Posttransplantation Lymphoproliferative Disorder Initially Seen as Iris Mass and Uveitis

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Primary ocular posttransplantation lymphoproliferative disorder is rare. Epstein-Barr virus is implicated as the cause as a result of systemic immunosuppression after transplant surgery. We studied a patient who developed ocular posttransplantation lymphoproliferative disorder after orthotopic liver transplantation. Slitlamp and light microscopic photographs confirmed the diagnosis.


In April 1996, the patient had an elevated EBV titer associated with gastrointestinal distress that resolved with oral acyclovir. In March 1998, the patient developed tonsillitis and underwent tonsillectomy. Histologic analysis failed to definitively diagnose PTLD.

In November 1999, the patient had sand thrown into her right eye. Her ophthalmologist diagnosed a corneal abrasion with reactive anterior uveitis. The abrasion healed rapidly, but the uveitis persisted. Three days after the injury, the patient was referred to the University of Wisconsin–Madison pediatric eye clinic for evaluation.

When first seen by us, the patient’s medications included oral cyclosporine, 0.7 mg twice daily; oral prednisone, 5 mg every other day; 5% homatropine hydrobromide, 1 drop in the right eye 4 times daily; ciprofloxacin hydrochloride, 1 drop in the right eye every 3 hours; and prednisolone acetate, 1 drop in the right eye every 2 hours. On examination, the best-corrected visual acuity was 20/30 in the right eye and 20/20 in the left. Ocular motility was normal, as were the results of external examination. There was anisocoria, with the right pupil greater than left, without a relative afferent pupillary defect.

Slitlamp examination disclosed normal conjunctiva and sclera in both eyes. Large mutton-fat keratic precipitates were seen bilaterally, more severe in the right eye than the left (Figure 1). Seven to 10 inflammatory cells per 2-mm slit beam were seen in the right anterior chamber, and 5

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to 7 were seen in the left. Examination of the irises showed prominent nodularity in the right eye at the 6, 9, and 12 o’clock positions, while the iris in the left eye was normal (Figure 1). The lenses were clear bilaterally. Funduscopic examination disclosed a few anterior vitreous cells in the right eye, a clear vitreous in the left eye, and normal optic nerves and retinas. Anterior segment ultrasonography was consistent with iris masses in the right eye.

In this immunosuppressed child with iris nodules, there was suspicion of infectious uveitis, secondary malignancy (leukemia or lymphoma), or posttransplantation lymphoproliferative disorder. A joint decision was made with the transplant team and the pediatric oncology service to pursue further workup, to include a cerebrospinal fluid analysis, bone marrow aspiration biopsy, and iris biopsy of the right eye.

The bone marrow was normal. The cerebrospinal fluid showed a mild lymphocytosis with normal-appearing lymphocytes. Results of physical examination were normal, as was a complete blood cell count and a computed tomographic scan of the pelvis, abdomen, and chest. A biopsy of the right iris was performed with the patient under general anesthesia.

A 2 × 2 × 1-mm piece of iris tissue was received for histopathologic examination. Microscopic examination showed a dense infiltrate of the iris stroma, consisting predominantly of plasma cells, with accompanying lymphocytes with mild atypia (Figure 2). Immunohistochemical staining was strongly positive for κ light chains and negative for λ light chains (Figure 3). The CD3 staining was moderately intense and the CD20 staining was moderate (Figure 4).

The immunohistochemical staining was interpreted as follows: The strong positivity for κ light chains and the negative λ light chains indicate monoclonality of the predominant population of cells, the plasma cells. The positive CD3 and CD20 staining represents the polymorphism of the infiltrate and the accompanying T (CD3-positive) and B (CD20-positive) cells. The final diagnosis was of a polymorphic infiltrate with a predominant monoclonal plasma cell population consistent with PTLD of the iris. No studies for evidence of EBV were performed on the iris specimen.

**COMMENT**

Posttransplantation lymphoproliferative disorder develops in approximately 3% of patients who receive systemic immunosuppression for liver transplantation. The association between immunosuppression after organ transplantation and lymphoproliferative disorders has been known since the early 1970s; however, most of these tumors were originally diagnosed as non-Hodgkin lymphoma. In 1977, Hertel et al were the first to present these tumors as a lymphoproliferative disorder unique to patients who have undergone organ transplantation. In the 1980s, Hanto et al fully described the syndrome of PTLD.

Three distinct varieties of PTLD have been described. The first is a mononucleosilike syndrome of fever, adenopathy, tonsillitis, and sore throat, which is self-limited. The second variety of PTLD consists of widespread lymphoproliferative disease that usually leads to death. Our patient was initially seen by us with localized organ involvement, the third variety of PTLD. Localized PTLD most commonly affects the gastrointestinal tract, central nervous system, tonsils, and salivary glands.
Epstein-Barr virus is implicated as the cause of PTLD. One theory suggests that EBV causes B-cell proliferation, which would normally be down-regulated by cytotoxic T cells and natural killer cells. Posttransplant immunosuppressive medications inhibit T-cell function, and thus B-cell proliferation goes unchecked. Serologic evidence supporting the association between EBV and PTLD was strongly supported by Ho et al.²

Histopathologically, PTLD usually consists of a B-lymphocyte or plasma cell proliferation. The spectrum ranges from polyclonal benign typical-appearing B-cell proliferations to mononclonal aggressive atypical-appearing B-cell and plasma cell proliferations. Occasionally T-cell lymphomas are recognized as PTLD. In a histopathologic study of 83 specimens in 43 cases of PTLD by Nalesnik et al., most (71 of 83) were classified as polymorphic or minimally polymorphic, whereas only 12 of 83 were monomorphic. In the same study, clonality was determined in 30 cases. Twelve were monoclonal, 13 were polyclonal, and 5 cases had separate lesions that were both monoclonal and polyclonal. The case presented here is consistent with the most common type of PTLD, a polymorphic infiltrate with a monoclonal predominant subpopulation.

Treatment of PTLD consists of systemic ganciclovir and lowering the dosage(s) of immunosuppressive agents to achieve a balance between organ rejection and PTLD. Surgical resection of localized PTLD tumors or systemic antilymphoma agents are options in select cases.

Outcomes vary depending on the type and extent of the tumor. Previous reports of ocular occurrence of PTLD exist,³-⁵ 2 of which were first seen as iris masses,⁵,⁶ 2 as vitreitis mimicking lymphoma,⁷,⁸ and 1 as an orbital mass.⁹

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