver transplantation. Diagnostic positron emission tomography (PET) scan demonstrated multiple sites of abnormal fluorodeoxyglucose (FDG) uptake within the larynx, distal esophagus, cervical lymph nodes, and abdomen concerning for PTLD. Laryngeal biopsy demonstrated Epstein–Barr virus (EBV) positive cells confirming the diagnosis. Rituximab therapy and reduction of immunosuppression resulted in resolution of his laryngeal disease in 3 months. An extensive literature search to review the existing data on pediatric PTLD of the larynx and trachea revealed 14 reported cases.
Conclusions: PTLD of the pediatric airway is an EBV-associated disease that requires a high index of suspicion as patients can often present with non-specific signs and symptoms but progress to have significant airway compromise. Evaluation consists of peripheral blood polymerase chain reaction (PCR) assays, biopsy, and PET/CT imaging. Management options include reduction of immunosuppression and/or systemic therapies.

Contents

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1. Introduction

Post-transplant lymphoproliferative disorder (PTLD) is a well-known complication of pharmacologic immunosuppression after solid organ transplantation. PTLD typically results from Epstein–Barr virus (EBV) infection, which causes an abnormal proliferation of B cells. In an immunosuppressed patient, the severity of this proliferation ranges from lymphoid hyperplasia to malignant lymphomas [1]. Of the pediatric patients diagnosed with PTLD, 25–63% will present with symptoms involving the head and neck [2,3]. Given the relative rarity of PTLD in the pediatric airway, we aim to present a case and review the existing limited literature on this subject. Our goal is to provide a framework for clinicians during the evaluation and treatment of this rare entity.

2. Methods

A retrospective chart review was performed to identify a pediatric patient with laryngeal PTLD treated at Boston Children's Hospital. The patient's hospital records were reviewed to identify demographics, transplant history, symptoms, lesion location, imaging, surgical approach, management, and post-treatment course. An extensive review of PTLD of the larynx and/or trachea in the English-language literature was also performed. Multidisciplinary expertise was elicited to provide a comprehensive overview.

3. Results

3.1. Case presentation

Our patient was diagnosed with fetal/embryonal hepatoblastoma at two years of age. He underwent several courses of chemotherapy and local control surgery but experienced disease recurrence in the liver ultimately undergoing a liver transplant at 3-1/2 years of life. Four months post-transplant, an EBV PCR resulted at 110,690 copies, but the patient remained asymptomatic. Tacrolimus was titrated to achieve target immunosuppression, and he returned to his home institution. Two months later, he began to develop fevers, hoarse voice, snoring, and cough. CT imaging demonstrated right epiglottic/aryepiglottic fold and supraglottic soft tissue thickening with edema. EBV viral DNA assayed by PCR of the plasma, previously negative, was then positive at < 50 IU/mL. Otolaryngology was consulted and direct laryngoscopy was performed, which revealed a mass on the posterior aspect of the false vocal cords extending to the laryngeal aspect of the epiglottis. Unfortunately a biopsy of the region was non-diagnostic. His EBV levels continued to rise, peaking at 79,844 IU/mL; recurrent intussusception led to resection of an abdominal lymph node with histology demonstrating polymorphic EBV-associated PTLD. Immunosuppression was reduced and EBV levels declined. However, continued intermittent fevers and bilious emesis prompted reevaluation at Boston Children's Hospital.

Upon arrival, an EBV PCR resulted at 974,612 copies. A PET/CT scan demonstrated multiple sites of abnormal FDG uptake within the larynx, distal esophagus, cervical lymph nodes, and abdomen (including the retroperitoneum, bowel, and porta hepatis), which were concerning for PTLD (Fig. 1). Repeat direct laryngoscopy demonstrated no masses or lesions in the oral mucosa; however, a progressive ulcerative laryngeal lesion involving the right side of the epiglottis and extending inferiorly along the right aryepiglottic fold with obliteration of the right hemilarynx was biopsied (Fig. 2). The trachea and distal airway appeared normal. On histopathology, the laryngeal mass was characterized by a mixed population of lymphocytes, histiocytes, neutrophils and apoptotic debris. Immunohistochemically, lymphocyte markers revealed a mixture of CD20 and CD79a positive B cells and numerous CD3 positive T cells. Scattered EBV positive cells were observed with Epstein–Barr encoding region (EBER) in situ hybridization and these cells appeared to correspond to the CD20 immunoreactive lymphocytes. While it is plausible that this constellation of findings was indicative of acute EBV infection, the final histopathology, imaging, and clinical symptoms were felt consistent with a diagnosis of PTLD (Fig. 3).

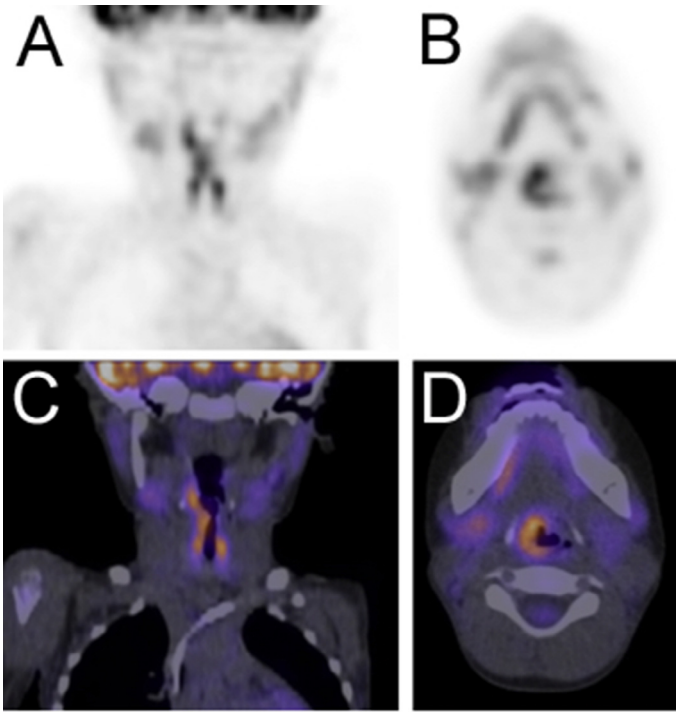

Fig. 1. (A) Coronal and (B) axial FDG-PET images, as well as fused images (C and D). PET/CT images show abnormal increased laryngeal FDG accumulation, with prominent uptake present around the vocal cords, extending both cephalad and caudally in the soft tissues surrounding the larynx. Physiologic FDG uptake commonly seen in the lymphoid tissue of the tonsils and adenoids (not shown) was clearly separable from the laryngeal uptake seen here.

The patient received four doses of 375 mg/m^2 rituximab administered weekly and tacrolimus was further decreased. His EBV PCR peaked at 2.6 million copies just prior to initiation of therapy but normalized weeks later with no detectable virus after only two doses of rituximab. A repeat PET scan following the four weekly rituximab treatments demonstrated only mild residual laryngeal avidity with