CORNEAL RESEARCH

Investigators examine challenges in treating infectious keratitis and the association between thyroid function and keratoconus status.

BY FARHAD HAFEZI, MD, PHD, FARVO

THE PERSISTENT DILEMMA OF MICROBIAL KERATITIS: GLOBAL BURDEN, DIAGNOSIS, AND ANTIMICROBIAL RESISTANCE

Ung L, Bispo PKM, Shanbhag SS, Gilmore MS, Chodosh J[1]

Industry support: No

ABSTRACT SUMMARY

In this review article, Ung et al note that "current epidemiological data suggest that microbial keratitis may be epidemic in parts of the world—particularly within South, Southeast, and East Asia—and may exceed at least 2 million cases per year worldwide." They found that etiologic patterns differ between economically developed and developing regions: Bacterial keratitis was the predominant form in developed countries (principally due to contact lens use), and fungal keratitis was predominant in developing countries (where agriculture and trauma to the eye caused by vegetable matter are common). The investigators review the challenges of diagnosing microbial keratitis. They note that cultures and staining methods achieve positive results approximately 50% of the time with bacterial causes and 27% to 62% of the time with fungal causes, which makes choosing a targeted antimicrobial agent challenging.

These trends are worrisome in the context of emerging antimicrobial resistance. Ung and colleagues devote a section of their literature review to this topic. They state that there is "a clear trend toward resistance to commonly prescribed empirical antibiotics, which include fluoroquinolones and fortified antibiotics," and that "bacterial resistance to the leading fourth-generation fluoroquinolone antibiotic, moxifloxacin, is already at concerning levels."

For example, 26% of all organisms cultured at Wills Eye Hospital in Philadelphia were found to be resistant to moxifloxacin,[2] as were 35% of all *Staphylococcus* and *Streptococcus* species isolated at the Francis I. Proctor Foundation in San Francisco.[3] In India, susceptibility to moxifloxacin for coagulase-negative *Staphylococcus* species and methicillin-sensitive *Staphylococcus* has been reported to be as low as 61.2% and 53.1%, respectively.[4]

DISCUSSION

It is no secret that there is a paucity of new antibiotics in the

STUDY IN BRIEF

▶ Ung and colleagues performed a literature review of all English-language articles listed on PubMed, Medline, Embase, and Web of Science that contained the keywords *microbial keratitis*, *bacterial keratitis*, *fungal keratitis*, *infective keratitis*, and *acanthamoeba keratitis* published since 2000 that involved more than 200 patients and/or corneal scrapes for which the identification of etiologic agents was available. The investigators identified 65 studies matching these criteria and reported the prevalence of infectious keratitis in different regions of the world, the diagnostic accuracy of tests to ascertain which pathogen is present, and the success rates of different antimicrobial agents (eg, antibiotics and antifungal drugs) for treatment.

WHY IT MATTERS

Infectious keratitis is a fast-moving, sight-threatening disease that can be caused by a number of different organisms. Determining the pathogen or mix of pathogens present in an ulcer is challenging because cultures and stains are slow to perform and often fail to give a result. Exacerbating these problems is an increase in antimicrobial resistance of the causative organisms. This study illustrates the true scale of the disease and the challenges faced by ophthalmologists when trying to treat it.

pipeline and that antimicrobial resistance is increasing. With several million cases globally per year, infectious keratitis has been described as a *silent epidemic* by the World Health Organization. This situation may rapidly become catastrophic if novel antimicrobial agents or other approaches to treating corneal infections do not become available. This study by Ung and colleagues also makes it clear how challenging infectious keratitis is to diagnose accurately and treat appropriately, even with currently effective treatments.

Given that infectious keratitis can cause scarring and permanent visual impairment, its consequences for patients, their families, and society in general can be profound. This is particularly true in countries where patients' access to care from eye care specialists is limited and costly, the population is mostly rural and poor, and surgical ORs for procedures such as keratoplasty to treat corneal scarring are expensive and concentrated in major cities.

ASSOCIATION BETWEEN KERATOCONUS AND THYROID GLAND DYSFUNCTION: A CROSS-SECTIONAL CASE-CONTROL STUDY

El-Massry A, Doheim MF, Iqbal M, et al[5]
Industry support: No

ABSTRACT SUMMARY

Investigators assessed the corneas and thyroids of every patient in this study. Corneal topography was measured (flat, steep, and maximum simulated keratometric readings) with the Pentacam (Oculus Optikgeräte). Blood serum concentrations of thyroid-stimulating hormone, free triiodothyronine, and free thyroxine were measured using an enzyme-linked immunosorbent assay. Patients with thyroid-stimulating hormone, free triiodothyronine, or free thyroxine readings that were outside of normal reference ranges were referred to experienced endocrinologists for further examination.

The investigators found that 10 of 187 (5.3%) patients with keratoconus had thyroid gland dysfunction compared to two of the 187 (1.1%) control patients (P = .036). Predictably, there were also significant differences in the mean flat, steep, and maximum simulated keratometric values in each group (P < .001). Of the 10 patients with keratoconus and thyroid gland dysfunction, two of eight were men.

STUDY IN BRIEF

▶ In this cross-sectional case-controlled study, investigators sought to determine whether there is an association between thyroid gland dysfunction and keratoconus. The study enrolled 187 patients with keratoconus (Amsler-Krumeich grades 1–4) and 187 age- and sex-matched control patients who did not have keratoconus. Thyroid dysfunction was present in significantly more patients with keratoconus (5.3% vs 1.1%, P = .036).

WHY IT MATTERS

The prevalence of keratoconus is considerably greater than was once thought,[6-9] as has been demonstrated by studies that have used modern diagnostic techniques such as corneal topography and tomography to detect corneal irregularities. These diagnostic approaches are revealing more patient groups who are at increased risk of developing keratoconus and other corneal ectasias, including those that can occur after refractive surgery. Identifying these patients, treating them, and excluding them from laser refractive surgery is therefore important.

DISCUSSION

This study is the first in the literature to compare cases and controls for sex, age, and relevant comorbidities. Its results support and reinforce previous studies that have found a positive association between thyroid dysfunction and keratoconus.[10-16] There is plenty of evidence: At the molecular level, tear thyroxine levels have been found to be two to 50 times higher in patients with keratoconus than in patients without ocular disease. These levels rise as keratoconus progresses and decline as the condition stabilizes.[17]

Despite the significant association between keratoconus and thyroid gland dysfunction observed in this study, a significant majority of patients with keratoconus did not display signs of thyroid dysfunction, which adds to the evidence that a multitude of factors can cause keratoconus. ■

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