

Ocular Manifestations of Systemic Diseases: The Eyes are the Windows of the Body

Heeyoon Cho

Department of Ophthalmology, Hanyang University College of Medicine, Hanyang University Guri Hospital, Guri, Korea

An ocular manifestation of a systemic disease is an eye condition that directly or indirectly results from a disease process originating from another part of the body. There are many diseases known to cause ocular or visual changes as a result of systemic disease. Diabetes, for example, is the leading cause of new cases of blindness in those aged 20-74, with ocular manifestations such as diabetic retinopathy and macular edema affecting up to 80% of those who have had the disease for 15 years or more. Other diseases such as acquired immunodeficiency syndrome (AIDS) and hypertension are commonly found to have associated ocular symptoms. Physicians need to consider that systemic disease can involve the eyes and it is important for ophthalmologists to understand that they may be the first to suggest a diagnosis due to underlying systemic disease. According to the quote “The eyes are the windows of the soul”, ophthalmologists should view the eyes as not only windows of the soul but also a window to the physical state of the entire body.

Systemic hypertension is a major risk factor for the development of retinal vascular diseases including hypertensive retinopathy, retinal vein or artery occlusion, and embolic events. High blood pressure also increases the risk for the development and progression of diabetic retinopathy. Signs of hypertensive retinopathy are predictive of target-organ damage including cardiovascular and cerebrovascular diseases [1]. High blood pressure affects the heart, kidney, brain, large arteries, and also the eyes. Retinal, choroidal, and optic nerve circulations undergo pathophysiological changes resulting in clinical signs referred to as hypertensive retinopathy,

hypertensive choroidopathy, and hypertensive optic neuropathy. Systemic hypertension also increases the risk for the development of retinal vein and artery occlusion, retinal-arteriolar emboli, and diabetic retinopathy.

Diabetic retinopathy is one of the common causes of blindness. It is an ocular manifestation of diabetes, which affects up to 80 percent of all patients who have had diabetes for 20 years or more. Diabetic macular edema is the most common cause of visual dimness in patients with diabetic retinopathy. Dr. Lee will discuss the challenges and current treatments to prevent the visual disturbance related to diabetic macular edema [2].

Systemic lupus erythematosus (SLE) is an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue in many parts of the body. SLE is a potentially life-threatening multisystem disease that is commonly associated with ocular manifestations. The purpose of this review is to outline the ocular manifestations of SLE and treatments [3]. Ocular complications have been reported in up to one-third of patients with SLE. Ocular manifestations can be associated with significant morbidity and eye issues may play a role as a marker for systemic disease activity.

Keratoconjunctivitis sicca is the most common ocular problem in patients with SLE. When ophthalmologists see patients complaining of dry eye symptoms, determining the underlying reason as to why these patients are suffering from dry eye symptoms is important. The hypo-secretion of tears is one cause of dry eye symptoms.

Sjögren Syndrome (SS) is one of the most frequent systemic au-

Correspondence to: Heeyoon Cho

Department of Ophthalmology, Hanyang University Guri Hospital, 153 Gyeongchun-ro, Guri 11923, Korea
Tel: +82-31-560-2165, Fax: +82-31564-9479, E-mail: hych@hanyang.ac.kr

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

toimmune disorders, mainly involving the eyes and mouth due to inflammation of the lacrimal and salivary glands. Exocrine glands affected with a typical focal lymphocytic infiltration potentially lead to dry eyes and dry mouth. In addition to the known pathogenic mechanism of SS through autoimmunity, the diagnostic criteria of SS has recently changed as proposed by the American College of Rheumatology/Sjögren's International Collaborative Clinical Alliance (ACR/SICCA) in 2012. The main change is that the ocular surface staining score is the only required test for ocular manifestations of SS; however, other diagnostic methods evaluating tear film status, although excluded from the new criteria, are still worth investigating for staging of the disease and treatment planning, including direct observation of tear film, tear film break up time, Schirmer test, and measurement of the tear film levels of inflammatory mediators. Eye-specific signs and symptoms and ocular treatment options for SS will be discussed in this issue by Dr. Song and Dr. Lee [4].

Sarcoidosis is a granulomatous disease that can include ocular involvement, and although its incidence is relatively high, communication can be challenging during collaborative treatments owing to differences in terminology. It is also difficult for a non-ophthalmologist to achieve understanding of the types of ophthalmologic complications and each of their characteristics. Thus, Dr. Kim will present literature regarding ocular sarcoidosis that will give insight into this disease for ophthalmologists [5].

Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare and sometimes life-threatening hypersensitivity mucocutaneous disease triggered mostly by medications and infections. Major involving tissues are the mucous membranes of oral, gastrointestinal, respiratory, integument and gynecologic tissues. Even after recovering from skin problems without sequelae, survivors can have serious ocular complications leading to blindness despite local and systemic therapy. There are no definite effective systemic and local treatment for SJS/TEN. Early detection and aggressive treatment is important for the long-term prognosis of eye. Eyelid margin and palpebral conjunctiva and fornix should be checked thoroughly to detect the cicatricial changes that make chronic ocular surface failure such as limbal cell deficiency and complete ocular surface keratinization. Amniotic membrane transplantation and cultivated oral mucosal graft are benefit to reduce the risk of ocular surface failure. Dr. Kang will discuss the pathogenesis, diagnosis and treatment of this destructive ocular surface disease [6].

Ocular manifestations can occur in various systemic disease of pediatrics. Although we cannot deal with ocular manifestations of all pediatric systemic disease in this paper, Dr. Oh will give us the review of particular diseases that are interested to the general physician and pediatric ophthalmologists [7]. Ocular manifestations of Hyperthyroidism, Hypoparathyroidism, Diabetes mellitus, Porphyria, Cystinosis, Mucopolysaccharidosis, Wilson disease, Juvenile idiopathic arthritis, Systemic lupus erythematosus, Marfan syndrome, Weill-Marchesani syndrome, Child abuse will be described.

Thyroid ophthalmopathy (TO) is an autoimmune inflammatory disorder involving the orbit characterized by inflammation and swelling of the extraocular muscles and an increase in orbital fat and connective tissue. Despite extensive research, TO continues to be a difficult condition for the patient to cope with and for the clinician to treat. Current treatments consist of systemic immunosuppression, orbital irradiation, and surgery. It is promising for patient refractory to conventional therapy that pathogenesis of TO at molecular level which advance development of new therapies targeting cellular immunity are now better understood. Future therapies targeting immune system or specific molecules are under investigation and show promise for the future. This review will describe current trends in the management of TO, from well-established therapies such as glucocorticoids, orbital irradiation and orbital decompression to more innovative therapies targeting immune system or specific molecules involved in TO pathogenesis [8].

Systemic infections that are caused by various types of pathogenic organisms can be spread to the eyes as well as to other solid organs. Bacteria, parasites, and viruses can invade the eyes via the bloodstream. Despite advances in the diagnosis and treatment of systemic infections, many patients still suffer from endogenous ocular infections; this is particularly due to an increase in the number of immunosuppressed patients such as those with human immunodeficiency virus infection, those who have had organ transplantations, and those being administered systemic chemotherapeutic and immune-modulating agents, which may increase the chance of eye involvement. Dr. Lee focused on the conditions that ophthalmologists encounter most often and that require cooperation with other medical specialists and clinical information about ocular manifestations associated with various systemic infections will be reviewed in this issue [9].

This issue did not cover all ocular manifestations of systemic diseases but, it includes the representative disorders resulting seri-

ous morbidity such as diabetes, autoimmune disorders, and infections.

REFERENCES

1. Ma DJ, Yu HG. Window to heart; ocular manifestations of hypertension. *Hanyang Med Rev* 2016;36:146-50.
2. Lee JE. A multimodal approach to diabetic macular edema. *Hanyang Med Rev* 2016;36:151-4.
3. Cho H. Ocular manifestations of systemic lupus erythematosus. *Hanyang Med Rev* 2016;36:155-60.
4. Song IS, Lee SM. Ocular manifestations of sjögren syndrome. *Hanyang Med Rev* 2016;36:161-7.
5. Kim YT. Ocular manifestations of sarcoidosis: an ophthalmologist's view. *Hanyang Med Rev* 2016;36:168-73.
6. Kang MH. Ocular Manifestations of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Hanyang Med Rev* 2016;36:174-81.
7. Lim HW, Oh SY. Ocular manifestations of pediatric systemic disease. *Hanyang Med Rev* 2016;36:182-5.
8. Kang S, Sa HS. Current trends in the management of thyroid ophthalmopathy. *Hanyang Med Rev* 2016;36:186-91.
9. Moon BG, Lee JY. Ocular inflammation associated with systemic infection. *Hanyang Med Rev* 2016;36:192-202.