Post-Transplant Lymphoproliferative Disease (PTLD) Presenting as Progressive Stridor

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ABSTRACT

Objectives: Case presentation of Epstein-Barr Virus (EBV) negative post-transplant lymphoproliferative disorder (PTLD) with severe enlargement of the epiglottis and aryepiglottic (AE) folds resulting in airway compromise. Present a literature review of laryngeal findings in PTLD. Study Design: Case report and literature review. Methods: The case of a 15 month old male who presented to a tertiary care academic medical center with six month history of stridor is reported and reviewed. The patient’s pertinent history, clinical findings, radiologic and pathologic findings are examined. Radiographic and pathologic slides will demonstrate surgical specifics. Results: The patient had a history of orthotopic liver transplant at age six weeks for fulminant liver failure. Seven months after surgery the patient developed progressive audible inspiratory stridor at rest with positional upper airway obstruction but without prolonged cyanotic episodes. The patient was admitted for anemia and thrombocytopenia and diagnosed with Evans Syndrome. Due to the patient’s progressive stridor, an airway fluoroscopy was performed. Findings included irregular thickening of the epiglottis and aryepiglottic folds, which was confirmed by flexible video laryngoscopy. Biopsy of the epiglottis and aryepiglottic folds revealed EBV negative PTLD. The patient received intravenous gamma globulin (IVIG), rituximab, and reduction of tacrolimus immunosuppression, which resulted in prompt resolution of the patient’s stridor and upper airway obstruction. Conclusion: EBV negative PTLD presenting as upper airway obstruction is a very rare entity. Early suspicion, with particular attention to the airway, and tissue diagnosis are critical for early therapeutic intervention in this potentially life-threatening condition.

INTRODUCTION

Post-transplant lymphoproliferative disease (PTLD) occurs in patients treated with cyclosporine or tacrolimus after organ transplantation. Associated with Epstein-Barr virus (EBV) infection, PTLD may be insidious, resembling infectious mononucleosis, or may present as an aggressive form of lymphoma. Its prevalence has been reported to be 4% among children compared to 8.8% among adults. Lesions occur in the head and neck, gastrointestinal tract, and the transplanted allograft. Although PTLD commonly causes upper airway-narrowing in children, previously reported cases have primarily involved Waldeyer’s ring. We describe a case of PTLD with severe enlargement of the epiglottis and aryepiglottic folds causing progressively worsening stridor and cyanotic spells for a six month period.

CASE REPORT

A 15 month old male who had an orthotopic liver transplant for idiopathic fulminant hepatic failure at five weeks of age was admitted with thrombocytopenia. His medications included tacrolimus and he had been followed closely by the Transplant Service without problems. During his workup, it was noted that the patient had a six month history of progressively worsening stridor. The stridor was mild at rest, with minimal subcostal retractions, but worsened with agitation. There was no concern regarding weight gain or failure to thrive; however, he did have intermittent emesis with food intake. Patient had been seen by multiple otolaryngologist’s and diagnosed with laryngomalacia despite never having a diagnostic laryngoscopy secondary to thrombocytopenia. The patient’s thrombocytopenia was attributed to viral suppression and diagnosed as idiopathic thrombocytopenic purpura (ITP). Viral serologies were positive for hepatitis C.

Further evaluation at our hospital included an airway fluoroscopy revealing mild tracheomalacia and irregular thickening of the epiglottis and aryepiglottic folds, greater on the right than the left concerning for a focal lesion such as a hemangioma. Sleep study noted frequent, repetitive, relative desaturations with arousals often during periods of snoring. The lowest SPO2 was 83%.

He was taken to the operating room for a direct laryngoscopy and bronchoscopy. Laryngeal polypoid transformation was noted extending circumferentially around the epiglottis extending along the aryepiglottic folds. A 3.5 endotracheal tube was placed without difficulty. A biopsy was performed on the epiglottis which revealed dense subepithelial lymphoplasmacytic infiltrate. Biopsied tissue was a mixture of T and B-lymphocytes with maintained cytoarchitecture, suggesting diagnosis of polymorphic PTLD. The biopsied tissue was EBV-negative. Tacrolimus immunosuppression was discontinued and changed to prednisolone. He ultimately was weaned from prednisolone and started on sirolimus. The patient’s stridor and cyanotic spells resolved with the alteration in medications. A subsequent laryngoscopy and bronchoscopy seven months after the first procedure revealed normalization of the supraglottis and mild laryngomalacia with resolution of the polypoid changes in the epiglottis and aryepiglottic folds.

DISCUSSION

PTLD was originally described as a complication of immunosuppressive therapy in 1968. Since that time, PTLD has been associated with cyclosporine and tacrolimus (FK506) immunosuppression. Each of these agents depresses specific immune mechanisms normally active against EBV, particularly T-cell function.

The incidence of PTLD in the pediatric transplantation population has been reported to be 4% to 11%. The disease is more common in pediatric than in adult transplant recipients. Literature suggests that the increased incidence of disease in pediatric patients is attributable to their increased tendency to be infected with EBV. Younger children are more likely to develop PTLD than older children, with the 2 to 5 year old range having the highest incidence for similar reasons.

Otolaryngological manifestations are present in up to two thirds of the patients who present with PTLD. The most common area affected in the head and neck is the Waldeyer ring. The process can be insidious or rapid, requiring emergent airways stabilization and adenosotonsillectomy. One case of respiratory arrest from PTLD-induced acute airway obstruction has been reported and underlines the importance of early diagnosis and airway management.

The diagnosis of PTLD is made by pathologic evaluation. EBV-associated PTLD may be divided into three types. Type 1 represents polymorphic diffuse B-cell hyperplasia without evidence of malignancy. Type 2 represents polymorphic B-cell lymphoma. This disorder may progress from a polyclonal to a monoclonal B-cell proliferation, or non-Hodgkin’s lymphoma (Type 3). Therapy for PTLD consists of antiviral therapy, reduction or cessation of immunosuppressive therapy, and surgical excision as indicated.

Successful treatment involves early diagnosis and relief of airway obstruction. Surgical intervention is recommended for supportive and diagnostic purposes only. Certainly, the symptoms caused by PTLD-induced local airway disease can be improved with surgical debulking as noted in our case report.

CONCLUSION

Fortunately, PTLD presenting as airway compromise or worsening stridor is a relatively rare clinical entity. Further studies are needed to better elucidate the most effective long-term treatment protocols. Early suspicion, with particular attention to the airway and tissue diagnosis, is critical for early therapeutic intervention.

REFERENCES