Graves' Eye Disease

By John McCann, M.D.

Introduction: The triad of exophthalmos, tachycardia and goiter was initially described in 1835 by Robert James Graves. Today the term Graves' eye disease is used to describe patients who may have eyelid retraction, exophthalmos or diplopia.

Etiology: Graves' disease is an autoimmune disorder that affects the thyroid gland and connective tissues of the orbit. Auto antibodies bind to the thyrotropin receptor in the thyroid gland and thus mimic the effects of thyroid stimulating hormone, resulting in hyperthyroidism. Recent research suggests that the insulin-like growth factor-1 receptor (IGF-1R) is the antigen that reacts with auto antibodies in the orbit of patients with Graves' disease. Autoimmune stimulation of IGF-1R on the orbital fibroblast results in an increase in the volume of fat and enlargement of the extraocular muscles. The increased volume of fat and muscle displaces the eye out of the boney orbit. The swollen extraocular muscles become inflexible, which contributes to diplopia and retraction of the upper and lower eyelids.

Disease spectrum: Graves' eye disease encompasses a wide clinical spectrum. Only about 5 percent of patients with Graves' eye disease will have disease severe enough to require surgical intervention.

In the least severely affected patients, the disorder tends to mimic allergic conjunctivitis. Patients complain of watering eyes, and pale swelling of the conjunctiva is evident. One can differentiate early onset Graves' disease from allergic conjunctivitis because in Graves' disease the symptoms are not seasonal and are not associated with itching.

One of the earliest signs of Graves' disease is retraction of the upper eyelids. The normal position for the upper eyelid

is 1 mm below the intersection of the sclera and the cornea (limbus). In Graves' disease the upper lid is retracted, allowing one to see the white sclera above the superior limbus.

In more severe cases, the patient may begin to note diplopia. Initially this is only present when looking to the side. Patients may also note bulging forward of the eyes and in many cases this will be unilateral.

In the most severely impacted patients, the combination or eyelid retraction and exophthalmos causes lagophthalmos. If untreated, this can result in permanent visual loss from corneal ulceration or scarring. Marked enlargement of the extraocular muscles in the orbital apex can compress the optic nerve and result in permanent loss of vision.

Graves' disease is three to four times more common in women than men and tends to impact middle-aged patients. However, the eye disease tends to be most severe in older men and in smokers.

Diagnosis: Graves' eye disease is a clinical diagnosis that cannot be excluded with any laboratory test. The most sensitive clinical sign of the disorder is eyelid retraction. Hyperthyroid state supports the diagnosis but as many as 25 percent of patients have euthyroid Graves' eye disease. Elevated anti-thyroid hormone levels support the diagnosis but will be normal in many cases. Orbital imaging can demonstrate enlarged extraocular muscles, but some patients have normal extraocular muscles and only demonstrate an increase in the volume of orbital fat. In cases where the diagnosis is in question, referral to an orbital disease specialist is appropriate.

Disease course: Graves' eye disease runs a stereotypical course with an initial active inflammatory phase followed roughly a year later by some spontaneous improvement and loss of inflammatory signs such as eye watering and swelling of the conjunctiva. The disease then enters an inactive phase and in 90 percent of patients remains stable throughout life. The active inflammatory phase of the disease may cause permanent changes in the orbital soft tissue that require surgical intervention.

Nonsurgical treatment: In all phases of Graves' eye disease, it is important to protect the cornea by frequent use of artificial tears during the day and lubricating ointment at night. For patients with minor degrees of diplopia, putting prisms in the spectacles can be useful. A smoking cessation plan should be discussed. Euthyroid state does not generally improve Graves' eye disease. In fact radioactive ablation of the thyroid gland has been linked with worsening of the eye disease and when possible should be avoided by using antithyroid medications in patients with Graves' eye disease.

Prednisone at 1mg/kg can reduces the active inflammatory component of the disorder. Systemic complications of prolonged high dose prednisone limit use to patients with severe or vision-threatening disease. Retrobulbar Kenalog injections can help reduce symptoms of orbital pain without the systemic complications of oral steroids. Some have advocated for orbital radiation; however, a number of large studies have called into question the efficacy of this treatment. Hopefully, research will lead to specific anti-inflammatory treatment with fewer side effects than systemic steroids.

Surgical treatment: Surgical treatment of Graves' disease is generally delayed until patients are in the stable phase of the disease. The one exception to this is when patients have vision threatened by optic neuropathy or corneal ulceration that is not responsive to systemic steroids. In these cases emergent orbital decompression is appropriate and typically very successful in sparing the patient's vision.

Surgical rehabilitation in Graves' disease can involve as many as three stages: orbital decompression, extraocular muscle surgery and eyelid surgery. These surgeries are most commonly performed by an ophthalmic plastic surgeon. Surgery is customized to the individual patient's needs. In the most severe cases, all three stages of surgery are required because each phase of surgery can impact the next stage. In less severe cases it may only be necessary to do eyelid surgery.

Graves' eye disease typically impacts middle-aged patients. The alteration in facial appearance is as disturbing to these patients as the alteration in visual function.

In the last decade, many improvements have been made in the efficacy and safety of surgical rehabilitation, resulting in a

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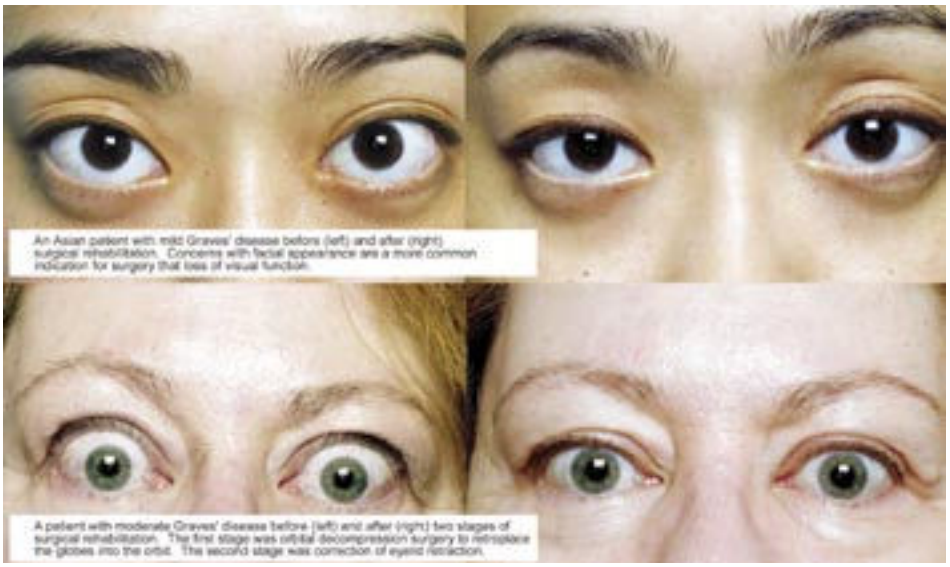

An Asian patient with mild Graves' disease before (left) and after (right) surgical rehabilitation. Concerns with facial appearance are a more common indication for surgery that loss of visual function.

A patient with moderate Graves' disease before (left) and after (right) two stages of surgical rehabilitation. The first stage was orbital decompression surgery to retroplace the globes into the orbit. The second stage was correction of eyelid retraction.

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number of rooms that are currently available. This will mitigate any impact the construction might have on volume. The temporary ED site will not interfere with the AirMed air ambulance service.

The new entrance to the temporary ED will be located at the current entrance to the Cancer Treatment Center, which will accommodate both ambulances and walk-ins. A new parking plan calls for additional parking lots and the introduction of valet parking for patients.

The hospital currently treats more than 22,000 people annually in its Emergency Department and this expansion allows Ogden Regional to better manage the fast-growing population in the area. The renovation will include 17 private exam rooms.

The $11 million project is scheduled for completion in July 2007.

LDS HOSPITAL AGAIN RANKED ONE OF AMERICA'S BEST HOSPITALS IN *U.S. NEWS & WORLD REPORT* MAGAZINE'S 2006 RANKINGS OF NATION'S TOP HEALTH CARE CENTERS

For the fourth year, LDS Hospital has been ranked as one of best hospitals in America, according to *U.S. News & World Report* magazine's 2006 rankings of the top medical facilities in the nation.

LDS Hospital, Utah's largest medical facility, is the only hospital in the state ranked among the nation's top 50 centers in four different medical specialties.

U.S. News & World Report ranks LDS Hospital 37th in the nation for orthopedic care, 41st for the treatment of respiratory disorders and pulmonary medicine, 43rd for endocrinology or diabetes care and 49th for urology.

Out of nearly 5,200 hospitals, only three percent — 176 in all — are ranked by the magazine in one specialty. Even fewer are ranked in multiple specialties, like LDS Hospital.

"This is wonderful recognition for our incredible medical staff and all of our employees who strive to make a difference in the lives of our patients each and every day," says Mikelle Moore, LDS Hospital Administrator. "This honor is yet another confirmation of what residents of the Intermountain West already know: the most comprehensive care available in the world is right here in our own community. I want to extend my deepest appreciation to all of our team at LDS Hospital for their dedication and commitment to excellence."

Hospitals were ranked in 16 different categories. Initial eligibility for these data-driven specialties required ranked hospitals to meet any of three standards: membership in the Council of Teaching Hospitals, affiliation with a medical school or availability of at least nine out of 18 key technologies like shaped beam radiation, advanced cancer therapy, etc. This year, less than a third of the hospitals qualified.

Hospitals were then judged on mortality rates, reputation and a mix of care-related factors such as nursing (that is, nurse/patient ratios and magnet designated hospitals) and other patient services.

The objective of the Best Hospitals in America survey is to identify centers that take on and excel at tough procedures and conditions — rare cancers, worsening heart failure, seeming untreatable leg-artery blockages, according to the magazine.

"That's why most of the institutions ranked are referral centers, where the sickest patients are sent for advanced care. Such hospitals follow — and often pioneer — new treatment guidelines. They conduct bench-to-bedside research. And they use the latest advances in imaging, surgical devices and other technologies to ensure the highest quality of care for patients," writes *U.S. News & World Report*.

LDS Hospital, which has served the Intermountain West for 102 years, serves as a major referral center for more than 75 hospitals throughout the Intermountain Region. LDS Hospital is one of only two Level I adult trauma centers serving Utah and is actively involved in more than 200 clinical research projects. ■

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widening of the indications for surgery. Historically, surgery was only available for patients with imminent loss of vision. Today a desire to have facial appearance reverted to the premorbid state is a more common indication for orbit and eyelid surgery than alteration in visual function.

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