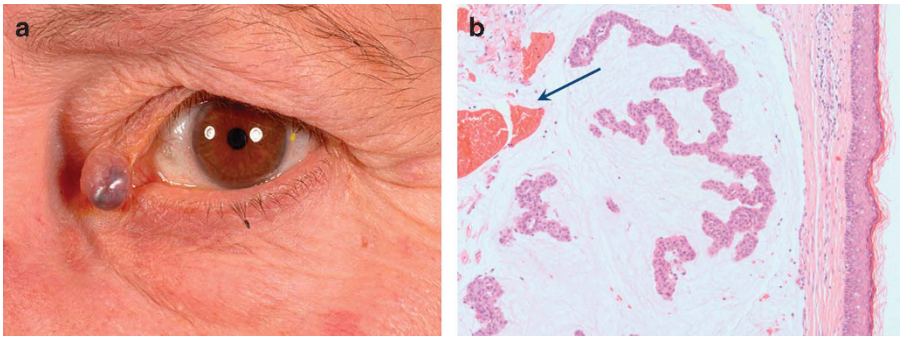

Figure 1 (a) Clinical appearance of the cystic lesion on the medial aspect of the left upper lid with telangiectatic vessels on the surface and localised purple–blue discolouration inferiorly. (b) Subcutaneous cyst lined predominantly by papillary apocrine and conventional double-layered hidrocystoma epithelium, and containing small lakes of blood (arrow) within the luminal basophilic myxoid material (H&E ×10).

dome-shaped, thin-walled cysts. They are usually translucent, skin-coloured lesions, but are occasionally lightly or deeply pigmented. Histologically, they are characterised by a unilocular or multilocular cystic space in the dermis with a lining consisting of a double layer of epithelial cells.[1] Although there is a single case report of a giant apocrine hidrocystoma presenting as a tense haematoma of the scalp,[3] to the best of our knowledge there are no published reports of eyelid hidrocystomas presenting with spontaneous bleeding within the lesion. A possible predisposing factor for intralesional bleeding in our case was regular use of clopidogrel, an antiplatelet agent that has been associated with spontaneous haematomas at other sites.[4,5]

Conflict of interest

The authors declare no conflict of interest.

References

1 Sarabi K, Khachemoune A. Hidrocystomas—a brief review. *MedGenMed* 2006; **8**: 57.
2 Buckel TB, Helm KF, Ioffreda MD. Cystic basal cell carcinoma or hidrocytoma? The use of an excisional biopsy in a histopathologically challenging case. *Am J Dermatopathol* 2004; **26**: 67–69.
3 El Demellawy D, Babay S, Elkhawaga S, Alowami S. A brief report of a rare case of giant apocrine hidrocystoma presenting as a scalp hematoma. *Pol J Pathol* 2011; **62**: 116–117.
4 Ozlu T, Ozlu MF, Ayhan A. Spontaneous ovarian hematoma in a patient treated with clopidogrel. *Int J Gynaecol Obstet* 2008; **102**: 293–294.
5 Ruiz-Tovar J, Aguilera A, Sanchez-Picot S, Rojo R, Garcia-Villanueva A. [Spontaneous haematoma of the psoas muscle with femoral neuropathy associated with antiplatelet treatment with clopidogrel: is surgical decompression indicated?]. *Cir Esp* 2010; **88**: 335–336.

E Novitskaya[1], C Rene[1] and A Dean[2]

[1]Ophthalmology Department, Addenbrooke's Hospital, Cambridge, UK

[2]Department of Histopathology, Addenbrooke's Hospital, Cambridge, UK
E-mail: elena.novitskaya@googlemail.com

Eye (2013) **27,** 782–783; doi:10.1038/eye.2013.57; published online 12 April 2013

Sir,

Purtscher retinopathies: Are we aiming at the wrong target?

We welcome, and read with interest, the systematic review of Purtscher retinopathies by Miguel *et al*,[1] who described the systemic aetiologies underlying Purtscher's, the clinical features, the efficacy of corticosteroid therapy, and visual outcomes.

The discovery of effective therapies for Purtscher-spectrum retinopathies requires identification of the mechanism underlying Purtscher-related microvasculopathy. Despite the sporadic treatment of Purtscher's with corticosteroids, only 8 of the 17 Purtscher-associated aetiologies identified by the authors are primary inflammatory disorders, 5 of which necessitate systemic steroid therapy (Table 1). Ocular inflammation is not a feature of Purtscher retinopathies.

We observed that 14 Purtscher-associated aetiologies were recognized precipitants of thrombotic microangiopathy (TMA) (Table 1)—a systemic syndrome that triggers widespread microvascular thrombosis in response to a range of primary disorders.[2] Ocular features of Purtscher's include cotton wool spots, retinal haemorrhages, Purtscher-flecken, and arteriolar obstruction with late leakage on fluorescein angiography.[1] Thrombotic microangiopathy may account for all features through terminal arteriole and capillary hyaline thrombosis—pathological hallmarks identified in patients as early as 1924.[2]

The molecular pathophysiology of TMA is heterogeneous, varying according to systemic aetiology. TMA involves a complex, interdependent dysregulation of haemostatic, thrombotic, and complement cascades with endothelial dysfunction and inflammation—

Table 1 Causes of Purtscher retinopathies, inflammation, and thrombotic microangiopathy

Cause of Purtscher's spectrum retinopathy identified by Miguel et al[1]	*Cause of thrombotic microangiopathy (TMA)*	*Primary inflammatory disorder*	*Steroids used to treat the underlying disorder*	*Treatment*
Trauma	Yes	Inflammatory component	No	Supportive Fresh frozen plasma Protein C concentrate Blood/platelet transfusion
Acute pancreatitis[a]	Yes	Yes	No	Supportive Management of complications
Valsalva manoeuvre	No	No	No	Supportive
Thrombotic thrombocytopenic purpura	Yes	Inflammatory component	Adjunctive In refractory cases	Supportive Fresh frozen plasma exchange +/− steroids Haemodialysis High-dose steroids
Haemolytic uraemic syndrome	Yes	Inflammatory component	Adjunctive In refractory cases	Supportive Fresh frozen plasma exchange +/− steroids Haemodialysis Plasmapheresis Eculizumab[b] High-dose steroids
Hepatitis C-related cryoglobulinaemia	Yes	Yes	Adjunctive	Treatment of HCV with interferon/ribavirin Steroids Cyclophosphamide Azathioprine Plasmapheresis
Pregnancy-related HELLP syndrome	Yes	Inflammatory component	No evidence	Delivery of fetus Magnesium sulphate Transfusion Fresh frozen plasma
Lupus	Yes	Yes	Yes	Steroids Mycophenolate mofetil/ cyclophosphamide
Retrobulbar anaesthesia	No	No	No	Supportive
Pancreatic carcinoma	Yes	No	No	Surgery +/− chemotherapy/radiotherapy
TMA following chemotherapy	Yes	Inflammatory component	No evidence	Supportive Drug cessation
Necrotizing vasculitis with lung cancer	Yes	Yes	Yes	Steroids Immunosuppressive agents
Acute allograft rejection	Yes	Yes	Yes	Steroids Immunosuppressive agents
Renal scleroderma	Yes	Yes	Yes	Steroids Immunosuppressive agents
Nephrotic syndrome	Yes	Inflammatory component	Yes	Steroids Cyclophosphamide/ levamisole
Multiple myeloma	Yes	No	Adjunctive	Chemotherapy +/− steroids
Coil embolization of carotid aneurysm	No	No	No	Supportive

[a] Corticosteroids are a recognized cause of acute pancreatitis.
[b] Monoclonal antibody raised against complement proteins.

corticosteroids address only the inflammatory component. Research efforts have identified decreased activity of ADAMTS-13, a von Willebrand clotting factor, in association with TTP[3] and HELLP syndrome[4] and antibodies against CD36, the ADAMTS-13 endothelial receptor in haemolytic uraemic syndrome. Novel molecules offer fresh therapeutic targets;[2] recent reports suggest success in depleting the ADAMTS-13 antibody in TTP with the novel biologic agent Bortezomib.[5]

The lack of efficacy demonstrated with corticosteroids is logical given the diverse aetiologies of Purtscher's, which may demonstrate a primary inflammatory trigger, such as acute pancreatitis, but later perpetuate through consumptive thrombocytopenia, coagulopathy, and/or complement activation associated with TMA. These secondary processes are unlikely to be steroid responsive.

We suggest consideration of the hypothesis that Purtscher retinopathies are manifestations of thrombotic microangiopathy. Research into the molecular pathogenesis of TMAs with identification of novel molecules in physiological and pathological cascades—such as ADAMTS-13—may offer more promising therapeutic targets for future patients with Purtscher retinopathies.

Conflict of interest

The authors declare no conflict of interest.

References

1 Miguel AI, Henriques F, Azevedo LF, Loureiro AJ, Maberley DA. Systematic review of Purtscher's and Purtscher-like retinopathies. *Eye (Lond)* 2013; **27**(1): 1–13.

2 Chapman K, Seldon M, Richards R. Thrombotic microangiopathies, thrombotic thrombocytopenic purpura, and ADAMTS-13. *Semin Thromb Hemost* 2012; **38**(1): 47–54.
3 Bettoni G, Palla R, Valsecchi C, Consonni D, Lotta LA, Trisolini SM *et al.* ADAMTS-13 activity and autoantibodies classes and subclasses as prognostic predictors in acquired thrombotic thrombocytopenic purpura. *J Thromb Haemost* 2012; **10**(8): 1556–1565.
4 Hulstein JJ, van Runnard Heimel PJ, Franx A, Lenting PJ, Bruinse HW, Silence K *et al.* Acute activation of the endothelium results in increased levels of active von Willebrand factor in hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome. *J Thromb Haemost* 2006; **4**(12): 2569–2575.
5 Shortt J, Oh DH, Opat SS. ADAMTS13 antibody depletion by bortezomib in thrombotic thrombocytopenic purpura. *N Engl J Med* 2013; **368**(1): 90–92.

IH Yusuf and S-L Watson

The Royal Berkshire Hospital NHS Foundation Trust, Reading, UK
E-mail: imranyusuf@doctors.org.uk

Eye (2013) **27,** 783–785; doi:10.1038/eye.2013.47; published online 5 April 2013

Sir,

Response to Yusuf and Watson

We thank Yusuf and Watson[1] for their insightful comments regarding our recent publication.[2] Indeed, ocular inflammation is not always evident in Purtscher and Purtscher-like retinopathies (PuR). The hypothesis of a common pathological molecular pathway between PuR and thrombotic microangiopathy (TMA) deserves further exploration.

Both PuR and TMA share a mechanism of microvascular occlusion, which has been suggested for PuR by many authors in the past years[3,4] and include arteriolar precapillary occlusion and microvascular infarct of the retinal nerve fiber layer. Both include complement activation[5] and capillary endothelial damage.[3] However, there is no current evidence of a common pathway in some pathological mechanisms of PuR, such as microembolization,[3] fat emboli[6] or a rheological event[7] that results in vascular endothelial dysregulation (as recently suggested as an alternative etiology).

These issues must be addressed in further studies to identify and characterize the etiology and mechanisms of PuR. Afterwards, new molecular targets can be explored for the treatment of Purtscher and Purtscher-like retinopathies.

Conflict of interest

The authors declare no conflict of interest.

References

1 Yusuf IH, Watson S-L. Purtscher retinopathies: Are we aiming at the wrong target? *Eye* 2013; **27**(6): 783–785
2 Miguel AI, Henriques F, Azevedo LF, Loureiro AJ, Maberley DA. Systematic review of Purtscher's and Purtscher-like retinopathies. *Eye (Lond)* 2013; **27**(1): 1–13.
3 Kincaid MC, Green WR, Knox DL, Mohler C. A clinicopathological case report of retinopathy of pancreatitis. *Br J Ophthalmol* 1992; **66**(4): 219–226.
4 Agrawal A, McKibbin M. Purtscher's retinopathies: a review. *Surv Ophthalmol* 2006; **51**: 129–136.
5 Craddock PR, Hammerschmidt D, White JG, Dalmosso AP, Jacob HS. Complement (C5-a)-induced granulocyte aggregation in vitro. *J Clin Invest* 1977; **60**(1): 260–264.
6 Chuang EL, Miller FS, Kalina RE. Retinal lesions following long bone fractures. *Ophthalmology* 1985; **92**: 370–374.
7 Harrison TJ, Abbasi CO, Khraishi TA. Purtscher retinopathy: an alternative etiology supported by computer fluid dynamic simulations. *Invest Ophthalmol Vis Sci* 2011; **52**(11): 8102–8107.

AIM Miguel[1,2], F Henriques[1], LFR Azevedo[2], AJR Loureiro[1] and DAL Maberley[3]

[1]Ophthalmology Department, Central University Hospital of Coimbra, Coimbra, Portugal
[2]Center for Research in Health Technologies and Information Systems (CINTESIS) and Department of Health Information and Decision Sciences, Faculty of Medicine, University of Porto, Porto, Portugal
[3]Retinal Division, Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, British Columbia, Canada
E-mail: myworld_ana@hotmail.com

Eye (2013) **27,** 785; doi:10.1038/eye.2013.48; published online 5 April 2013