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Review Article

Ocular manifestations of systemic disease

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ABSTRACT

Ocular changes are common in the course of many systemic infections and inflammatory diseases. The human eye as an organ can offer critical clues to the presence of systemic illness. A thorough ophthalmic examination including visual acuity, pupillary reaction, ocular motility, confrontation, field testing, external inspection, direct ophthalmoscopy and fluorescein staining should be completed. This article describes ocular signs and symptoms associated with systemic diseases like diabetes, hypertension, autoimmune disorders, infections, inflammatory conditions, malignancy and acquired immune deficiency syndrome and their serious ocular sequelae.

Key Words- Eye, Systemic Diseases, Diabetes, Arthritis, Hypertension.

INTRODUCTION

An ocular manifestation of a systemic disease is an eye condition that directly or indirectly results from a disease process in another part of the human body. There are many systemic, infectious, inflammatory and autoimmune diseases known to cause ocular or visual changes. The eye is composed of many different types of tissues. This unique feature makes the eye susceptible to a wide variety of diseases as well as provides insights into many body systems which may be connected with the eyes by those similar tissue types. Also, eyes are the only organs where we can have a direct look at the end arterioles and look for any inflammatory or atherosclerotic or proliferative changes in these. This information, once gleaned is not only helpful in achieving a diagnosis but often aids in the institution of timely management regarding the patient as well as gives an insight about the prognosis of the disease as well as its impact on other critical organ systems like the heart and kidney. Almost any part of the eye can give important clues to the diagnosis of systemic diseases. Signs of a systemic disease may be evident on the outer surface of the eye (eyelids, conjunctiva and cornea), middle of the eye (anterior chamber, iris, lens and vitreous cavity) and at the back of the eye (choroid and retina)[21]. Problems in the eye may be a first presentation of the systemic disease or patients with known systemic problems may need to have their eyes specifically checked for complications. Awareness of these associations is the first step in diagnosis and management of these often complex patients.

Review:

Diabetes Mellitus: The most important ocular complication in Diabetes is diabetic retinopathy (DR) and is the leading cause of blindness in the working age population. The prevalence of diabetic retinopathy is markedly higher in patients who have type I diabetes (estimated at 40% to 80%), but it also affects 20% to 30% of patients who have type II diabetes[1,2]. Main types of diabetic retinopathy depending on spectrum of progression of ocular changes are background DR, pre-proliferative, proliferative and advanced DR.

Background Retinopathy:
Signs of microvascular leakage (hemorrhage and exudates) away from the macula. Vision is normal.
Pre-proliferative Retinopathy:
Evidence of occlusion (cotton wool spots). The veins become irregular and may show loops. Vision is normal

Proliferative Retinopathy:
Occlusive changes lead to the release of vasoproliferative substances from the retina resulting in neovascularisation of the optic disc or elsewhere in the retina. Neovascularisation may also occur on the iris causing severe glaucoma. Vision is normal. Sight threatening.

Advanced Diabetic Retinopathy:
Proliferative changes result in bleeding into vitreous or between the vitreous and retina. The retina may also be pulled away from its underlying pigment epithelium. Vision is reduced, often acutely with vitreous haemorrhage. Sight threatening.

Maculopathy:
Exudates and haemorrhages within the macular region, evidence of retinal edema and evidence of retinal ischemia.
Diabetic patients are at risk for ocular vaso-occlusive events, presumably due to a hypercoagulable state[1]. Complications include central retinal artery occlusion, central retinal vein occlusion and ocular motor nerve palsies. Ocular infections that occur primarily in diabetic patients are bacterial endophthalmitis and rhinocerebral mucormycosis.

Hypertension: hypertension, especially when long standing 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 ophthalmological conditions[3].

Acute changes:
Elevated blood pressure- a severe acute rise causes fibrinoid necrosis of the vessel-wall which results in lipid exudates, nerve fibre layer infarcts (cotton wool spots), flame shaped haemorrhages and sometimes and sometimes edema of retina. In malignant hypertension, optic disc swelling also occurs.

Chronic changes:
Arteriolar sclerosis- ophthalmoscopic features include changes in the arteriolar light reflex, attenuation of the retinal arterial vessels (copper and silver wiring) and by the presence of nipping of the retinal vein where it is crossed by an arteriole.
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.

Malignancy: Malignancy of the eye can be primary or secondary due to metastases. They usually arise from the breast or lung and infiltrate the choroid but may also affect the optic nerve or an extraocular muscle. Lymphoma and leukemia may also occur in the eye with conjunctival or optic nerve infiltration.

Acquired immune deficiency syndrome: ocular findings may provide important clues to HIV related disease. Anterior ocular segment complications of AIDS include infectious

keratitis and anterior uveitis[4,20]. Posterior segment eye complications occur in as many as 75% of AIDS patients and often can lead to visual impairment or blindness[5,19]. Retinal microangiopathy and cytomegalovirus (CMV) retinitis are most common, affecting 30% to 40% of AIDS patients[6,16]. 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)[5,6]. Neuro-ophthalmic complications of AIDS related intracranial infections or tumors may also occur. Central toxoplasmosis is most common and can present with cranial nerve palsies, visual field loss or papilledema[6].

External ocular disease in AIDS patients manifests as opportunistic infections and tumors. The range of opportunistic infections include viral (herpes zoster ophthalmicus, herpes simplex, molluscum contagiosum, human pappilomavirus), protozoal (microsporidium) and fungal (candida and cryptocaccus)[6,7,8].

Secondary bacterial infections may occur with opportunistic eye infections and can result in corneal ulcers. A higher incidence of pre-septal cellulitis is also reported in AIDS patients. Kaposi's sarcoma is an AIDS-defining opportunistic tumor caused by human herpes virus 8. Kaposi sarcoma lesions may appear as eyelid mass or conjunctival mass.

Autoimmune diseases:

Rheumatoid arthritis, juvenile rheumatoid arthritis, Sjogrens syndrome, the seronegative spondyloarthropathies, systemic lupus erythematosus, multiple sclerosis, giant cell arthritis and Graves disease are autoimmune disorders commonly encountered by physicians. These autoimmune disorders can have devastating systemic and ocular effects.

Rheumatoid arthritis:

Approximately 25% of patients with rheumatoid arthritis (RA) will have ocular manifestations. These may include keratoconjunctivitis sicca, scleritis, episcleritis, keratitis, peripheral corneal ulceration and less common entities such as choroiditis, retinal vasculitis, episcleral nodules, retinal detachment and macular edema[9,10].

Juvenile rheumatoid arthritis:

Juvenile rheumatoid arthritis accounts for approximately 80% of cases of uveitis in children[9,10,11]. Delay in diagnosis can lead to cataracts, glaucoma and blindness.

Sjogrens syndrome:

The primary ocular manifestation of Sjogren's syndrome is keratoconjunctivitis sicca.

Spondyloarthropathies:

Among the seronegative spondyloarthropathies uveitis in ankylosing spondylitis is the most common ocular manifestation. It occurs in approximately 25% of patients with ankylosing spondylitis, in up to 37% of patients with Reiter's syndrome, in approximately 20% of patients with psoriatic arthritis and in up to 9% of patients with enteropathic arthritis (arthritis associated with Crohn's disease or ulcerative colitis)[12,13,14].

Systemic lupus erythematosus:

Ocular disease occurs in 20% of patients with systemic lupus erythematosus. External ocular manifestations include keratoconjunctivitis sicca, conjunctivitis, uveitis, episcleritis, scleritis, keratitis and a discoid lupus rash over eyelids[15,16]. Typical complications include optic neuritis, ischemic optic neuropathy, hemianopia, amaurosis, internuclear ophthalmoplegia,

papillary abnormalities, oculomotor abnormalities, pseudotumor cerebrii and visual hallucinations[15].

Multiple sclerosis:
Optic neuritis is diagnosed in 75% of patients with MS and is the presenting symptom in 14 to 25% of cases[17,18]. Dysmetria, nystagmus and cranial nerve palsies, especially involving the sixth and third nerves, may result from lesions of the brain stem and cerebellum.

Giant cell arteritis:
Up to 50% of patients present with ocular symptoms that include pain, diplopia, visual loss and amaurosis fugax, in addition to headache, jaw claudication and neck pain[19,20].

Graves disease:
Common sequelae of thyroid disease is exophthalmos with retraction of the upper and lower eyelids. This may result in corneal exposure leading to exposure keratopathy with corneal ulceration. Diplopia may be present due to restrictive extra-ocular muscle palsy and optic nerve compression is caused by enlarged extra ocular muscles.

Systemic infections: the most common systemic infections arise from AIDS include candidiasis and herpes zoster. Candidiasis may occur in compromised patients with candida growing in blood cultures. Typically involves a seriously ill ICU patient with a central parenteral feeding line. Retinitis and vitreous fungal balls may be seen. Herpes zoster, affecting the 1st division of trigeminal (Vth) nerve, typically causes a conjunctivitis or keratitis in addition to the characteristic dermatomal dermatitis, Anterior uveitis and retinitis or optic neuropathy may also occur.

CONCLUSION:

A wide array of ocular changes is possible in many systemic diseases. Careful screening of visual acuity, a complete external eye examination and fundoscopic examination as well as slit lamp examination are needed in any patient with eye complaints and especially when progression of known systemic diseases is suspected. Many ocular complications of systemic diseases also require urgent ophthalmologic evaluation to ensure that the best possible treatment outcomes are achieved.

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