Necrotic adenoids in post-transplant lymphoproliferative disorders

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Abstract. Necrotic adenoids in post-transplant lymphoproliferative disorders. Problem: Post-transplant lymphoproliferative disorders (PTLD) are a potentially fatal complication after solid organ transplantation. The majority of cases are associated with Epstein Barr virus infection (EBV). The first manifestations of PTLD are frequently observed in the ENT area with adenoidal and/or tonsillar enlargement.

Methodology: We present the case of a 12-year-old girl with a total nasal obstruction and tonsillitis five months after a kidney transplantation for bilateral congenital kidney hypoplasia.

Results: The EBV genome was detected by polymerase reaction three months after surgery. Fiberoptic examination revealed an obstructive necrotic mass in the naso-pharynx. The anatomic-pathologic analysis revealed necrotic adenoids.

Conclusions: Necrotic tonsillitis is common. Necrosis of the adenoids, although rarer, can also occur and explains the important respiratory distress. Since two thirds of PTLD patients present with clinical symptoms in the ENT area, the otorhinolaryngologist should be aware of this complication.

Introduction

Post-transplant lymphoproliferative disorders (PTLD) are a well-recognised and potentially fatal complication after bone marrow or solid organ transplantation. These include a spectrum of disorders ranging from benign hyperplasia to invasive malignant lymphoma. The majority of cases are associated with Epstein Barr virus (EBV)-driven tumour formation in B-cells, and are a consequence of the detrimental effect of immunosuppressive agents on the immune-control of EBV.

Adenotonsillar tissue is a principal reservoir for EBV replication. Indeed, the first manifestation of PTLD in children is most frequently observed in the Waldeyer’s ring with adenoidal and/or tonsillar enlargement.

We present the case of a child with necrotic adenoids after kidney transplantation.

Case report

A 12-year-old girl was referred to our ENT department with respiratory distress. The patient presented with total nasal obstruction and tonsillitis. She also complained of dental abscess and colitis. This situation caused important weight loss and cachexia. The patient had a medical history of bilateral congenital kidney hypoplasia and underwent a kidney transplantation at the age of 11 years. For 9 months, she was on oral immuno-suppressive therapy consisting of azathioprine 50 mg once daily, tacrolimus 3 mg twice daily, and prednisolone 5 mg once daily. The adolescent was seronegative for EBV before the transplantation, but the EBV genome was detected by polymerase chain reaction three months after the transplantation surgery. A high EBV viral load (3,990,270 copies/ml) was confirmed by blood analysis. She was also anaemic and had important peripheral neutropenia and an inverted CD4/CD8 ratio. Internists had already prescribed aciclovir 800 mg twice daily few days earlier.

Examination by flexible nasofibroscopy revealed an obstructive, necrotic, white-coloured mass in the nasopharynx. The differential diagnosis included...
nasopharyngeal carcinoma, lymphoma, or necrotic adenoids post EBV infection. Moreover, the patient had bilateral serous otitis media.

A CT scan and a MRI of the head and of the neck were performed later and showed some adenopathies and an obstructive mass that completely occupied the nasopharynx and pressed the soft palate outward (Figures 1-3). Because of these findings, the patient underwent biopsies of the necrotic mass, the posterior pharyngeal wall, the rhino-pharynx, and the oropharynx. During the biopsy of the obstructive mass, the mass became unhooked from the nasopharynx in one piece. This allowed an analysis of the entire mass and improved the patient’s respiratory distress. During the same surgical intervention, we inserted trans-tympanic tubes.

The anatomic-pathologic analysis revealed a necrotic mass of 0.2 × 3 centimetres in diameter and a lymphoid infiltrate of the oro- and nasopharyngeal mucous membrane. The immunocytochemical analysis showed positive staining for the CD20 and CD79 markers that are specific for a B-cell infiltrate. There were no cellular abnormalities.

These analyses provided the diagnosis of acute infectious mononucleosis in PTLDs and a major necrosis of adenoids.

The treatment consisted of aciclovir 800 mg four times daily and anti CD20, B cell-specific monoclonal antibodies. We stopped azathioprine and tacrolimus for 10 days and increased the prednisolone to 15 mg once daily. Initially, this treatment improved the general condition of our patient and reduced the EBV viral load by 65% (1,345,000 copies/ml). However, one month later the girl developed a Pneumocystis carinii infection and required a tracheotomy. This infection caused major bronchial damage and our patient died 10 months after the kidney transplantation.

Discussion

PTLD is a well-known complication of paediatric organ transplantation. The first symptoms are often in the ear, nose, or throat area with adenotonsillar enlargement, and rhino-sinusal or laryngeal involvement. To our knowledge, this is the first reported case describing necrosis of the adenoids.

PTLD can be difficult to diagnose and to distinguish from a nasopharyngeal lymphoma. Zeglaoui et al.\(^1\) reported two paediatric cases of nasal NK/T-cell lymphoma and showed that a high index of malignant suspicion can be provided by imaging studies (bony erosion, extension, and destruction of the sinuses and orbits). In our case, histological analysis provided the final PTLD diagnosis and showed lymphoid infiltrate with or without cellular abnormalities and lymphoid markers for B cells (CD20), T-cells (CD3), or natural-killer cells (CD56 & CD57). In situ hybridisation (ISH) can detect EBV mRNA in tissue sections and cytological preparations. Some centres consider ISH the gold standard for detecting cases of disease associated with EBV.\(^2\)

The reported incidence of PTLD in adult transplant
recipients ranges from 1% to 2%.\(^7\) In the paediatric population, a greater incidence has been reported (5-15%) due to a higher percentage of EBV seronegative patients at the time of transplant, pointing out EBV as one of the major factors involved in the pathophysiology of PTLD.\(^7\)

Long-term immunosuppression is a well-recognised risk factor. High blood levels of cyclosporine and tacrolimus have both been linked to the occurrence of PTLD. Notably, PTLD in bone marrow recipients occurs from less than 1% to as many as 24% in those receiving T-cell depleted bone marrow, presumably because of the immunosuppressive effect of removing EBV-specific T-cells, which further promotes PTLD development.\(^8\)

At present, reduction of immunosuppression with the aim of restoring natural EBV-specific immune-surveillance is widely accepted as the first-line treatment for PTLD in solid organ recipients. This produces successful tumour regression in approximately 20-50% of cases.\(^6\) In our case, a more aggressive surgical strategy, such as tonsillectomy or adenotony, since adenotonsillar tissue is a principal reservoir for EBV replication, could be beneficial. But there are no reports that this treatment produces reduction in the EBV viral load. Only a minority infectious mononucleosis in the normal population will result in tonsillectomy. These cases are usually florid or atypical, and generate the most concern for a possible diagnosis of lymphoma.\(^7\) In some instances of PTLD in patients with localised lesions, surgical resection has successfully led to tumour eradication and improvement in respiratory distress, like in our patient.\(^8\) Some authors discuss the potential of prophylactic adenotonsillectomy to prevent possible PTLD and rhino- and oropharyngeal tissue enlargement in all transplanted paediatrics patients with an EBV seronegative status.\(^8\) This kind of surgical prophylaxis could also decrease the incidence of general ENT infections for these immuno-suppressed patients. The anti-viral drugs aciclovir and ganciclovir are commonly administered, although no evidence exists to support their clinical utility. Monoclonal antibodies directed against a variety of B-cell surface antigens have been investigated as a potential PTLD treatment. Several studies addressing the use of rituximab, a chimeric human/mouse anti-CD20 monoclonal antibody, have reported successful anti-tumour responses.\(^10,11\) The good results first reported in our case were probably caused by all these treatments. Unfortunately, our patient died from another detrimental consequence of the immuno-suppressive drugs.

**Conclusion**

PTLD are difficult to diagnose and to treat. Prompt diagnosis is important to improve patient survival. Tonsillar hypertrophy and adenoidal enlargement are the most frequently encountered manifestation of PTLD. To our knowledge, our case is the first to describe necrosis of the adenoids. Because two thirds of PTLD patients present with clinical symptoms in the ENT area, the otorhinolaryngologist should be aware of this complication.

**References**


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