Sir,
The use of Campath in severe peripheral ulcerative keratitis associated with Wegener's granulomatosis

Wegener's granulomatosis (WG) is a rare multisystem granulomatous disease. The ocular presentations of WG include episcleritis, scleritis, peripheral ulcerative keratitis (PUK), obstruction of the nasolacrimal duct, uveitis, and optic nerve involvement. Corneal melting has been reported in 11–16% of patients with WG.¹

Case report

A 43-year-old woman presented to our clinic with severe PUK and systemic features of WG. She had multiple negative C and P-ANCA. Clinically, she had a flattened nasal bridge and bilateral dacryocystorhinostomies and on ENT assessment was found to have a septal perforation. A conjunctival biopsy showed a granulomatous inflammation with the histological appearance of WG.

The PUK decompensated and her cornea perforated while on methotrexate 20 mg weekly. Previously she was on cyclophosphamide but had to discontinue as she developed haemorrhagic cystitis. At the time of perforation, she was admitted and treated with pulse intravenous (i.v.) methylprednisone 500 mg/day and eventually required a patch graft as her perforation and thinning worsened. She was discharged on mycophenolate mofetil 500 mg b.d. and prednisone 40 mg o.d. 3 days later she was reviewed in the outpatient clinic with further corneal melting at the edge of the patch graft (Figure 1). She was commenced on i.v. methylprednisone 1 g o.d., but after 3 days the PUK worsened. It was decided to start her on a course of Campath 10 mg i.v. daily (four doses). Her PUK stabilized over the ensuing months and she was kept on a maintenance dose of mycophenolate sodium 1440 mg

Figure 1 Active peripheral ulcerative keratitis (PUK), showing corneal thinning, at the edge of the corneal patch graft (arrow).

b.d. and a tapering dose of prednisone to 10 mg o.d., and 18 months after Campath therapy the PUK has remained in remission.

Comments

WG is a rare disease that usually affects patients in their fourth to sixth decades. It most commonly occurs in Caucasians with a male preponderance. The American College of Rheumatology stipulates that the presence of two or more of the following four criteria is associated with a sensitivity of 88% and a specificity of 92% for WG: abnormal urinary sediment, abnormal chest X-ray, oral ulcers or nasal discharge, and granulomatous inflammation.² A negative ANCA does not exclude the diagnosis of WG. Pathologically, the finding of a necrotizing granuloma confirms the diagnosis of WG.

Campath is indicated for the treatment of B-cell chronic lymphocytic leukaemia in patients who have been treated with alkylating agents and who have failed fludarabine therapy. Campath has also demonstrated a transient benefit in other conditions such as rheumatoid arthritis and multiple sclerosis.³ Recently, it has been shown to be useful in refractory ocular disease such as non-infectious retinal vasculitis, sympathetic ophthalmia, Behçet's disease as well as recurrent corneal graft rejection.^{4,5} Campath is a humanized anti-T-cell monoclonal antibody that recognizes the pan lymphocyte antigen CD52, inducing an antigen-specific unresponsiveness and immunoregulation.⁶ The main complications of Campath treatment, usually during the first i.v. infusion, include fever, rigor, nausea, vomiting, and hypotension responsive to steroids. Immunosuppression resulting from normal B- and T-lymphocyte depletion is frequent, resulting in an increased risk for opportunistic infections.⁷ There are many and varied immunosuppressive agents used in the treatment of PUK that usually have good effect. Cyclophosphamide, methotrexate, azathioprine, chlorambucil, and azathioprine have been utilized with good success.⁸ Cyclophosphamide is the drug of choice for almost all PUK associated with connective tissue disorders. Methotrexate, azathioprine, cyclosporine A, and chlorambucil have been found to be effective.⁸ To our knowledge, Campath has not been described as a treatment for PUK associated with WG.

References

- 1 Bullen CL, Liesegang TJ, Macdonald TJ, DeRemee RA. Ocular complications of Wegener's granulomatosis. *Ophthalmology* 1983; **90**: 279–290.
- 2 Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP. The American College of Rheumatology 1990

- criteria for the classification of Wegener's granulomatosis. *Arthritis Rheum* 1990; **33**: 1101.
- 3 Isaacs JD, Watts RA, Hazleman BL, Hale G, Keogan MT, Cobbold SP *et al*. Humanised monoclonal antibody therapy for rheumatoid arthritis. *Lancet* 1992; **340**: 748–752.
 - 4 Dick AD, Meyer P, James T, Forrester JV, Hale G, Waldmann H *et al*. Campath-1H therapy in refractory ocular inflammatory disease. *Br J Ophthalmol* 2000; **84**: 107–109.
 - 5 Newman DK, Isaacs JD, Watson PG, Meyer PA, Hale G, Waldmann H. Prevention of immune-mediated corneal graft destruction with the anti-lymphocyte monoclonal antibody, Campath-1H. *Eye* 1995; **9**: 564–569.
 - 6 Waldmann H, Cobbold S. How do monoclonal antibodies induce tolerance? A role for infectious tolerance? *Annu Rev Immunol* 1998; **16**: 619–644.
 - 7 Pangalis GA, Dimopoulou MN, Angelopoulou MK, Tsekouras C, Vassilakopoulos TP, Vaiopoulos G *et al*. Campath-1H (anti-CD52) monoclonal antibody therapy in lymphoproliferative disorders. *Med Oncol* 2001; **18**(2): 99–107.
 - 8 Tauber J, Sainz de la Maza M, Hoang-Xuan T, Foster CS. An analysis of therapeutic decision making regarding immunosuppressive chemotherapy for peripheral ulcerative keratitis. *Cornea* 1990; **9**(1): 66–73.

MS Wertheim, AH Ross and DM Tole

Department of Ophthalmology, Bristol Eye Hospital, Lower Maudlin Street, Bristol, Avon BS1 2LX, UK

Correspondence: MS Wertheim,
Tel: +44 117 9230000;
Fax: +44 117 9233000.
E-mail: drwertie@hotmail.com

Eye (2006) **20**, 1453–1454. doi:10.1038/sj.eye.6702330;
published online 7 April 2006

Sir,
An unusual late complication of orbital floor fracture repair

We read with interest the recent article by Vose *et al*¹ about an unusual late complication of orbital fracture. As mentioned in their article, complications associated with alloplastic implants are rare.² When complications occur years after the initial surgery, the new symptoms may not be immediately associated with the previous orbital floor fracture repair. We report here another case of unusual late complication of orbital floor fracture repaired 25 years ago.

Case report

A 69-year-old, previously fit female presented to the eye casualty with recurrent episodes of right lower lid

swelling with purulent discharge (Figure 1). Visual acuities were normal, with no evidence of proptosis, chemosis, or ocular motility disturbance. She was treated as preseptal cellulitis with oral antibiotics. With each course of antibiotics, the cellulitis subsided but subsequently recurred with purulent discharge. After multiple casualty visits over a 6-month period, the possibility of a fistula was raised and referred to the oculoplastic clinic. On further questioning, the patient recalled right orbital floor fracture sustained during a road traffic accident 25 years ago, which was repaired with a silastic implant.

A computed tomography scan of the orbits and sinuses showed persistent defect in the right orbital floor. There was a displaced curvilinear intermediate-density structure lying freely in the right maxillary sinus, suggesting silastic implant. There was also complete opacification of the right maxillary sinus (Figure 2).

Figure 1 Right lower lid fistula.

Figure 2 Coronal view of CT scan orbits and sinuses showing a defect in the right orbital floor and a curvilinear opacity of intermediate density lying freely in the right maxillary sinus. There is complete opacification of the maxillary sinus.