# **Ophthaproblem**

## **Answer to Ophthaproblem** continued from page 1303

## 4. Nonproliferative diabetic retinopathy

Diabetic retinopathy (DR) is a leading cause of vision loss in working-aged individuals in Canada. 1,2 Indeed, some estimates suggest that retinopathy prevalence rates are as high as 40% in patients with diabetes.<sup>2</sup> As symptoms are not exhibited in the early stages of DR, most patients are unaware of any signs of retinopathy. This underscores the need for routine screening of diabetes patients with dilated fundoscopic examinations, thereby allowing the detection of retinopathy at its early stages and the timely initiation of treatment aimed at preventing vision loss. Unfortunately, diabetic screening programs have not been efficiently implemented and many patients do not benefit from the screening recommendations of current clinical guidelines.3

The risk of developing DR is directly related to the adequacy of diabetes control and how long a patient has had diabetes. For example, at 5, 10, and 15 years of disease duration, 25%, 60%, and 80% of patients with type 1 diabetes will develop retinopathy, respectively.4 For type 2 diabetes patients, 40% taking insulin and 24% not taking insulin will have retinopathy at 5 years, increasing to 84% and 53%, respectively, at 19 years. 5 Poor glycemic control, hypertension, smoking, hyperlipidemia, anemia, and nephropathy are all associated with DR progression.6

Diabetic retinopathy is diagnosed clinically with dilated fundoscopic examination and is categorized into either nonproliferative or proliferative types. There are several features of nonproliferative retinopathy. Microaneurysms are believed to be the first sign of DR and occur in retinal capillaries, in areas where vascular endothelial cells lose pericytes. Intraretinal hemorrhages occur when microaneurysms, capillaries, and venules rupture (Figure 1). Hard exudates refer to the waxy, yellow depositions typically seen in the macular area (Figure 1). These exudates represent the accumulation of serum lipoprotein extravasated from dysfunctional blood vessels. Such dysfunctional blood vessels are also the cause of macular edema, which in turn leads to vision loss; in fact, most cases of vision loss in patients with DR are attributed to macular edema.7 Macular edema is more common and usually more severe in patients with type 2 diabetes, and can be detected with careful fundoscopy or by using ocular imaging devices such as optical coherence tomography. Optical coherence tomography has emerged as a very important tool in diagnostics, as well as in monitoring response to treatment.

Another feature of nonproliferative retinopathy is cotton-wool spots. These lesions tend to occur in more advanced nonproliferative retinopathy and represent infarction of the nerve fibre layer of the retina due to occlusion of retinal arterioles. Finally, intraretinal microvascular anomalies refer to abnormalities within capillaries that occur in areas of retinal ischemia. Proliferative retinopathy refers to the stage of retinopathy in which neovascularization occurs on the optic disk or elsewhere

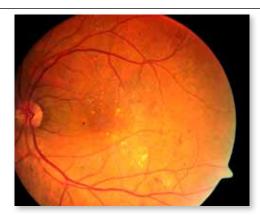


Figure 1. Colour fundus photograph of the left eye showing some characteristic features of nonproliferative diabetic retinopathy, including microaneurysms, hard exudates, and intraretinal hemorrhages

in the retina owing to the presence of vasoproliferative factors, which are released in response to retinal ischemia. These new vessels grow along the anterior portion of the retina, and might cause substantial visual loss by inducing preretinal or vitreous hemorrhage, or worse, tractional retinal detachment.

The main causes of visual loss in DR include macular edema, macular ischemia, vitreous hemorrhage, and tractional retinal detachment.6 Fluorescein angiography is useful as an ancillary test for assessing the integrity of the retinal vasculature and can help guide therapeutic decision making.

### Management

Patients with nonproliferative retinopathy should be monitored with regular dilated fundoscopic examinations.1 The 2008 Canadian Diabetes Association clinical practice guidelines suggest screening patients with type 1 diabetes within 5 years of diagnosis, while patients with type 2 diabetes should be referred at the time of diagnosis (as nearly 30% will already have DR).2 The frequency of follow-up examinations depends on the severity of the retinopathy at diagnosis. Typically, patients with early disease will require annual examinations while those with more advanced disease will require closer followup. Because pregnancy can exacerbate DR, women with diabetes should be assessed before conception and again during the first trimester. Teleophthalmology mobile screening programs can help screen patients who do not have ready access to eye physicians.3

Strict blood glucose and blood pressure control remain the most important strategies for decreasing both the risk of developing and the progression of DR. The Diabetes Control and Complications Trial showed that intensive blood glucose control reduced the incidence of DR by 76% when compared with standard blood glucose control in patients with type 1 diabetes after 7 years.4 The UK Prospective Diabetes Study

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showed similar results in patients with type 2 diabetes, with the relative risk of DR progression being reduced by 21% in 12 years in those with intensive blood glucose control compared with the conventional treatment group.5 It also showed that blood pressure control was associated with a nearly 50% reduction in relative risk of substantial vision loss at 8 years.

For patients with clinically meaningful macular edema, laser treatment can reduce the risk of moderate visual loss by 50%.8 The laser treatment is directed toward leaking microaneurysms and areas of retinal thickening. Clinicians often use pharmacologic agents delivered via intravitreal injections in concert with laser therapy to help reduce retinal edema. These agents include steroids, such as triamcinolone acetonide, and antivascular endothelial growth factor (anti-VEGF) agents, such as bevacizumab and ranibizumab.9 These agents can confer substantial reductions in retinal thickening and help speed visual recovery; a recent randomized clinical trial has shown that superior outcomes are attained when anti-VEGF agents in particular are used in combination with deferred laser in the treatment of diabetic macular edema.10

Panretinal photocoagulation is a laser treatment typically performed for proliferative retinopathy and can reduce the risk of severe vision loss by up to 50%.8 This type of laser treatment involves applying thermal laser burns to the retina, outside the macular region. It is purported that ischemic retina ablation reduces the ischemic drive, releasing vasoproliferative factors into the vitreous, which in turn causes neovascularization in the retina and subsequent ocular complications. The aforementioned anti-VEGF agents can also be used in such a scenario; however, these agents are temporizing measures and laser treatment must be administered for long-term effect.9

Finally, vitrectomy is an important option in some cases of DR. It improves vision in patients with nonclearing vitreous hemorrhage and is required in patients with tractional diabetic retinal detachment.

### Recommendations

This patient should be referred to an ophthalmologist for a dilated fundoscopic examination. Optical coherence tomography and fluorescein angiography imaging might be recommended to more accurately characterize the extent and pattern of retinopathy present. Anti-vascular endothelial growth factor therapy in combination with focal or grid laser therapy might be necessary if there is evidence of centre-involved macular edema.<sup>10</sup> Panretinal photocoagulation is generally recommended if there is evidence of proliferative retinopathy. Surgery (ie, vitrectomy) is reserved for cases of nonclearing vitreous hemorrhage and tractional detachment.

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#### Competing interests

None declared

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