Retinal vein occlusion disease and platelet activation: Will antiplatelet therapy be a promising therapeutic strategy for patients with retinal vein occlusion disease in the future?

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Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy and represents an important cause of permanent visual loss (1). The prevalence of RVO has been reported to be between 0.7% and 1.6% and increases with age (1). Overall, 90% of patients who develop vein occlusion disease are over 50 years of age (2). Retinal vessels are affected to a different extent, from central retinal vein occlusion (CRVO), to hemicentral retinal vein occlusion (HCRVO) and branch retinal vein occlusion (BRVO) (3). The precise mechanism leading to thrombosis in RVO has not been clearly elucidated. The most frequent site of occlusion is the tract of the central retinal vein passing through the lamina cribrosa (3). Several reasons have been discussed for this localisation. Collagen tissue of the lamina cribrosa becomes thicker and stiff with age causing compression of the vascular wall, and degenerative processes of the central retinal artery with positive arterial remodelling may cause compression of the adjacent venous wall resulting in the formation of an endoluminal thrombus (3). Others favour the hypothesis that open-angle glaucoma predisposes to RVO due to increased intra-ocular pressure and compromised venous outflow (4).

Many of the acquired and inherited risk factors and conditions associated with deep venous thrombosis have been sought in subjects with RVO. Over the last years literature has accumulated on the possible role of different haemostatic factors in the pathogenesis of RVO. Some studies state an association between thrombophilic risk factors such as deficiency of antithrombin, protein S or protein C, elevated levels of PAI-1, activated protein C resistance, different polymorphisms of the prothrombin gene or of the PAI-1 gene, whereas other studies do not (5). Most of these data are predominantly based on retrospective retrieval of information from case records with small sample sizes. Prospective randomized studies on this subject, however, are missing. One meta-analysis (5) on this issue shows that there is only evidence for an association between hyperhomocysteinemia and anticardiolipin antibodies, factors that are known as risk factors for venous thrombosis as well as for arterial thrombotic disease. The minor effect of the factor V Leiden mutation and the protrombin gene mutation (risk factors for venous thrombosis only) suggest that atherosclerosis might be the more important condition in the development of RVO (5). This hypothesis is supported by other studies showing an association between RVO and classical risk factors such as arterial hypertension, diabetes mellitus, hypercholesterolemia and hyperhomocysteinemia (6). The anatomy of retinal arteries and veins could be an explanation for this. RVO occurs at crossing sites where the retinal artery is passing anterior to the vein. During systemic atherosclerotic disease the retinal artery could thicken and hence cause compression of adjacent veins, because artery and vein are confined within a common advential sheath. Platelets play a pivotal role in atherosclerotic disease, but the role of platelets in the pathogenesis of RVO has been poorly evaluated so far.

In this issue of Thrombosis and Haemostasis Leoncini et al. (7) (see article beginning page 218) studied platelet response to collagen and signal transduction steps involved in platelet activation in a selected group of patients (n=38) with RVO. In resting and activated platelets isolated from these patients p72syk phosphorylation, phospholipase cγ2 phosphorylation, protein kinase C activation, intracellular calcium levels and nitric oxide (NO) formation were measured. The study group consisted of 18 patients with CRVO, 20 patients with BRVO and a control group comprising 40 age-matched healthy subjects. Platelets derived from patients with CRVO/BRVO were more responsive to collagen in comparison to the healthy controls in regard to phosphorylation of p72syk, activation of phospholipase cγ2 and protein kinase C. Furthermore, platelets from RVO patients showed enhanced rise in intracellular calcium and less formation of the antithrombotic mediator NO than healthy control subjects. Thus, the authors convincingly show that the increased platelet response to collagen might contribute substantially to thrombogenesis in RVO patients.

The idea that activated platelets are involved in the pathogenesis of RVO is not entirely new. There have been a few studies performed focusing on platelet aggregation and RVO. Watson et
References