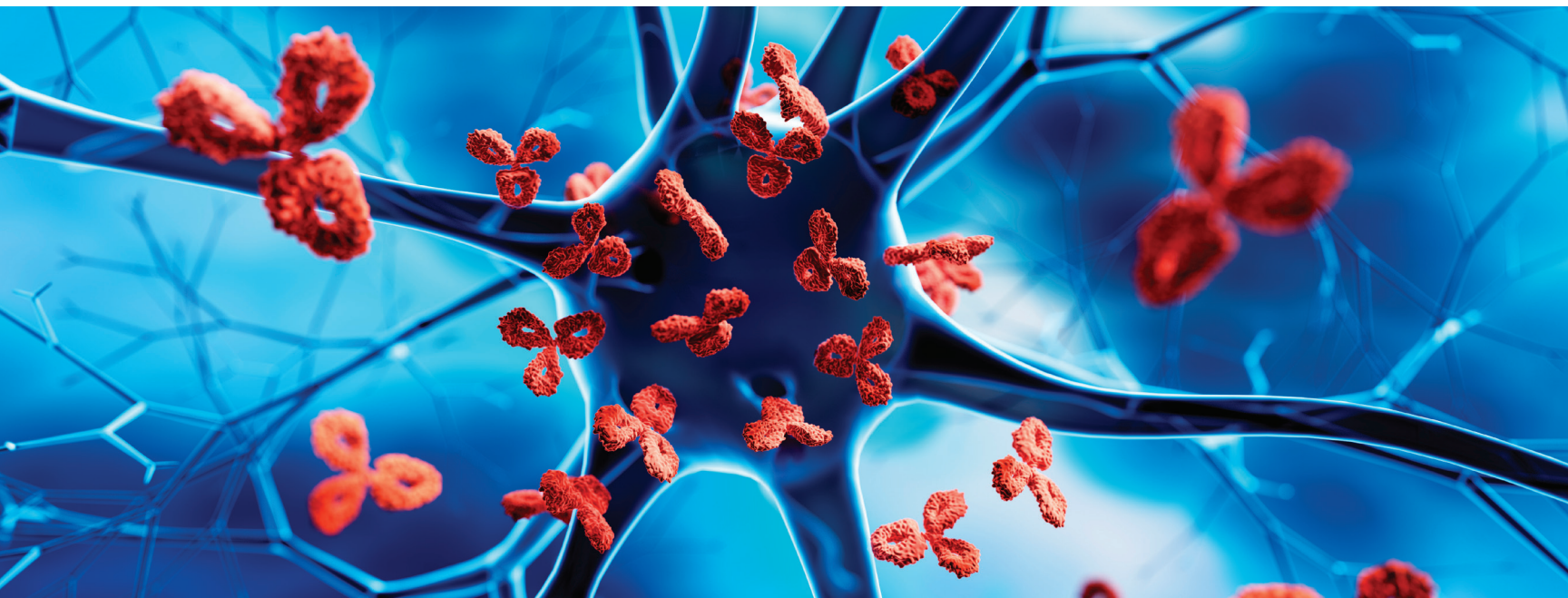




AUTOIMMUNE DISEASE AND THE EYE



Many affected patients will present with ocular signs and symptoms.

BY ANTHONY DEWILDE, OD, FAAO

Autoimmune diseases are a complex set of conditions, in which the immune system mistakenly targets healthy cells instead of foreign cells. This can lead to significant morbidity and mortality. Autoimmune disease is the second highest cause of chronic illness in the United States. All in all, there are more than 80 types of autoimmune diseases.¹

Diagnosing autoimmune diseases can be difficult, often due to lack of access to health care, testing options that are expensive and difficult to obtain, lack of specificity with testing modalities, and vague symptoms.

From initial symptoms to final diagnosis, the process typically takes an average of 4.5 years and involves up to four doctors.²

ODs are in a unique position to help patients with autoimmune disease, as many of these conditions manifest with ocular signs and symptoms. By understanding the association between autoimmune disease and the eye, we can detect early signs and symptoms, allowing earlier referral and treatment.

The number of autoimmune diseases that can affect the eye is vast. As such, this article will focus on the three main conditions that

I've encountered over the course of my career: myasthenia gravis (MG), thyroid eye disease (TED), and giant cell arteritis (GCA).

MYASTHENIA GRAVIS

MG is a chronic autoimmune disease where autoantibodies bind to the neuromuscular junction, blocking its ability to receive normal signals from acetylcholine. This manifests as muscle weakness and fatigue. Around 50% of patients with MG will initially present with ocular manifestations, such as ptosis and/or diplopia (Figure 1). Often, these manifestations are variable and worsen with increased heat and/or fatigue. Although ptosis and diplopia are common early manifestations of MG, 50% to 80% of patients progress to generalized MG within 2 years.³

Management

If MG is suspected due to ocular manifestations, case history, or symptoms, diagnostic testing should begin with laboratory evaluations, electrophysiology testing, or in-office testing. Care should be taken to rule out other causes of ptosis, such as third cranial nerve (CN) palsy, Horner syndrome, and age-related ptosis.

In-office testing can be completed by resting an ice pack on a patient's



Figure 1. A 62-year-old patient with acquired ptosis OS from MG.

closed eyelids to see if ptosis improves after 2 minutes. Another test attempts to fatigue the muscles by having the patient stare upward for 2 minutes. If MG is present, ptosis should manifest or worsen with fatigue. Although the ice pack test is highly sensitive for ptosis, it is not too sensitive to detect diplopia due to MG.⁴ Clinical suspicion should be heightened for the possibility of MG if a patient has variable diplopia or does not have other risk factors for microvascular CN palsy, such as diabetes mellitus or hypertension.

Treatment

Treatment for MG includes systemic therapies, such as anticholinergics, corticosteroids, and several new biologic therapies. Treating ocular-specific complications, such as ptosis and diplopia, can be challenging because of their variable nature. Eye drops can help ease ptosis.^{3,5} Patching, frosting lenses, and prism can help reduce diplopia symptoms.

THYROID EYE DISEASE

TED, or Graves disease, is an autoimmune thyroid disease where autoantibodies bind to thyrotropin-stimulating hormone receptors on the thyroid gland, leading to overactivity. The majority of patients with Graves disease manifest symptoms consistent with hyperthyroidism, such as increased energy, difficulty sleeping, and heat intolerance. Although most patients with autoimmune thyroid disease have hyperthyroidism, there is a subset that has hypothyroidism, or normal thyroid levels (euthyroid) on laboratory evaluation.^{6,7} A total of 30% to 50% of these patients experience ocular complications, such as exophthalmos, dry eye, eye ache, pain on eye movement, injection, and diplopia (Figure 2).^{6,7}

Management

The OD's role in the management of Graves disease is important, due to the disease's cosmetic appearance and

potential for irreversible vision loss. By recognizing early signs and symptoms of this condition, we can recommend laboratory evaluation and imaging and referral to a specialist. If the patient has no systemic symptoms or has a normal laboratory evaluation, recommend close follow-up, as 80% of patients with euthyroid will develop thyroid complications over the following 18 months.^{6,7}

Treatment

Treatment for systemic complications of Graves disease consists of calming acute exacerbations of the autoimmune process through corticosteroids, stabilizing the thyroid, and reversing any complications that may arise along the way.⁶⁻⁸

Ocular treatment for Graves disease involves managing signs and symptoms, such as redness, dryness, and diplopia. If conservative treatments, such as eye drops and glasses, fail to alleviate symptoms, patients traditionally have two options available: corticosteroids and orbital decompression.

Due to the potential complications of orbital surgery and the systemic side effects of corticosteroids, medications such as teprotumumab-trbw (Tepezza, Horizon Therapeutics) are often preferred. Teprotumumab works by targeting insulin-like growth factor to downregulate orbital inflammation. Although the response is typically greater for patients who have active Graves disease, teprotumumab works on both active and chronic forms of the condition.^{9,10}

GIANT CELL ARTERITIS

GCA is an immune-mediated vasculitis that causes focal ischemic lesions in medium- and large-sized arteries. Patients can present with a variety of different symptoms, including headache, scalp tenderness, jaw claudication, and vision loss.^{11,12}

Vision loss is typically a result

AT A GLANCE

- Many autoimmune diseases manifest with ocular signs and symptoms.
- By understanding the association between these diseases and the eye, we can detect early signs and symptoms, allowing earlier referral and treatment.
- The three main conditions that I've encountered are myasthenia gravis, thyroid eye disease, and giant cell arteritis.

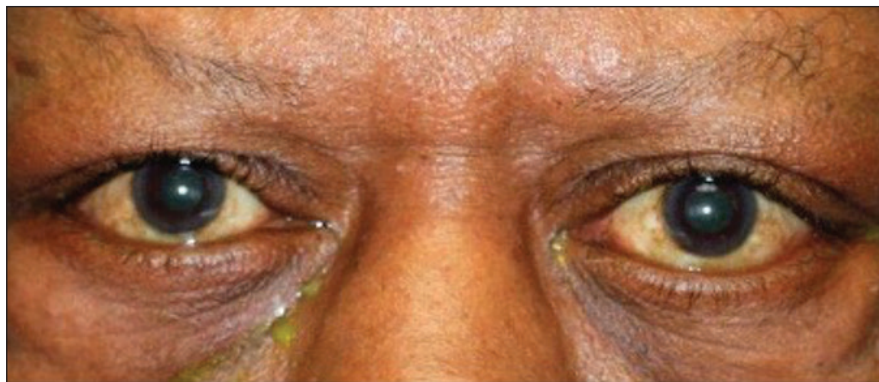


Figure 2. A 68-year-old patient with mild exophthalmos OS from Graves disease.

of arteritic anterior ischemic optic neuropathy. Patients present with sudden, painless vision loss that is usually profound. Funduscopy evaluation reveals pallid-appearing unilateral optic nerve edema. One-third of patients will develop bilateral optic nerve edema within 14 days if untreated.^{11,12} Although the likelihood of GCA increases with age, there have been case reports of GCA developing in patients as young as in their 40s.

Management

Generally, the recommendation is to evaluate all patients who are 50 years of age and older and present with ocular or systemic symptoms, regardless of their optic nerve status. The recommended testing protocol involves Westergren erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and complete blood cell count with differentiation.

Sohan Singh Hayreh, MD, found that certain symptoms are more suggestive of GCA than others

in patients who present with a unilateral swollen optic nerve, such as jaw claudication, neck pain, and anorexia. Dr. Hayreh also found that combining ESR > 47 mm and CRP > 2.45 mg/dL yielded 100% sensitivity and 97% specificity in the detection of GCA.¹³

Typically, the combination of age, ocular signs, systemic symptoms, and laboratory evaluation can accurately diagnose GCA. If there remains doubt with any of these markers, temporal artery biopsy is considered the gold standard for diagnosis, although it is not used on every patient who is suspected of having GCA due to cost, difficulty arranging testing, potential complications, and accuracy of other testing modalities.^{13,14}

Treatment

Treatment for GCA has remained oral corticosteroids (80-100 mg/day) for years.^{11,12,14} This approach helps calm the autoimmune response and prevent further ocular and systemic complications. Due to the many side

effects of corticosteroids and the high recurrence rate when tapering, other medications are sometimes used instead of or in combination with corticosteroid treatment.

Tocilizumab (Actemra, Genentech) is an immune-suppressing biologic medication that binds to interleukin-6 receptors. It has been shown to improve overall outcomes of GCA, including reducing the recurrence rate and decreasing the total amount of steroids taken.¹⁵

A MULTIDISCIPLINARY APPROACH

Our role in the ocular and systemic health of patients is vital. Because many autoimmune diseases manifest in the eye, a multidisciplinary approach is required, involving assessment of ocular and systemic manifestations, referral to appropriate health care providers, and management of complications. ■

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