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Sir,

Epstein-Barr virus dacryoadenitis as a complication of bone marrow transplant in a child with combined immunodeficiency

Dacryoadenitis may result from bacterial or viral infection or granulomatous disease such as sarcoidosis and may affect up to 1 in 300 people with acute Epstein-Barr virus (EBV) infection.¹ The clinical course in the immunocompetent patient is usually mild and self-limiting.

We present a case of severe acute bilateral dacryoadenitis in a child who had recently undergone a bone marrow transplant. Concurrent EBV infection was demonstrated in blood and tears by polymerase chain reaction (PCR).

Case report

An 8-year-old girl presented with a 1 week history of pain and redness around both eyes. Ocular examination revealed reduced aqueous tear secretion and mild conjunctival injection with no follicular or papillary changes. Visual acuities, anterior and posterior segments were all normal.

Two months previously she had undergone a 1DQ mismatched, T-cell replete, unrelated donor bone marrow transplant (using low-intensity conditioning²) to treat combined immunodeficiency (with an autoimmune component which included poliosis). Her post-transplant course was not smooth and she remained neutro- and lymphopenic. She had also developed anorexia and a mild skin rash suggestive of mild graft-versus-host disease (GVHD). Her ocular findings were thought to be consistent with GVHD. She was commenced on tear film supplements and mild topical steroid drops.

Two days later she had increased pain and upper lid oedema. Examination showed bilateral palpable tender swollen lacrimal glands but no pre-auricular or submandibular lymphadenopathy (Fig. 1). There were bilateral temporal small perilimbal subconjunctival haemorrhages with mild punctate epithelial keratitis and minimal conjunctivitis. Samples taken over the previous 2 weeks for plasma PCR detected a rapid rise in EBV viral load from none to 165 000 copies/ml. She was commenced on foscarnet and the anti-CD20 monoclonal

Fig. 1. (A) Face showing bilateral periorbital oedema, especially in the region of the lacrimal glands. (B) Right eye showing temporal subconjunctival haemorrhage. (C) Left eye showing temporal subconjunctival haemorrhage.

antibody, rituximab (as prophylaxis against post-transplant lymphoproliferative disorder³). PCR of the tear film detected EBV DNA.

Over the following few days her symptoms improved and her lacrimal gland swelling resolved. Her aqueous tear secretion remained slightly subnormal, however, requiring occasional tear film supplements. After 1 month EBV DNA was undetectable in her plasma and tears. Autoantibodies to extractable nuclear antigen including Ro and La were negative.

Comment

Following bone marrow transplantation, ocular complications are very common and correlate strongly with GVHD.⁴ These include keratoconjunctivitis sicca, conjunctivitis (including pseudomembrane formation and cicatrization), keratitis and uveitis. Chronic GVHD may induce T cell infiltration of lacrimal glands, resembling collagen vascular disease histologically and resulting in stasis of secretions without inflammation. Systemic immunosuppression may be required while ocular surface disease may be treated with tear film supplements, topical steroids or topical cyclosporin.⁵ Other causes of ocular surface disease include the original pathology, treatments (such as drugs and radiation for myeloablation and immunosuppression) and infections including viruses.

EBV infects 90% of humans, manifesting as infectious mononucleosis and resulting in lifelong latent infection of B lymphocytes.⁶ EBV may play a role in the pathogenesis of Sjögren syndrome via the induction of IL-12 expression.⁷ Infected B cells can undergo transformation and proliferation, but in immunocompetent hosts this is usually suppressed by EBV-specific cytotoxic T lymphocytes. After bone marrow transplantation EBV may cause post-transplant lymphoproliferative disorder (PTLD) which may progress to lymphoma.⁸ Risk factors include a mismatched donor and a diagnosis of primary immunodeficiency, as in this case. In this unit, regular surveillance for opportunistic infection after bone marrow transplant includes PCR monitoring of EBV, cytomegalovirus and adenovirus DNA. Ganciclovir and foscarnet are active against replicating EBV but not against EBV-transformed B cells. Rituximab is a rituxin-conjugated, human-mouse chimeric monoclonal antibody against CD20, a B cell antigen. In direct contrast to GVHD, treatment of EBV and PTLD may require reduction of immunosuppression. PTLD may cause uveal infiltration resulting in cells in both aqueous and vitreous with iris or choroidal masses,⁹ none of which were exhibited by our patient.

The clinical features of this case suggest dacryoadenitis while the rapid rise in plasma EBV DNA suggests this virus as the most likely cause. Our patient had minimal conjunctivitis although her inflammatory response may have been modified by her immunodeficiency. The finding of EBV DNA in tears may simply reflect her high systemic viral load; EBV has

previously been isolated from tears of patients with HIV but has not been correlated with clinical eye disease.¹⁰ Although this patient had autoimmune pathology, primary Sjögren syndrome was unlikely as no specific autoantibodies were found. Her antibody production, however, is likely to be compromised following her recent bone marrow transplant.

In this case the high EBV viral load helped to differentiate the condition from GVHD and, in view of the risk of PTLD and the availability of specific treatment, EBV should be considered in any immunodeficient patient presenting with painful, red eyes.

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