Ophthalmologic Complications of Systemic Disease

Jean E. Klig, MD, FAAP

Division of Pediatric Emergency Medicine, Boston University School of Medicine, Boston Medical Center, 1 Boston Medical Center Place, Boston, MA 02118, USA

The human eye, as an organ, can offer critical clues to the presence of systemic illness. Ocular changes are common in the early course of many systemic infections and inflammatory diseases that may be diagnosed in the emergency department. A careful and thorough eye examination is paramount during routine evaluation in the emergency department because it can provide primary information on otherwise undetected systemic illness and corroborative data for known problems. This article reviews various ophthalmologic complications of systemic disease that can be detected by an emergency department provider, as well as key findings that can be discerned with specialty consultation.

Acquired syphilis

Infection with Treponema pallidum affects most organ systems if untreated. In fact, acquired syphilis was a common cause of ocular inflammation before the introduction of effective antimicrobial treatment. Although the prevalence of acquired syphilis has diminished overall in the post-antibiotic era, it still remains an important clinical entity [1]. Current worldwide estimates suggest the occurrence of approximately 12 million new cases of syphilis each year, 90% of which are in developing countries [1]. Rates of primary and secondary syphilis infection in the United States have risen markedly since 2000, primarily among male homosexuals. Although ocular syphilis is now rare overall, prolonged untreated syphilis-related ocular disease can produce destructive changes in the eye; therefore, clinical suspicion is vital to early intervention. If present, ocular syphilis will manifest during the second or third stages of clinical illness. A key triad that should prompt
clinical suspicion of syphilis infection is persistent headache, red eyes or eye pain, and an unexplained elevated erythrocyte sedimentation rate (ESR) [2].

There are no signs that are pathognomonic of ocular syphilis, and it can readily mimic other ocular disorders. Madarosis, or loss of the eyelashes or eyebrows, can occur. Uveitis is the most common eye finding [3], accounting for the red eyes or eye pain in the triad detailed previously. Eye involvement usually is evident beyond the primary stage of syphilis, but a primary chancre of the conjunctiva is possible [4]. Anterior segment eye findings that may be evident to the emergency department physician on direct and slit lamp examination include keratitis (interstitial or stromal) and iridocyclitis or anterior uveitis [1,4]. Prolonged syphilitic interstitial keratitis can result in closed angle glaucoma, which can be a presenting sign of the disease [5]. Acute iridocyclitis occurs in approximately 4% of patients with secondary syphilis, with bilateral involvement in approximately 50% of cases [4]. A red eye–type finding that the emergency department provider may note is dilated iris capillaries, or roseolae, often in early iridocyclitis. Roseolae may progress to discrete papules and then to larger yellow nodules [4].

Posterior segment ocular changes in syphilis include chorioretinitis (unifocal, multifocal, or neuroretinitis), posterior uveitis, vaso-occlusive retinal changes, and retinal detachment [1,4]. The emergency department provider is most likely to detect associated visual changes and eye redness or ocular pain on examination, although it may be possible to discern inflammatory changes to the fundus. Neuro-ophthalmologic changes that may be appreciated are an Argyll Robertson pupil (unilateral or bilateral small pupils that accommodate to near vision but do not react to light), third and sixth cranial nerve palsies, and visual field defects from brain involvement. Ophthalmologic consultation is important in cases of suspected ocular syphilis, because many of the changes that occur are reversible if detected and monitored during treatment. In addition to a more extensive examination of the fundus that is performed by an ophthalmologist, additional testing via MRI, angiography, and other modalities may be performed. Ophthalmologic consultation is critical in HIV patients with evidence of ocular syphilis because more severe eye disease and greater rates of complication are common [4]. In turn, HIV testing should be considered in patients with suspected ocular syphilis given the common risk factors for both diseases [3].

**Varicella-zoster virus infection**

Varicella and herpes zoster infections are due to the same human herpes virus 3, also known as varicella-zoster virus (VZV). Immunization against varicella has diminished the incidence and severity of the disease overall; however, primary infections and reactivation as herpes zoster continue to occur in persons who are un-immunized or immunocompromised, or as “break-through disease” in vaccinated patients [6]. Ocular manifestations of primary varicella infection are generally uncommon. Nonetheless, the
following have been reported as isolated or combined findings during primary varicella illness: lid, conjunctival, and corneal vesicles; iridocyclitis; glaucoma; cataracts; chorioretinitis; optic neuritis or atrophy; and internal ophthalmoplegia [7]. The common viral prodrome and typical skin lesions of varicella infection will precede or accompany any ocular involvement. Ocular changes can also be seen as a late complication of primary varicella illness [7].

Herpes zoster infection (shingles) results from reactivation of latent VZV in sensory nerve ganglia, with migration down the nerves to the related dermatome where severe pain and characteristic skin lesions result [8]. Risk factors for herpes zoster include advanced age, poor nutrition, immune compromise, fatigue, and physical or emotional stress [9]. The lifetime risk of herpes zoster is about 10% to 20% overall; approximately 10% to 25% of cases involve the ophthalmic division of the trigeminal nerve, which is known as herpes zoster ophthalmicus (Fig. 1). Ocular lesions develop in approximately half of patients with herpes zoster ophthalmicus [8]. Damage to the eye and surrounding structures occurs owing to inflammation of sensory nerves, with the potentially serious sequelae of chronic ocular inflammation, vision loss, or severe pain [9]. Although acute herpes zoster ophthalmicus typically entails the classic VZV rash in the specific dermatome, ocular changes can occur with minimal or no rash [8,9]. Up to one third of patients with herpes zoster ophthalmicus also have involvement of the nasociliary nerve that innervates the tip of the nose. This involvement is known as Hutchinson’s sign and is a strong predictor of ocular inflammation and corneal denervation [8,10]. Patients with Hutchinson’s sign are reported to have twice the incidence of ocular changes overall. Patients

Fig. 1. Herpes zoster ophthalmicus. (From Wipf JE, Paauw DS. Ophthalmologic emergencies in the patient with diabetes. Endocrinol Metab Clin North Am 2000;29(4):825; with permission.)
without Hutchinson’s sign may have eye involvement in up to one third of cases [8,9].

External ocular manifestations of acute herpes zoster ophthalmicus that may be observed by the emergency department provider include blepharitis, conjunctivitis, episcleritis, and scleritis. Blepharitis can entail vesicular lesions on the eyelids or lid edema and inflammation. The latter may cause ptosis on the affected side [9]. Conjunctivitis is a common early complication of herpes zoster ophthalmicus that is associated with vesicles on the lid margin; the conjunctivae will appear red and swollen and may have petechial hemorrhages [8]. Episcleritis may be seen in as many as one third of herpes zoster ophthalmicus cases and includes erythema, pain, and swelling of the episclera that can be masked by overlying conjunctivitis. Scleritis is a less common but more serious late finding of herpes zoster ophthalmicus following a week of illness, and the cornea is usually also involved (sclerokeratitis).

Corneal involvement occurs in 65% of patients with acute herpes zoster ophthalmicus, and a high level of suspicion for this entity is warranted if vision loss is reported by the patient or detected on visual acuity testing in the emergency department [9]. Symptoms of eye pain or light sensitivity may also occur. The spectrum of corneal changes in herpes zoster ophthalmicus correlates with the progression of disease and includes epithelial keratitis, anterior stromal keratitis, and disciform keratitis. Epithelial keratitis is usually a transient early finding of herpes zoster ophthalmicus that is initially seen on slit lamp examination as multiple swollen lesions which stain with fluorescein or rose bengal dye. VZV dendrites may appear later in a branching or “medusa-like” pattern with similar staining and examination via Wood’s lamp or slit lamp [9]. Anterior stromal keratitis, or nummular keratitis, occurs in as many as 30% of patients with herpes zoster ophthalmicus during the second week of disease and likely reflects an antigen–antibody response to viral proliferation in the overlying epithelium [11]. On slit lamp examination, multiple patchy fine granular infiltrates with a halo can be seen in the anterior stroma below areas of previous epithelial keratitis [8,9]. Disciform keratitis is a late event in herpes zoster ophthalmicus that occurs in about 5% of cases, usually about 3 weeks after the onset of disease. It reflects an extension of anterior stromal keratitis that can herald chronic changes of scarring, lipid deposition, and vascularization, all of which can compromise vision.

Anterior uveitis, or inflammation of the iris and ciliary body, occurs in approximately 40% of patients with herpes zoster ophthalmicus. Patients with the Hutchinson’s sign (involvement of the nasociliary nerve) are at a higher risk for anterior uveitis. Herpes zoster ophthalmicus iritis is generally mild, with small keratic precipitates and a faint flare in the anterior chamber that can be seen on slit lamp examination. A mild elevation in intraocular pressure frequently occurs. Complications of iris atrophy (20%), secondary glaucoma (10%), secondary cataracts (rare), and ischemia
of the ciliary body (phthisis bulbi, very rare) can occur [8]. Timely ophthalmologic referral and treatment is essential. See the article by Mueller and McStay elsewhere in this issue for a discussion of treatment options.

Herpes zoster ophthalmicus is commonly associated with many cases of acute retinal necrosis. Presenting symptoms include blurred vision or pain in the affected eye. Peripheral patches of retinal necrosis may be evident on fundoscopic examination. Emergent ophthalmologic consultation is warranted because retinal detachment can occur.

Lyme disease

Lyme disease is endemic to many areas of the United States and Europe but is an uncommon cause of significant ocular disease [12]. The rare ocular manifestations of Lyme disease are largely known through case reports and small case series; epidemiologic studies of patients with Lyme disease have reported only a few cases of ocular involvement [13]. Ocular complications of Lyme disease can be similar to those of syphilis, presenting with both early and late findings [14]. Patients with severe ocular manifestations of Lyme disease likely have a more chronic form of the disease [15].

Clinical findings in stage 1 Lyme disease include the erythema chronicum migrans rash and flulike symptoms. Eye changes that may be noted in as many as 11% of patients are conjunctivitis, periorbital edema, and mild photophobia [14,15]. Stage 2 Lyme disease develops days to months later and reflects clinical progression of the illness that may include a relapsing migratory monoarthritis, neurologic disease (cranial neuropathy, meningitis, or radiculopathy), and cardiac atrioventricular block. Ocular manifestations that may occur in stage 2 Lyme disease result from intraocular inflammation that leads to granulomatous iridocyclitis with or without uveitis that may be seen on slit lamp examination. Further involvement of the retina may occur as retinal vasculitis, disk edema, or choroiditis. Neuroophthalmic symptoms of blurred vision, headache, Bell’s palsy, cranial neuropathy, and diplopia may also be present [15]. Decreased color vision and visual field changes can occur. Other more rare ocular complications in late stage 2 Lyme disease are paralytic mydriasis, Horner’s syndrome, the Argyll Robertson pupil, orbital myositis, and temporal arteritis [15].

Stage 3 Lyme disease occurs months to years afterwards and reflects persistent infection that manifests as prolonged chronic or recurrent arthritis or chronic neurologic syndromes. The severe ocular complications of Lyme disease seen during stage 3 are episcleritis, stromal keratitis, orbital myositis, vitreitis, or pars planitis. Episcleritis entails redness, pain, and swelling of the episclera that can be seen on direct examination. Complaints of photophobia or blurred vision can occur with stromal keratitis; scattered nummular opacities can be seen on slit lamp examination. Findings in orbital myositis can range from pain on movement of the affected ocular muscle to an inability to move the eye in the direction of the affected muscle.
Vitreitis is evidenced as multiple inflammatory nodules that may be seen on fundoscopic examination ("snowbank exudates"). It is referred to as pars planitis when stromal keratitis is also present. Ophthalmologic consultation is appropriate to confirm these findings and screen for additional rare complications of Lyme disease [15].

**Acquired immunodeficiency syndrome**

It is estimated that since the early 1980s over 50 million people have been infected with HIV worldwide, and more than 22 million deaths have resulted from AIDS [16]. The advent of highly active antiretroviral therapy has produced a remarkable decline in all manifestations of HIV infection, including ocular complications [16]. Nonetheless, ocular findings may provide important clues to HIV-related disease.

Conjunctival microvascular disease affects as many as 75% of HIV-infected patients. Changes of the conjunctiva can appear similar to sickle cell disease and are best observed on the inferior perlimbal bulbar conjunctiva [17]. Slit lamp examination may reveal capillary dilations, microaneurysms, variable short vessel segments or isolated vessel fragments, or a granular appearance of blood within dilated vessels [18]. Other common findings in HIV disease include dry eye, keratoconjunctivitis sicca, and chronic allergic conjunctivitis [17].

External ocular disease in AIDS patients manifests as opportunistic infections and tumors. The range of opportunistic infections includes viral (herpes zoster ophthalmicus, herpes simplex keratitis, molluscum contagiosum, human papillomavirus), protozoal (microsporidium), and fungal (candida and cryptococcus) sources [16–18]. Secondary bacterial infections (*Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa*) may occur with opportunistic eye infections and can result in corneal ulcers. A higher incidence of preseptal cellulitis is also reported in AIDS patients. Kaposi’s sarcoma is an AIDS-defining opportunistic tumor caused by human herpesvirus 8. As many as 20% of patients with Kaposi’s sarcoma may have ocular involvement [19]. Kaposi’s sarcoma lesions may appear on the eyelids or conjunctivae as an irregular mass that is red to purple in color, but they also appear similar to a hordeolum (stye) [17]. Conjunctival Kaposi’s sarcoma lesions are possible and can be mistaken for subconjunctival hemorrhages which do not resolve [16]. Squamous cell carcinomas (associated with human papillomavirus infection) may also be seen as external ocular manifestations of AIDS disease.

Anterior ocular segment complications of AIDS include infectious keratitis (due to the organisms detailed previously) and anterior uveitis. The latter affects more than half of AIDS patients [20]. Mild iridocyclitis often results from VZV or herpes simplex virus infections, with inflammatory changes of the iris and anterior ciliary body seen on slit lamp examination [16]. More severe anterior uveitis occurs in association with posterior
segment infections. Symptoms may include photophobia, pain, redness, decreased vision, or lacrimation.

Posterior segment eye complications occur in as many as 75% of AIDS patients and often can lead to vision impairment or blindness [19]. Retinal microangiopathy and cytomegalovirus (CMV) retinitis are most common, affecting 30% to 40% of AIDS patients overall [16]. The former is of non-infectious origin and is characterized by cotton-wool spots on fundoscopic examination that may be asymptomatic and transient. Retinal hemorrhages and microaneurysms may also be reported on examination by an ophthalmologist. CMV retinitis is usually associated with low CD4 T-lymphocyte levels and severe systemic disease, although it may be a rare presenting manifestation of AIDS [19]. Symptoms of CMV retinitis include floaters, blurred vision, and visual field loss [16]. Ophthalmologic consultation is needed given that retinal detachment (30%) and optic nerve involvement (5%) are possible. The range of optic findings includes granular retinitis, hemorrhagic retinitis, and perivascular retinitis. Other posterior eye segment AIDS-related infections are retinitis due to other viruses (VZV, herpes simplex) or bacteria (ocular syphilis), choroiditis (Pneumocystis carinii, Cryptococcus neoformans, Mycobacterium tuberculosis), and retinochoroiditis (Toxoplasma gondii) [16,19]. Neuro-ophthalmic complications of AIDS-related intracranial infections or tumors may also occur. Cerebral toxoplasmosis is most common and can present with cranial nerve palsies, visual field loss, or papilledema [16].

Reiter’s syndrome

Reiter’s syndrome is a multisystem disease that entails a symptom triad of urethritis, conjunctivitis, and arthritis with negative serology [21,22]. It is an uncommon disease overall that is diagnosed more frequently in men (typically those aged more than 30 years) but can also occur in women [23]. The onset of Reiter’s syndrome is often preceded by genitourinary infection or bacterial enteric infection [22]. As many as 75% of patients with Reiter’s syndrome test positive for HLA-B27 histocompatibility antigens.

The most consistent ocular manifestation of Reiter’s syndrome is a mild bilateral mucopurulent conjunctivitis that is part of the diagnostic triad and that occurs in up to 58% of patients [24]. Mucopurulent eye discharge will be noted, and a papillary or follicular reaction is also common [24]. The conjunctivitis may occur up to 2 weeks after the onset of symptoms of urethritis but often precedes the onset of arthritis. Acute iritis that is detectable on slit lamp examination develops in as many as 20% of patients with Reiter’s syndrome [25]. Keratitis may also be evident as subepithelial opacities (keratic precipitates) with overlying punctate lesions [24–26]. These findings of anterior uveitis are more common in patients who test positive for HLA-B27 antigens [26,27]. Other eye complications of Reiter’s syndrome that have been reported include scleritis, episcleritis, disk edema, retinal edema, and retinal
vasculitis [24]. Chronic recurrent ocular inflammation may occur following the acute eye changes and can result in posterior synechiae, glaucoma, cystoid macular edema, and cataracts [24].

Infectious endocarditis

Ocular complications of infectious endocarditis typically result from some type of septic embolic event to the retina. Emergency department providers may be familiar with the finding of a Roth’s spot, which is commonly seen in endocarditis and other diseases. A Roth’s spot is a cluster of superficial retinal hemorrhages that can be seen on fundoscopic examination as oval hemorrhages with pale centers, often located near the optic disk [28]. In endocarditis, this cluster represents red blood cells which surround inflammatory cells that have collected in the area in response to a septic embolus [29].

A full spectrum of retinal complications may occur in patients with infectious endocarditis. Most are described in case reports and include focal retinitis, embolic retinopathy, subretinal abscesses, choroidal septic metastasis, choroiditis, endophthalmitis (Fig. 2), papillitis, and optic neuritis [30–36]. Clinical vigilance for symptoms of ocular pain, injection, and vision loss is critical in patients with known or suspected endocarditis. Any of these symptoms should prompt an immediate complete examination of the eyes and consultation with an ophthalmologist.

Kawasaki’s disease

Mucocutaneous lymph node syndrome, or Kawasaki’s disease, is an acute multi-organ vasculitis that primarily affects children aged 1 to 8 years.

Fig. 2. Enophthalmitis. (From Wipf JE, Paauw DS. Ophthalmologic emergencies in the patient with diabetes. Endocrinol Metab Clin North Am 2000;29(4):821; with permission.)
It presents with fever and the following symptoms: (1) bilateral bulbar conjunctivitis without exudates; (2) dryness of the lips and oral cavity, with reddening of the mucosa; (3) polymorphous truncal rash without vesicles or crusts; (4) erythema and edema of the palms and soles, or periungual desquamation; and (5) acute nonpurulent cervical lymphadenopathy [37,38]. Incomplete or atypical presentations of Kawasaki’s disease are also possible [38]. The primary ocular manifestation of Kawasaki’s disease is bilateral bulbar conjunctivitis (often with limbal sparing); any additional inflammatory eye changes are similarly bilateral [39]. A recent study of conjunctival swabs from patients with Kaposi’s sarcoma bulbar conjunctivitis reported a predominance of neutrophils, or “neutrophilic conjunctivitis,” as a cytopathologic change that can be followed as Kawasaki’s disease progresses [40].

Anterior uveitis can occur in 25% to 50% of patients with Kawasaki’s disease [38]. The initial bulbar conjunctivitis can readily progress to bilateral iridocyclitis. Symptoms of photophobia, pain, redness, decreased vision, or lacrimation may occur. Subconjunctival hemorrhages or circumcorneal injection with a violaceous hue may be noted on examination of the eyes. Slit lamp examination may reveal superficial punctate keratitis, keratitic precipitates, vitreous opacities, or aqueous cells and a flare response [39,41].

Posterior segment changes have also been reported in Kawasaki’s disease. Papilledema may occur, for which fluorescein angiography is needed to detect vasculitis-related changes [39,42]. Retinal ischemia may also occur as the Kawasaki’s disease vasculitis progresses [43]; therefore, prompt ophthalmologic consultation is necessary, particularly if more advanced Kawasaki’s disease ocular complications are suspected. Dacrocystitis has been reported as an eye complication following resolution of acute Kawasaki’s disease [37].

Temporal arteritis

Giant cell arteritis, or temporal arteritis, is the most common vasculitis in patients over 50 years of age. The disease involves T cell–mediated inflammation of medium-to-large caliber arteries which produces tissue destruction, vascular occlusion, and end organ ischemia [44,45]. Although giant cell arteritis may affect the vascular supply of any organ, cranial ischemic complications are common and often include the eyes. Patients with giant cell arteritis have a significant risk of irreversible blindness [45]. As many as 90% of patients with giant cell arteritis initially complain of headache, but a wide array of symptoms is possible, including a classic symptom of jaw pain or claudication [44]. An elevated ESR is also commonly noted, but a normal ESR does not exclude the disease. Key symptoms of eye involvement in giant cell arteritis include variable loss of vision, amaurosis fugax, diplopia, and eye pain [46,47]. Amaurosis fugax has been reported to be a significant predictor of subsequent irreversible blindness in patients with giant cell arteritis [45].
Anterior ischemic optic neuropathy is the most common cause of visual loss in giant cell arteritis. Changes may be seen on fundoscopic examination as a pale or chalky white swelling of the optic nerve, and splinter hemorrhages may also be present [44]. Diminished intraocular pressure and hypotony of the ciliary body with decreased pupillary response may also be evident [48–50]. These findings can occur in both eyes [51]. Other ocular ischemic lesions that can result from giant cell arteritis but may elude detection on routine examination are central retinal artery occlusion, cilioretinal artery occlusion, posterior optic neuropathy, and choroidal ischemia [50,51]. Overall, emergency ophthalmologic consultation is essential to ensure detection of potential ocular complications of giant cell arteritis.

Giant cell arteritis–related eye changes can progress to irreversible blindness within weeks without immediate treatment. Early diagnosis and a high level of clinical suspicion for eye complications are vital to achieve the best possible outcomes. The treatment of temporal arteritis is discussed in more detail by Vortmann and Schneider elsewhere in this issue.

Hypertension

Hypertension, especially when longstanding or inadequately controlled, causes a broad array of end organ damage. Ocular complications of hypertension result from direct effects on the eye, as well as secondary effects of other ophthalmologic conditions [52]. Although hypertensive eye changes are a major risk factor in patients with diabetes, 2% to 14% of non-diabetic patients aged more than 40 years are also at risk [53,54]. The primary effects of hypertension on the eye cause pathologic changes to the retina through a range that begins with vasoconstriction and progresses to leakage at the blood–retinal barrier and arteriosclerotic changes.

Hypertensive retinopathy is classically described by four grades of retinal change based on advanced ophthalmologic examination [55]; however, clinicians may observe an array of eye findings on simple fundoscopy that correspond to mild, moderate, and severe hypertensive changes [52]. Mild retinopathy entails arteriolar narrowing, often seen as arteriovenous “nicking” or “nipping.” Moderate hypertensive retinopathy can entail findings of “flame” or “blot” hemorrhages, cotton-wool spots, microaneurysms, and hard exudates [52]. All of these findings may occur with severe retinopathy, as well as swelling of the optic disk. When blood pressure is extremely high, increased intracranial pressure with resultant optic ischemia (hypertensive optic neuropathy) will be evident as papilledema on fundoscopic examination [52]. Overall, hypertensive retinopathy is a well-established sign of systemic vascular disease and is associated with subsequent stroke [52].

Other retinopathies that are known complications of hypertension are as follows: retinal vein occlusion, retinal emboli, retinal artery occlusion, retinal macroaneurysm, ischemic optic neuropathy, and diabetic retinopathy. Many of these conditions have common findings, and urgent
ophthalmologic consultation is essential for a correct diagnosis and prompt treatment. Retinal vein occlusion is a common disorder from which vision loss can occur. Patients typically present with poor visual acuity; fundoscopic findings may include retinal hemorrhages, cotton-wool spots, and edema of the macular and optic disk. Retinal emboli may be single or multiple and are often asymptomatic with transient changes, although frank retinal artery occlusion can occur [52]. These emboli may be seen as punctate pale defects on fundoscopy. Retinal emboli signal a high risk of thromboembolic stroke and cardiovascular disease [52]. Retinal artery occlusion is most common in hypertensive patients over 60 years old and presents with symptoms of a painless and sudden unilateral vision loss. A “cherry red spot” may be seen on fundoscopic examination. A retinal arterial macroaneurysm is a more rare disorder that is somewhat unique to patients with hypertension. It can present with acute vision loss but is more likely discovered incidentally on advanced ophthalmologic examination of an asymptomatic patient. Ischemic optic neuropathy is the most common acute optic neuropathy of patients aged more than 50 years and is more common in patients with diabetes. Up to 90% of cases are anterior and present with abrupt vision loss and edema of the optic disk. Diabetic retinopathy is detailed in the following section.

**Diabetes**

Emergency department providers are likely to encounter many of the complications of type 1 and type 2 diabetes mellitus, especially as the overall incidences of diabetes and obesity continue to rise. Ocular complications of diabetes are no exception. Indeed, diabetic retinopathy remains the most common cause of legal blindness in patients between 18 and 74 years of age. Early recognition with prompt treatment can dramatically affect outcome [56]. Other ocular complications of diabetes include vascular events and severe eye infections.

The prevalence of diabetic retinopathy is markedly higher in patients who have type 1 diabetes (estimated at 40% to 80%), but it also affects 20% to 30% of patients who have type 2 diabetes [56,57]. Hypertension is also a significant risk factor for diabetic retinopathy. Intensive medical control of blood glucose levels has been shown to significantly reduce both the incidence of new retinopathy and the progression of pre-existing retinopathy. Moreover, control of hypertension with angiotensin-converting enzyme inhibitors can reduce the progression of diabetic retinopathy. Despite the routine monitoring for diabetic retinopathy as a standard, diabetic patients may still present to the emergency department with complaints of vision change. In these cases, prompt ophthalmologic consultation is required for an optimal outcome.

Three main types of diabetic retinopathy form the spectrum of progression of ocular changes: non-proliferative (background), pre-proliferative,
and proliferative retinopathy [57]. Non-proliferative diabetic retinopathy may be evident on simple fundoscopic examination as dilated veins, microaneurysms temporal to the macula, and small hemorrhages in either a “dot and blot” pattern (deeper) or flame shape (more superficial) [56]. More extensive ophthalmologic examination and imaging may reveal additional findings of hard exudates, retinal edema, and arteriovenous shunting. Pre-proliferative diabetic retinopathy entails lesions resulting from retinal ischemia. The lesions may be evident on simple fundoscopic examination as multiple cotton-wool spots, vascular changes (narrowed arterioles; dilated veins in bead, loop, or sausage-like patterns), or dark blot hemorrhages [56]. The last change is more likely seen on further retinal examination or fluorescein angiography, along with capillary non-perfusion filling defects, macular edema, and intraretinal microvascular abnormalities. Proliferative diabetic retinopathy is best detected by an ophthalmologist. Findings include retinal scars (retinitis proliferans), new vessel formation, vitreous hemorrhage, and retinal detachment [56].

Diabetic patients are at risk for ocular vasocclusive events, presumably due to a hypercoaguable state [56]. Complications include central retinal artery occlusion (Fig. 3), central retinal vein occlusion, and ocular motor nerve palsies. Central retinal artery occlusion presents with sudden near complete or complete vision loss. Fundoscopic examination may reveal retinal edema and pallor and a darkened macula; further findings are possible on fluorescein angiography [56]. Central retinal vein occlusion presents with a slower onset of blurred vision and variable loss of vision. Fundoscopic examination may show retinal edema, dilated and twisted retinal veins, and retinal hemorrhages with cotton-wool spots (“blood and thunder”) [56]. Ocular motor nerve palsies can result from ischemic cranial nerve injuries, which in diabetic patients most commonly involve the oculomotor (third)
nerve. The sixth and fourth nerves can also be affected but in decreasing order of frequency. Symptoms of third nerve palsy can include diplopia, ptosis, and sometimes headache and eye pain; a slight anisocoria may be noted, although the pupil is usually spared. Interestingly, ocular motor nerve palsies usually occur in diabetic persons who do not have diabetic retinopathy.

Severe eye infections are rare in diabetes but are uniformly destructive when present. Two ocular infections that occur primarily in diabetic patients are bacterial endophthalmitis (see Fig. 2) and rhinocerebral mucormycosis. The former is a severe ocular complication that often results in blindness. A wide array of bacterial causes is possible and includes *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*. Presenting symptoms include pain, photophobia, floaters, and reduced vision. Hypopyon (pus) can be seen in the anterior chamber on examination. Rhinocerebral mucormycosis is a rare but serious fungal complication of type 1 diabetes that presents in combination with diabetic ketoacidosis. Initial clinical symptoms include eye pain, headache, and nasal stuffiness. Periorbital swelling and proptosis may be noted, along with necrotic lesions on the palate and nasal mucosa. Further complications include cavernous sinus thrombosis, internal carotid artery thrombosis, and death.

Summary

A wide array of ocular changes is possible in many systemic diseases. Emergency department providers may encounter ophthalmologic signs or symptoms during the evaluation of a patient with known systemic disease, or in a patient with as yet undiagnosed illness. Careful screening of visual acuity, a complete external eye and fundoscopic examination, as well as slit lamp examination are needed in any patient with eye complaints and especially when progression of known systemic disease is suspected. Emergent ophthalmology consultation is critical if any degree of vision loss is reported or detected on screening. Many ocular complications of systemic disease also require urgent ophthalmologic evaluation to ensure the best possible treatment outcomes are achieved.

References


