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Post-transplant Lymphoproliferative Disease May Present with Severe Airway Obstruction

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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 and 0.8% among adults.[1,2] 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.[3] We describe a case of PTLD with severe enlargement of the epiglottis and aryepiglottic folds causing life-threatening airway obstruction after the induction of anesthesia.

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Case Report

A 14-month-old boy who had a liver transplant for biliary atresia at the age of 6 months presented with progressive stridor. The stridor was mild at rest, with minimal subcostal retractions, but worsened with crying. Despite normal liver function, weight gain was poor (weight, 8.4 kg). Fiberoptic examination of the airway at an outside hospital revealed laryngomalacia and possible tracheomalacia. Viral serology revealed past infection with EBV. Further evaluation at our hospital included normal fluoroscopy of the trachea and a sleep study that noted three 6- to 7-s episodes of obstructive apnea over 8 h, associated with a decrease in Sp_{O_2} from 97–99% to 89–90%. Fiberoptic examination of the airway revealed an enlarged epiglottis and aryepiglottic folds with minimal enlargement of the tonsils. The patient was scheduled for tonsillectomy and supraglottoplasty.

Medications included tacrolimus, prednisone, acyclovir, and trimethoprim-sulfamethoxazole.

Laboratory values included a hematocrit of 32% and a normal serum HCO_3^- of 23.

The pediatric otolaryngologist performing the procedures requested that the patient breathe spontaneously during direct laryngoscopy to allow assessment of vocal cord function. Anesthesia was

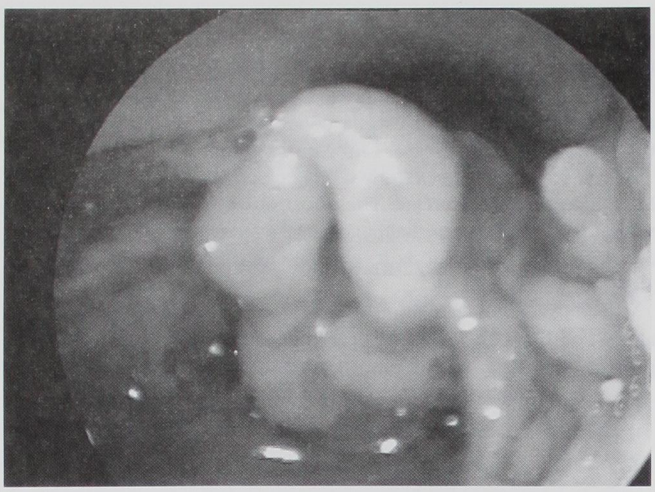

Fig. 1. The epiglottis is markedly enlarged, predisposing to complete obstruction of the glottic opening.

induced with intravenous thiopental, 20 mg, and halothane, 0.5–4.0%, *via* facemask. As the patient became unconscious, marked inspiratory stridor was noted. This persisted despite jaw thrust, oral and nasal airway placement, and administration of continuous positive airway pressure (CPAP) to 25 cmH_2O. Direct laryngoscopy revealed a markedly enlarged epiglottis, which was occluding the glottic opening, and thickened, redundant aryepiglottic folds (fig. 1). After administration of intravenous rocuronium, 8 mg, the patient's trachea was intubated with a 4.0-mm ID tracheal tube. Sp_{O_2}, which had decreased to 84% before tracheal intubation, increased to 100% while the patient's lungs were ventilated with an $F_{I_{O_2}}$ of 1.0.

During the 75-min procedure, anesthesia was maintained with propofol, 100–200 $\mu g \cdot kg^{-1} \cdot min^{-1}$, fentanyl, 15 μg, and rocuronium. Surgical excision of the tonsils, redundant aryepiglottic tissue, and one third of the epiglottis was performed.

Postoperatively moderate stridor was noted. Sp_{O_2} remained 100% with supplemental O_2 administration.

During the 24-h stay in the pediatric intensive care unit, intravenous dexamethasone and four doses of aerosolized epinephrine were given, and the stridor decreased. The patient was discharged home on postoperative day 10 without residual stridor.

Pathologic examination of the surgical specimens revealed PTLD (diffuse B cell hyperplasia) of the epiglottis and aryepiglottic folds, and reactive hyperplasia with EBV infection of the tonsils.

Discussion

Post-transplant lymphoproliferative disease was originally described as a complication of immunosuppressive therapy in 1968.[4] 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 cytotoxic T cell function.

Epstein-Barr virus-associated PTLD may be divided into three types.[5] Type 1 represents polymorphic, diffuse B cell hyperplasia without evidence for malignancy. Clinically the illness resembles infectious mononucleosis. Involved tissues show a polymorphous reactive proliferation, often limited to lymph nodes and tonsils. Type 2 represents polymorphic B cell lymphoma. This illness also resembles infectious mononucleosis, but tissues may show morphologic features of malignancy. Lymphoproliferation extends to extranodal organs, including the liver, and may be associated with fatal, progressive lymphoproliferation. 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 when indicated.

Ho *et al.* described 21 cases of EBV-associated PTLD in 1,467 transplant recipients in Pittsburgh from 1981 through 1985.[1] The frequency of occurrence in pediatric patients was 4% (11/253), whereas in adults it was 0.8% (10 of 1,214). All patients were treated with cyclosporine. Five children had a self-limited mononucleosis-like syndrome (Type 1). These cases presented with involvement of tonsils or cervical lymph nodes. Four children had a course that began similarly, but then progressed over the ensuing 2 months to widespread lymphoproliferation in internal organs and death (Type 2). Two cases were manifest by extranodal monoclonal B cell lymphoma (Type 3).

Reyes *et al.* reviewed 936 patients treated with tacrolimus (FK506) as the primary immunosuppressive agent after liver, kidney, or heart transplantation.[6] Fifteen cases of PTLD were noted, for an incidence of 1.6%. The incidence in children was 4.3% (6 of 141), whereas 1.1% of adult transplant patients were afflicted (9 of 795). The median time from transplantation to presentation was 4.4 months. Thirteen of 15 cases were in liver transplant patients; the other two cases were in kidney transplant patients. The range of pathology and site of presentation were similar to the series of Ho *et al.*

In a review of 14 children with PTLD at Children's Hospital of Pittsburgh, upper airway obstruction was the most common symptom, presenting in nine cases.[1] Ten patients had febrile illness with dysphagia, odynophagia, and hypertrophy of the tissues of Waldeyer's ring. Associated findings included cervical adenopathy, sinusitis, and otitis media. The majority of these children underwent uneventful tonsillec-

tomy or adenoidectomy and were discharged home. One patient had an intratracheal mass, presenting with biphasic stridor, and died after chemotherapy and radiation therapy. The other child had a paratracheal mass that presented with coughing episodes, underwent uneventful biopsy, and was doing well after a limited follow-up period.

We report a case of PTLD with isolated involvement of the glottic and supraglottic structures. Children with this manifestation of PTLD may be misdiagnosed as having laryngomalacia, tracheomalacia, tonsillar and adenoidal hypertrophy, or other disorders and may develop complete airway obstruction when given anesthetic or sedative-hypnotic drugs. An accurate diagnosis of this lesion before induction of anesthesia is important.

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