Progestogen and retinopathy due to stasis in the central retinal vein

Sir,
A 32-year-old lady presented with a one-day history of cloudy vision in her left eye on awakening. She was otherwise a healthy nonsmoker with no significant ophthalmic or medical history. She took no regular medication. However, on the previous morning she had taken 15 mg of Utovlan (norethisterone) as prescribed by her general practitioner in order to postpone menstruation for her wedding.

On examination, visual acuity was 6/5 in both eyes and there was no afferent pupillary defect. Anterior segments and intraocular pressures were normal. Dilated fundoscopy revealed retinopathy due to stasis in the central retinal vein [Figure 1], which was confirmed by fluorescein angiography [Figure 2]. There was no abnormality in the right eye.

Further investigations failed to identify any underlying risk factors. Blood pressure was 117/76 mmHg, pulse 72/min in sinus rhythm. Full blood count, plasma glucose, urea and electrolytes, serum immunoglobulin levels, hematocrit, erythrocyte sedimentation rate, C reactive protein, serum angiotensin converting enzyme, fasting lipid and homocysteine levels were all within their normal ranges. Antinuclear antibody, lupus anticoagulant and rheumatoid factor tests were negative. Factor V Leiden and Factor II (prothrombin) mutations were not detected and anti-phospholipid antibody and activated protein C resistance assays were within normal limits.

She was prescribed 75 mg aspirin daily and her fundal appearance
conclusive but it appears that they too may contribute to thrombogenesis. The type of progestogen used in the COC modifies the vascular event risk.\footnote{Gomes MP, Deitcher SR. Risk of venous thromboembolic disease associated with hormonal contraceptives and hormone replacement therapy: A clinical review. Arch Intern Med 2004;164:1965-76.} Furthermore, synthetic progestogens have been recorded to cause endothelial disruption, platelet activation and clot formation. This effect is not seen with natural progestogens or estrogens.\footnote{Lake SR, Vernon SA. Emergency contraception and retinal vein thrombosis. Br J Ophthalmol 1999;83:630-1.} A case of retinal arteriolar occlusion has been reported after high-dose progesterone only therapy.\footnote{Thomas T, Rhodin J, Clark L, Garces A. Progestins initiate adverse events of menopausal estrogen therapy. Climacteric 2003;6:293-301.}

To our knowledge this case represents the first report of retinopathy due to stasis in the central retinal vein in association with the use of progestogens in isolation. To assess the probability of Utovlan causing a retinopathy due to stasis in the central retinal vein the Naranjo algorithm was used. This scale suggests that there is a ‘probable’ probability that Utovlan caused this adverse reaction.\footnote{Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, \textit{et al.} A method for estimating the probability of adverse drug reactions. Clin Pharm Ther 1981;30:239-45.} This episode was reported as an adverse drug reaction to the Committee on Safety of Medicines who have no other recorded cases. Extensive investigation failed to identify any alternative cause. The relatively high dose of progestogen necessary for the purpose of delaying menstruation compared with the level in the COC or progestogen only pill is notable. While it is possible that the association in this case may be coincidental rather than causative in nature, it would seem prudent to consider the risks of venous thrombosis before prescribing any sex hormone.

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