Retinal Manifestations of Diabetes Mellitus and Hypertension

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The ophthalmoscope (Figure 1), which was invented in 1850 by Hermann von Helmholtz, allowed for the clinical correlation of retinal findings with many systemic diseases, such as diabetes mellitus, hypertension, hyperlipidemia, thyroid disease, vascular disease, and systemic infections. Although ocular signs are not necessarily disease specific (eg, signs seen in hypertensive patients also appear in diabetic patients), early recognition of these signs can help prevent unnecessary vision loss. Additionally, these signs in combination can help the physician determine which systemic disease is responsible for the patient’s retinopathy. A comprehensive discussion of all systemic diseases with ocular manifestations is beyond the scope of this article. Hence, this review focuses on retinal findings associated with two of the most common diseases seen in primary care: diabetes mellitus and hypertension. A brief review of the technique for ocular examination with the ophthalmoscope also is included.

Ocular Examination

A systematic routine should be used when examining the eyes and surrounding tissues. Generally, it is best to examine the eyes in the following sequence: visual acuity, extraocular muscle function, visual field testing, and then finally ophthalmoscopy. For optimum retinal examination, a mydriatic agent is used to dilate the pupil. Both tropicamide 1% (Mydriacyl) and phenylephrine hydrochloride 2.5% (Mydfrin) dilate the pupils in approximately 30 minutes. Once the patient’s eyes are dilated, the ophthalmoscope is held approximately 12 to 15 cm away from the patient’s eye. For examining the patient’s right eye, the examiner holds the ophthalmoscope in close proximity to his or her own right eye using the right hand. For examining the patient’s left eye, the examiner uses the left hand and left eye. The examiner then moves in closer to the patient’s eye while adjusting the lens settings for optimal focus. The physician also should keep his or her nonexamining eye open during this procedure.

Diabetes Mellitus

Diabetes mellitus is the leading cause of new cases of blindness in middle-aged Americans. Timely detection and treatment of diabetic retinopathy can substantially reduce the likelihood of blindness. Approximately half of adult diabetics in the United States, however, do not receive yearly eye examinations.

Type 2 diabetes mellitus is more common than type 1 diabetes, and the prevalence of type 2 diabetes increases with age. Type 2 diabetes may remain undetected for a long time. It has been estimated that 5 to 10 years of sustained hyperglycemia are needed to develop retinal manifestations. A high degree of correlation exists between glycemic control as measured by glycosylated hemoglobin levels and presence of early retinopathic manifestations.

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changes. As a rule, retinopathy precedes nephropathy. Therefore, early detection of the ocular manifestations of diabetes (Table 1) is important.

The initial stage of retinal changes in the diabetic patient is called nonproliferative diabetic retinopathy and includes the appearance of dot and blot hemorrhages (which are caused by intraretinal blood) and/or microaneurysms (Figure 2). Microaneurysms are seen as scattered red spots in the retina caused by weakened arterioles and capillaries leading to outpouching of the vessel walls. Dot and blot hemorrhages represent blood in the retina. The differentiation between a microaneurysm and a dot and a blot hemorrhage is based on size and is somewhat subjective. Distinguishing between a dot and blot hemorrhage and microaneurysm on direct ophthalmoscopy may be difficult.

Several years may pass before other lesions, such as retinal hemorrhages and exudates, develop. Hard exudates caused by leakage of proteins and lipids from the damaged arterioles appear as small white or yellow areas with sharp margins, often with a glistening appearance on the retina (Figure 3). As the disease progresses further, retinal changes occur, including macular edema and cotton-wool spots (Figure 4). Cotton-wool spots result from microinfarctions of nerve fibers caused by focal ischemia after occlusion of terminal retinal arterioles occurs. These spots appear as white fluffy spots on the retina. Macular edema is the principal mechanism of visual loss in nonproliferative retinopathy. Macular edema results from leakage from microaneurysms.

Proliferative diabetic retinopathy is a late stage of disease and is characterized by neovascularization (ie, new blood vessel formation), which is a response to continued retinal ischemia. Neovascularization results in vision loss due to vitreous hemorrhages and retinal detachment.

**Table 1. Subdivisions and Characteristic Lesions of Diabetic Retinopathy**

<table>
<thead>
<tr>
<th>Nonproliferative retinopathy</th>
<th>Microaneurysms</th>
<th>Hemorrhages</th>
<th>Hard exudates</th>
<th>Cotton-wool spots</th>
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<tr>
<td>Proliferative retinopathy</td>
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<td>Macular edema</td>
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<td>Neovascularization</td>
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**Figure 1.** A drawing of Hermann von Helmholtz’s original ophthalmoscope. (Reprinted with permission from Ravin JG. Sesquicentennial of the ophthalmoscope. Arch Ophthalmol 1999;117:1636.)

**Figure 2.** The arrow indicates dot and blot hemorrhages. Hard exudates also are visible.

**Figure 3.** The arrow indicates hard exudates. Dot and blot hemorrhages also are visible.
HYPERTENSION

The funduscopic changes in the eye noted with hypertension were first described in 1898. Since that time, little has changed in the terminology describing these characteristic retinal abnormalities. These characteristic retinal changes included arteriolar narrowing, arteriovenous crossing changes, alterations of light reflexes on arterioles, cotton-wool spots, microaneurysms, retinal hemorrhages, retinal edema, and blurred disc margins.

The first and most widely used grading system for hypertensive retinopathy was proposed by Keith et al. The classification system consists of 4 grades as follows:

- Grade I: mild narrowing of the retinal arterioles
- Grade II: arteriovenous nicking (ie, venous compression at arteriovenous crossings) (Figure 5)
- Grade III: cotton-wool spots, hemorrhages (Figure 6), retinal edema
- Grade IV: optic disc edema (Figure 7)

A newer more simplified grading system was recently proposed and divides the features, according to
prognosis, into 2 categories: nonmalignant and malignant hypertension.15 Nonmalignant findings include arteriolar narrowing and arteriovenous nicking; malignant findings consist of hemorrhages, hard exudates, cotton-wool spots, and optic disc edema. Hard exudates in the macula would suggest diabetic retinopathy versus hypertensive retinopathy in which the hard exudates would more likely appear in the peripheral retinal around a macroaneurysm. Optic disc edema can be caused by other conditions (eg, increased intracranial pressure); however, the presence of cotton-wool spots is highly suggestive of malignant hypertension as the etiology of disc edema.16 In the case of malignant hypertension, optic disc edema is caused by ischemic optic neuropathy.16 Papilledema develops within days to weeks of increased blood pressure and resolves within weeks to months following lowering of blood pressure.

Retinal vascular abnormalities, such as arteriolar narrowing and arteriovenous nicking, are irreversible long-term markers of hypertension. These nonmalignant hypertensive retinal vascular changes persist long term even after successful antihypertensive therapy.18 Retinal vascular abnormalities are useful risk indicators for cerebrovascular disease and stroke.19

Early detection of malignant hypertension is essential in reducing the likelihood of permanent visual damage.20 Malignant hypertensive retinal changes such as papilledema, cotton-wool spots, and hemorrhages resolve if blood pressure is well controlled.18 Malignant hypertensive retinal changes are likely findings in patients in hypertensive crisis, which is an abrupt elevation in blood pressure with a systolic blood pressure of greater than 210 mm Hg and a diastolic blood pressure of more than 120 mm Hg.

Ischemic optic neuropathy is a common cause of visual loss. Hypertension is the most frequently reported underlying disease. Ischemic optic neuropathy is a direct complication of hypertension, which affects the small arterioles supplying the anterior part of the optic nerve. Patients with ischemic optic neuropathy frequently report blurred vision, and funduscopic examination reveals optic disc edema.

CONCLUSION

Hypertension and diabetes are commonly encountered systemic diseases in primary care. A thorough eye examination can uncover retinal manifestations of these disease processes and thus prevent further damage leading to visual impairment. A basic understanding of these common retinal manifestations is essential in primary care.

REFERENCES