QUESTION

29

A Corneal Infiltrate Is Unresponsive to Topical Fluoroquinolones. Could This Be Acanthamoeba?

Elmer Y. Tu, MD

Acanthamoebae are free-living amoebae that form a resilient thick-walled cyst in harsh conditions. Keratitis is the most common human disease associated with *acanthamoeba* and should be considered in any patient with a corneal infiltrate that does not respond appropriately to traditional topical antibiotics because neither form is sensitive to these agents. Suspicion should be especially acute in contact lens-related (>85% to 90% of *acanthamoeba* keratitis (AK) cases in Western countries) infiltrates and/or exposure to non-sterile water as well as outdoor trauma.[1] However, fluoroquinolone resistance is not restricted to acanthamoeba, so this differential must include viral, fungal, other parasitic, and increasingly fluoroquinolone-resistant bacterial pathogens such as *Streptococcus species* and methicillin-resistant Staphylococcus aureus (MRSA).

Evaluation and Diagnosis

The clinical presentation of AK may range from diffuse epitheliitis, mild foreign body sensation with little or no stromal involvement (Figure 29-1) to the stromal ring-shaped infiltrate, radial keratoneuritis, and severe intractable pain nearly diagnostic of the infection (Figure 29-2). Disease is bilateral in up to 10% of AK and may be polymicrobial, previously identified concomitantly with viral, fungal, and bacterial pathogens.[2] Because of the specificity and long duration of therapy, definitive microbiologic diagnosis is preferred, including histologic smears of corneal scrapings (Giemsa, Wright, Diff-Quik, KOH prep,

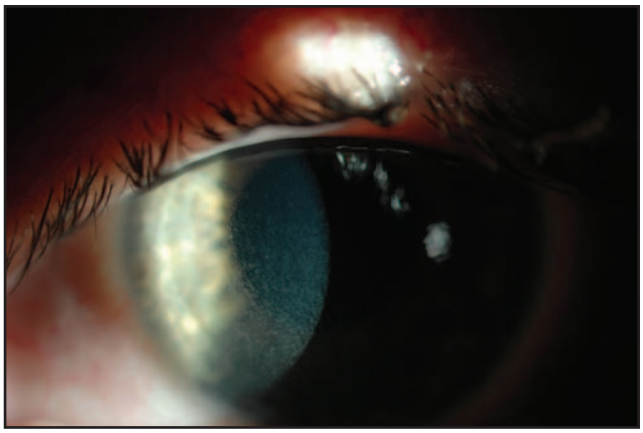

Figure 29-1. Slit-lamp photo of a contact lens wearer with AK clinically restricted to the epithelial layer. Smears and confocal microscopy were grossly positive for the organism.

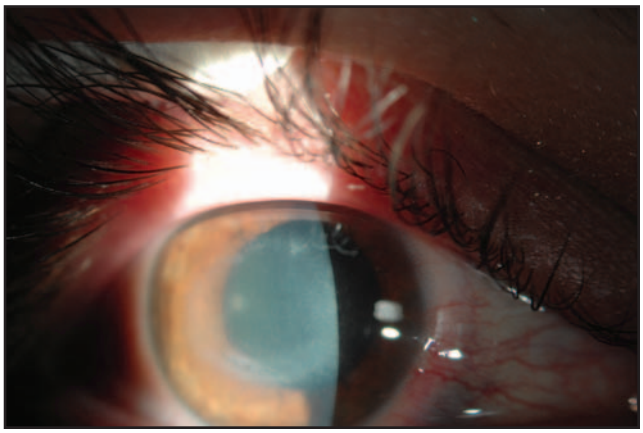

Figure 29-2. Slit-lamp photo of advanced *acanthamoeba* keratitis showing a classic immune ring infiltrate with central haze and minimal necrosis nearly pathognomonic for AK.

Calcafluor White, and others) or culture (non-nutrient agar with *Enterobacter* overlay). Of these methods, sensitivity and specificity is highest for histologic methods, while cultures are positive in only 0% to 50% of clinical cases of AK.[3] Corneal biopsy or polymerase chain reaction (PCR) may also be considered.

Confocal microscopy has been extensively used in the diagnosis of AK. Two units are currently available, the Confoscan 4 (Nidek Technologies, Padova, Italy) and the HRT Rostock Corneal Module (Heidelberg Engineering, Heidelberg, Germany), both of which offer *en face* serial sections of the cornea with high magnification and resolution, allowing in vivo imaging at a cellular level. Cysts are characteristically bright reflective circular opacities, sometimes with internal structures visible (Figure 29-3). In centers familiar with its use, sensitivity and specificity of confocal microscopy in the diagnosis may both exceed 90%.[3] Other imaging modalities have limited utility in AK.

Management

In the United States, no commercially available topical medications are effective for AK. We strongly recommend mechanical debridement of any clinically involved epithelium to debulk the infectious load and obtain tissue samples. Rarely, this alone may be curative in

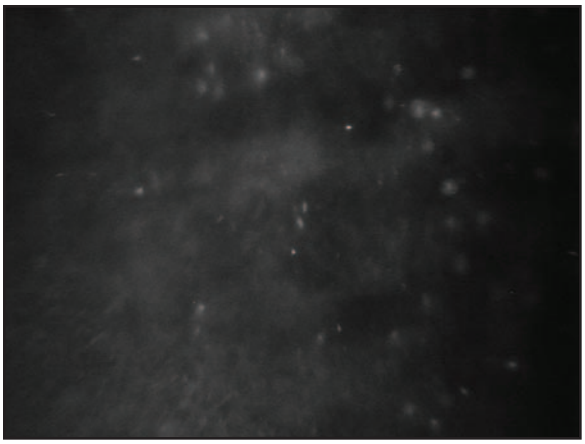

Figure 29-3. Confocal microscopy showing multiple bright centered cysts in the anterior stroma (upper and right portions of the scan). Note that the appearance varies significantly with lighting and position.

epitheliitis, but we only use this as an adjunct to specific medical therapy. Primary topical therapy for AK is either chlorhexidine gluconate 0.02% (CHG) or polyhexamethylene biguanide 0.02% (PHMB) (Bacquacil), available only from ophthalmic compounding pharmacies. We maintain hourly dosing for the first 3 to 7 days with a gradual taper over the first month to 4 times a day, continued for several months with a more gradual taper. However, the management is highly dependent on response to these medications with some patients treated for as little as a few weeks and others, usually those with deeper stromal involvement, requiring frequent dosing for an extended period of time. Because these agents have similar mechanisms of action, we do not commonly use them together, preferring to vary concentration and/or frequency. We prefer CHG because it is better tolerated and can be increased in concentration to 0.04% or 0.06% if needed,[4] although some AK will be more responsive to a change to PHMB.

The diamidines, propamidine isethionate 0.1% (Brolene) and hexamidine isethionate 0.1% (Desmodine), are mostly effective against the trophozoites and are prescribed hourly for the first few days with a rapid taper over the first month before surface toxicity ensues. Other previously described topical agents (eg, neomycin, clotrimazole, etc) have no role in our current treatment algorithm for routine AK.

When Should Systemic Therapy, Steroids, or Therapeutic Keratoplasty Be Considered?

Because topical therapy is usually sufficient, routine systemic therapy is unnecessary. In advanced or poorly responding cases of AK, oral itraconazole (suspension preferred for greater absorption) has been described, although our own experience has been disappointing. Intravenous pentamidine and some of the newer systemic antifungals may be more effective but have not been extensively studied. Therapeutic keratoplasty is successful in recalcitrant cases or in impending perforations but with a guarded prognosis for failure, secondary glaucoma, and recurrent infection. The role of corticosteroids, both topical and systemic, is controversial with no clear evidence of detrimental effect on final outcome. Practically, we attempt to rapidly discontinue, or reduce to the lowest effective level, topical and systemic corticosteroids in patients presenting with AK. Because most

extracorneal manifestations of AK are thought to be inflammatory, we will add or continue corticosteroids in cases of intractable limbitis, scleritis, and/or uveitis unresponsive to anti-acanthamoebal therapy.

How Should the Clinical Response Be Assessed and Duration of Treatment Determined?

The assessment of clinical response can be challenging in AK. The presence of epithelial infestation and radial keratoneuritis is easy to assess and usually resolves rapidly, although radial keratoneuritis may uncommonly scar exuberantly. Stromal disease is more difficult to evaluate because the borders of the keratitis are diffuse and inflammation does not always correlate with infectious activity. While some cases of post-infectious sterile corneal inflammation have been described, persistent keratitis, unlike the extracorneal manifestations, should be considered infectious unless proven otherwise. When corticosteroids are used, a constant level should be maintained to permit interval assessments of inflammatory activity as an indirect indicator of disease activity. It should be noted that viable amoeba have been recovered months to years after initial symptoms, but usually with continuing treatment. By convention, a period of 3 months of quiescence off of all medications should be observed before cure is assumed, but recurrences may rarely occur after this period.

References

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