Watch for Tattoo-Related Uveitis: **An Emerging Concern**

patient comes to you with nonspecific signs and symptoms of uveitis. You consider the potential causes and connections. Would tattoos be on your list?

In the last few years, a flurry of case studies and letters to the editor have pointed to an association between tattoos and uveitis—in which tattoo inflammation and ocular inflammation occur concurrently with no obvious systemic etiology. But the link is unclear. Is the tattoo triggering uveitis? Is there an underlying inflammation that is manifesting in both the eye and

Although tattoo-related uveitis is uncommon, its possibility should be considered in patients with tattoos, said Gary N. Holland, MD, at the University of California, Los Angeles. For one thing, there may be more cases than you think. According to a 2015 Harris poll, 29% of U.S. adults have a tattoo.1 Moreover, tattoo-related uveitis is not something you want to overlook. "It is likely to result in chronic inflammation that may need immunosuppression to prevent blinding complications," said Dr. Holland.

Presentation and Risks

Patients may present with either anterior uveitis or panuveitis, and the manifestations may run the gamut, said James P. Dunn, MD, at Wills Eye Hospital in Philadelphia.

Signs and symptoms. Typical signs and symptoms of severe anterior tattoo-related uveitis at onset include blurring of vision, pain, sensitivity to light, and redness, said Dr. Holland. "It is likely to show up as a sticky kind of uveitis with lots of posterior synechiae," added Dr. Dunn. "Most of the cases are bilateral or, if not, at least asynchronous anterior uveitis—more commonly nongranulomatous than granulomatous. Sometimes there is a lag period between the two eyes."

Ophthalmic complications. These patients are at risk for severe visionlimiting complications, said Dr. Holland, including cystoid macular edema, pupillary membranes, pupillary seclusion with iris bombe, and uveitic glaucoma.2

Some patients end up needing glaucoma surgery, added Kisha Piggott, MD, PhD, who recently published a case study about such a patient.3 "In our patient's case, however, we were able to control eye pressure with topical glaucoma medications," said Dr. Piggott, at the Washington University School of Medicine in St. Louis.

Other complications. Infection is another risk related to tattoos, said Dr. Holland. "Just as patients can get nontuberculous mycobacterial infections from contaminated equipment used in LASIK, they may also get infection of the tattoo from contaminated ink or other tattoo parlor equipment."



A SKIN-EYE ASSOCIATION. One of Dr. Dunn's patients diagnosed with tattoo-related uveitis presents with induration of his black tattoo.

What's the Link?

The association between tattoos and uveitis is not entirely clear, said Dr. Dunn. Depending upon the extent of the disease, different processes may be involved. "Some people just get tattoo granulomas and uveitis—perhaps a type of delayed hypersensitivity," he said. "For unknown reasons, others get more severe, systemic disease, where other factors such as genetics may have come into play."

Inflammatory response. The assumption has been that something in the tattoo itself is triggering the process, said Dr. Dunn. "However, it may be the other way around. An inflammatory process may actually be affecting the tattoos." He points to a report of a

BY ANNIE STUART, CONTRIBUTING WRITER, INTERVIEWING JAMES P. DUNN, MD, GARY N. HOLLAND, MD, AND KISHA PIGGOTT, MD, PHD.

French patient who developed tattoo granulomas and uveitis following initiation of immunotherapy.4 "This suggests that the tattoos may be a site of the inflammation, but not the primary cause."

Like sarcoidosis, but not? The inflammatory response in these cases can resemble sarcoidosis, said Dr. Holland, who calls it "sarcoidosis-like."

"Because it is so rare, tattoo-related uveitis has been difficult to study, and insufficient longitudinal patient followup exists," said Dr. Piggott. "Do patients with an otherwise negative systemic workup represent a subset of yet-to-bediagnosed sarcoid patients, or a distinct patient population?"

An allergic reaction? "If this were a true allergy, we would expect more diffuse inflammation of the entire tattoo," said Dr. Piggott. "But most cases have segmental inflammation or nodularity of the tattoo in different areas, which is more consistent with delayed hypersensitivity than an allergic response."

Typically, uveitis symptoms make an appearance at a minimum of six months after tattoo placement, said Dr. Piggott.

Delayed hypersensitivity reaction.

Her patient experienced a two-year delay and was referred to her with a history of inflammation in the eye, correlating temporally with tattoo inflammation, induration, and slight redness of the tattooed skin.

If this is a delayed hypersensitivity reaction, she said, it remains unclear whether it's due to a dye contaminant or to the heavy metals or other organic compounds that constitute the ink. In some individuals, said Dr. Holland, only one color in the tattoo will be associated with inflammation. "The cause is difficult to determine since the tattoo ink composition is largely unregulated," said Dr. Piggott.

Pinning It Down

The first step toward diagnosis is to get a complete history. Asking about tattoos is now a standard part of Dr. Dunn's review of systems. "You can't always see the tattoos, and patients often won't think to bring up induration of the tattoos," he said. "But if you don't ask about it, you may not consider it."

Questions to ask. It may be difficult for the patient to make the connection between skin and eye involvement, added Dr. Piggott. "Get more information and think broadly when obtaining the patient history. Include open-ended questions during the review of systems, allowing the patient to describe any atypical occurrences in the past few months or years."

If a patient has unexplained uveitis, said Dr. Holland, ask the patient, "Do you have any tattoos? Are any of your tattoos swollen or itchy?" That might unearth valuable clues, but it doesn't obviate the need to evaluate the patient for other more common causes, including sarcoidosis.

How will you know that the connection between skin and eye inflammation is not just coincidental? Dr. Holland said, "There is typically a temporal association: The uveitis and tattoo swelling will have started within a similar time period."

To rule out other potential causes, ask about any history of tuberculosis or sexually transmitted diseases, said Dr. Piggott. "The goal is to determine whether this is an infectious or inflammatory cause. When inflammation is present, the knee-jerk response may be to treat with local or systemic antiinflammatory medications, but we know that there are many infectious causes of inflammation."

Dermatological exam. If you're unsure about the diagnosis, but suspect that uveitis might be linked to tattoos, said Dr. Dunn, consider referring the patient to a dermatologist for a fullbody exam.

Potential tests. There is no standard workup, but testing is usually directed at possible causes of granulomatous disease. Some doctors will test for angiotensin-converting enzyme or C-reactive protein and use results as a marker of general inflammatory burden, said Dr. Dunn. Some may also conduct thyroid studies because of potential links to thyroid disease and other autoimmune diseases, he noted.

Although punch biopsies are rarely done, Dr. Piggott did order one of her patient's tattoo. "It was helpful in making the diagnosis after ruling out

other common causes." Dr. Dunn does not routinely refer patients for punch biopsies. However, he said, if the extent of skin disease indicates a greater likelihood of systemic disease, a punch biopsy might help confirm diagnosis.

Treatment-Resistant Problem

In some cases, patients will need what amounts to lifetime therapy for tattoorelated uveitis, but spontaneous remission is possible, said Dr. Dunn.

The goal is to figure out the underlying cause of the uveitis, said Dr. Piggott. The ocular inflammation can be treated with topical or periocular steroids, for example, but many patients require systemic treatment.

Work with a dermatologist. Although dermatologists are likely to be familiar with skin reactions from tattoos, some may not be aware that they can cause eye complications as well, said Dr. Holland. "It's important to work as a team to control both skin and eye reactions."

Manage patients' pain. The skin lesions can be extremely irritating; they may cause severe pruritis and a lot of pain, said Dr. Dunn. "The dermatologist may have therapy for the skin lesions that wouldn't necessarily respond well to systemic corticosteroids."

Suppress inflammation. "To prevent uveitic complications, initially suppress the anterior segment inflammation with local corticosteroids, as you would for any noninfectious cause of uveitis," said Dr. Holland. He added that maintaining suppression with corticosteroid eye drops is not an appropriate longterm strategy.

Immunomodulatory therapy may be needed. "When we tapered the topical corticosteroids in our most recent patient, the inflammation and symptoms came back," said Dr. Holland. In many cases, these patients require immunomodulatory therapy such as methotrexate to maintain control of the inflammation.

"The most striking finding for me has been the severity of the uveitis and how resistant it has been in some patients," said Dr. Dunn. "We've started patients on topical steroids, then moved to steroid injections or systemic

steroids. But immunosuppressants are often needed to get it controlled. Even then, uveitis has not always been consistently controlled and may recur."

As a result, he advised, "If you're not comfortable managing patients with aggressive immunosuppressant therapy, get them to a uveitis specialist quickly."

Is Tattoo Removal Appropriate?

Some data suggest that excising tattoos may alleviate the uveitis, said Dr. Dunn. "In our experience, however, most of these patients have multiple tattoos, and removing them is simply not practical, especially since it would be challenging to do adequate skin grafting."

If a patient wants a tattoo removed, the procedure may be done with laser. However, although the tattoo may no longer be visible on the skin, removal disperses the ink into the body. "If ink is the inciting factor, dispersing it won't make uveitis better—it might make it worse," Dr. Holland said. Newer dyes in development may be completely destroyed by laser.

1 https://theharrispoll.com/tattoos-can-take-any-number-of-forms-from-animals-to-quotes-to-cryptic-symbols-and-appear-in-all-sorts-of-spots-on-our-bodies-some-visible-in-everyday-life-others-not-so-much-but-one-thi/.

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- 3 Piggott KD, Rao PK. *JAMA*. 2019;321(7):699-700.
- 4 Reinhard R et al. *J Eur Acad Dermatol Venereol*. 2017;31:e375-e377.

Dr. Dunn is director of the uveitis unit at Wills Eye Hospital in Philadelphia. Relevant financial disclosures: None

Dr. Holland is director of the Ocular Inflammatory Disease Center at the UCLA Stein Eye Institute, at the University of California, Los Angeles. *Relevant financial disclosures: None.*

Dr. Piggott is an assistant professor of ophthalmology at the Washington University School of Medicine in St. Louis. *Relevant financial disclosures: None.*

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