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Sir,

Bilateral lacrimal gland enlargement due to post-transplant lymphoproliferative disorder

Over the years, post-transplant lymphoproliferative disorder (PTLD) has become increasingly reported as organ transplantation becomes more common. To our knowledge this is the first report of bilateral lacrimal gland enlargement secondary to PTLD.

Case report

A 49-year-old male, on oral cyclosporine A following renal transplantation performed 10 years previously for polyarteritis nodosa associated renal vasculitis, presented with a 2-week history of bilateral upper lid swelling secondary to bilateral nontender lacrimal gland enlargement. Examination was otherwise unremarkable. Significantly, he had been diagnosed with biopsy-proven cervical lymph node PTLD 6 weeks earlier.

Bilateral lacrimal gland incisional biopsy was performed. Histology of both lacrimal glands revealed atrophic acini and diffuse infiltration by a polymorphous population of small lymphocytes, plasma cells, and larger centroblast-like cells (Figure 1). Immunohistochemistry demonstrated that the majority of the cells, including the larger blasts, were B-cells, many aberrantly positive for the Epstein–Barr virus (EBV) upregulated T-cell antigen, CD43 (Figure 2). In situ hybridisation with the EBER mRNA probe (Figure 3) confirmed EBV infection and confirmed the diagnosis of EBV-positive polymorphic B-cell PTLD. Identical histology, immunohistochemistry, and in situ hybridisation appearances were seen in the cervical lymph node excised 6 weeks previously.

Under oncology supervision, the cyclosporin A therapy was withdrawn. However, due to the minimal response, treatment with monoclonal anti-CD20 (Rituximab, Roche) was started. Dramatic improvement ensued with shrinkage of both lacrimal glands and cervical lymphadenopathy. Unfortunately, the transplanted kidney underwent rejection, necessitating its removal. The patient remains well on dialysis with no recurrence of PTLD.

Discussion

PTLD, first described over 30 years ago,[1] represents a spectrum of lymphoproliferative disease, ranging from early polyclonal proliferations, often presenting with an infectious mononucleosis-like syndrome, to frank lymphoma, usually of the B-cell type.[2]

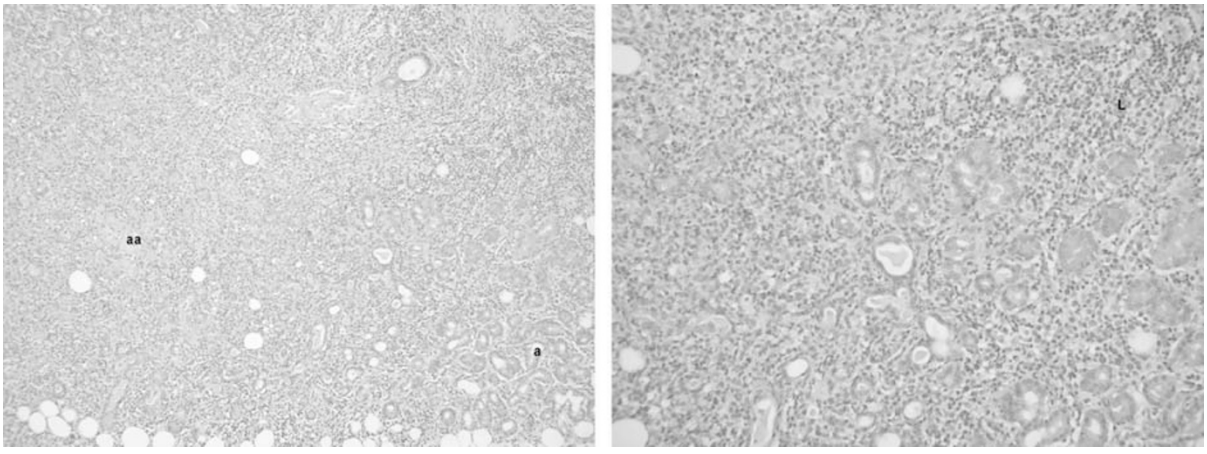

Figure 1 (Left) Histology of lacrimal gland incisional biopsy showing marked acinar atrophy associated with predominantly diffuse infiltrates of mature lymphocytes (aa—acinar atrophy, a—lacrimal gland acinus; H&E ×10). (Right) Higher power view showing diffuse infiltration of lymphocytes (L) among lacrimal gland acini (H&E ×20).

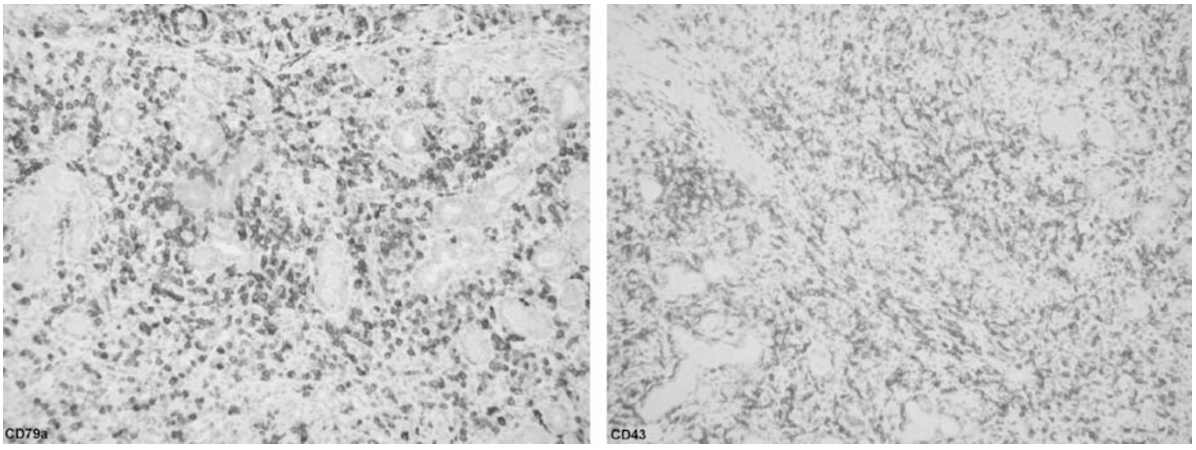

Figure 2 (Left) Immunohistochemistry showing positive staining for CD79a, a B-cell marker. (Right) Immunohistochemistry showing abnormally high staining for the T-cell marker CD43 in B-cells due to its upregulation caused by EBV infection (× 20).

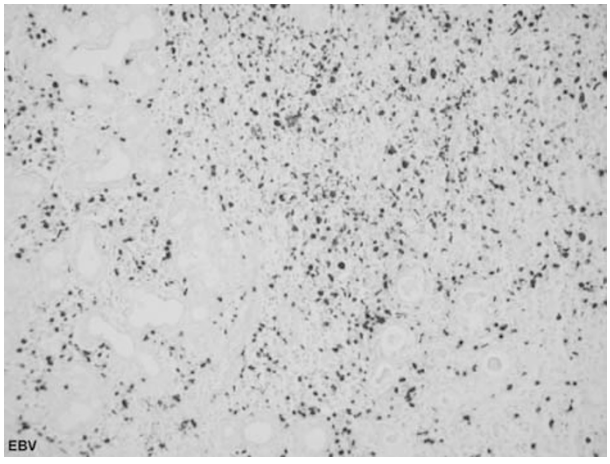

Figure 3 *In situ* hybridisation showing positive staining for Epstein–Barr virus with the EBER mRNA probe (× 20).

Four subtypes, which differ in histology and clonality, have been described—early lesions, polymorphic PTLD, monomorphic PTLD, and Hodgkin's lymphoma-like PTLD, sometimes with multiple subtypes presenting concurrently.[2–5] Disease severity is thought to be partially dependent upon the type of transplant received and associated immunosuppression protocol.[2,5,6]

The role of EBV is well recognised.[7–11] The vast majority of PTLD are thought to represent EBV-induced monoclonal, and less commonly, polyclonal, B-cell and T-cell proliferations, with EBV-positive PTLD presenting earlier than EBV-negative PTLD.

Interestingly, post-transplantaion MALTomas have also recently been reported and require differentiation from PTLD due to different managment and prognosis. Besides the histological differences of MALToma and PTLD, immunohistochemistry and in situ hybridisation differences also exist with the detection of EBV, which is characteristic for PTLD, so far unreported in transplantation-associated MALToma.[12]

The treatment of PTLD, which is dependent upon presentation, histological appearance (by both conventional morphology and immunohistochemistry) and molecular genetic analysis,[9,7,13,14] usually involves the risky initial step of reducing the level of immunosuppression.[15] Other treatment modalities include antiviral therapy,[14,16] chemotherapy, radiotherapy, immunotherapy,[17] and anti-B-cell monoclonal antibody preparations (eg anti-CD20, Rituximab).[5] However, despite treatment, prognosis remains poor, with mortality rates in excess of 60%.[2] Reports of PTLD remain sparse in the ophthalmic literature.[16–25] To our knowledge, this is the first report of lacrimal gland involvement by PTLD. It is important that ophthalmologists recognise PTLD, which is likely to become more common, as a cause of eye/orbital problems in transplant patients, since prompt treatment may improve patient survival.

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Sir,

Peyronie's disease following long-term use of topical timolol

Peyronie's disease (PD) is characterised by formation of a localised fibrous plaque of the tunica albuginea of the penis, which results in varying degrees of pain and