Atypical mycobacterial infections are frequent, late complications of human immunodeficiency virus infections and may have a variety of clinical manifestations. We describe a patient with end-stage acquired immune deficiency syndrome and disseminated atypical mycobacteriosis caused by *Mycobacterium avium-intracellulare* complex, with prominent iris nodules as the initial manifestation of a unilateral localized panophthalmitis. Acid-fast bacilli were identified cytologically from the iris nodule and aqueous aspirations. Topical, intracameral, and systemic treatments were used, but the infection progressed and enucleation was performed to avoid the impending scleral rupture. Histopathologic studies revealed an anterior panophthalmitis, with inferior scleral rupture due to acid-fast bacilli in the eye. *Mycobacterium avium-intracellulare* complex has been described as a cause of endophthalmitis in immunocompromised patients but, to our knowledge, this is the first report of a patient with iris nodules.


*Mycobacterium avium-intracellulare* complex is an endemic, atypical mycobacterium of minimal virulence in immunocompetent hosts. It consists of *M avium* and the morphologically and biochemically similar *M intracellulare*; they are grouped as *M avium-intracellulare* complex (MAC). Both belong to the Runyon atypical mycobacterium group 3 and are slow-growing, non-chromogenic pathogens that are distributed worldwide and throughout the environment. In immunocompetent hosts, colonization with MAC usually does not lead to clinically significant disease. In patients with acquired immune deficiency syndrome (AIDS), however, MAC is the most common cause of systemic bacterial infections in the United States. We describe a patient with end-stage AIDS and disseminated MAC presenting with iris nodules as the initial manifestation of an anterior panophthalmitis.

**REPORT OF A CASE**

A 46-year-old woman who was positive for the human immunodeficiency virus had a CD4 count of 0.005 × 10⁹/L had a 1-week history of pain, redness, and decreased visual acuity in the right eye. She reported fevers and weight loss but denied a productive cough and night sweats. The results of a purified protein derivative (tuberculin) test 10 months previously were negative; there was no record of a simultaneous anergy panel. There were intercurrent lower limb skin ulcerations, draining septic arthritides of several metacarpophalangeal joints, and oral candidiasis. Her medications included sulfamethoxazole-trimethoprim, zidovudine, and fluconazole.

Ophthalmologic examination findings revealed a best-corrected visual acuity of 20/300 OD and 20/20 OS. Intraocular pressures were 25 mm Hg OD and 18 mm Hg OS. Biomicroscopy of the right eye showed diffusely vasodilated conjunctiva and microcystic corneal edema with epithelial punctate staining and keratic precipitates. A 5% hypopyon with cells (++) and flare was evident in the anterior chamber. Numerous anterior iridic nodules measured up to 1 mm in diameter and were scattered midperipherally. A 3×3-mm lobulated mass at the 9-o’clock position extended from the iris surface to the pupillary border (Figure 1). The pupils showed...
no abnormalities. Dilated funduscopy disclosed rare cells in the anterior vitreous of the right eye and a normal fundus. The left eye showed no abnormalities.

Laboratory test results were notable for an elevated alkaline phosphatase level of 169 U/L (reference range, 30-115 U/L); leukopenia with a white blood cell count of 2.8 × 10^9/L (reference range, 4.8-10 × 10^9/L); and an erythrocyte sedimentation rate of 100 mm/h (reference range, 0-20 mm/h). A chest x-ray showed no abnormalities.

A paracentesis of the right anterior chamber, aspiration of the iris nodules, and metacarpophalangeal joint and leg ulcer scrapings were performed. Sputum and urine specimens were collected for microbiologic study. Cytologic examination of these specimens demonstrated numerous acid-fast bacilli (AFB) (Figure 2); however, only the sputum and urine cultures were positive for AFB after 6 weeks. The sputum bacilli were identified as MAC by DNA probing. Specific culture media for Mycobacterium tuberculosis, Mycobacterium marinum, and Mycobacterium haemophilum were used but failed to isolate AFB from any of the specimens. Blood cultures were also negative for various fungi and bacteria, including M tuberculosis and MAC.

The patient was treated with ethambutol hydrochloride, pyrazinamide, rifampin, and isoniazid with pyridoxine for disseminated M tuberculosis. Simultaneously she received topical prednisolone acetate and scopolamine hydrobromide to the right eye. During the initial 4 weeks of therapy, there was a good clinical response, with reduction of fever, gaining of weight, healing of skin lesions, and reduction of swelling around metacarpophalangeal joints. Total resolution of the iris nodules occurred and the visual acuity improved to 20/25 OD.

A relapse of the right endophthalmitis occurred 1 month later. The visual acuity measured 20/100 OD and the anterior chamber reaction was so florid it obscured fundus detail. The iris nodules recurred; the largest filled the anterior chamber and extended to the corneal endothelium. Intraocular pressure measured 56 mm Hg OD. Findings from a second cytologic examination of an anterior chamber aspirate confirmed the presence of AFB that again failed to grow on specific culture media.

Oral acetazolamide and ofloxacin and intramuscular amikacin were added to the systemic drug regimen and topical amikacin, ciprofloxacin, and timolol maleate drops were added to the right eye. Additionally, an intravitreal injection of amikacin was given. Over the ensuing 3 weeks, the right eye developed progressive scleral thinning inferiorly, a recalcitrant elevated intraocular pressure, and bare light perception visual acuity. Because of intractable pain and impending scleral rupture, the right eye was enucleated.

The enucleated globe grossly revealed marked anterior scleral thinning with an inferior limbal staphyloma. The cut surface of the transected globe demonstrated an inferior scleral rupture located 2 mm posterior to the limbus. A subconjunctival, dome-shaped mass of brown material was present (Figure 3, left). The anterior chamber was flat and the vitreous cavity contained scanty fluffy white material overlying the pars plana, inferiorly.

Results of a histopathologic study disclosed full-thickness scleral necrosis and rupture inferiorly, adjacent to the iris root (Figure 3, right). Overlying this area was a large subconjunctival mass of inflammatory cells and cellular debris. There was extensive necrosis of the iris and necrotic debris filled the anterior chamber. Scattered neutrophils, monocytes, melanophages, and free melanin pigment granules were observed within the vitreous, in the region of the pars plana, inferiorly. No inflammation was detected anywhere else in the sclera or choroid.

Numerous AFB were seen in the subconjunctival inflammatory mass, and in the adjacent corneoscleral lamellae, anterior chamber, iris, and ciliary body (Figure 4, left). These organisms were also demonstrated by electron microscopy intracellularly with phagosomes (Figure 4, right). Paraaffin-embedded tissue sections were used for polymerase chain reaction but failed to identify M tuberculosis, M haemophilum, or M avium.
The incidence of infections caused by atypical mycobacteria has increased with the onset of the AIDS pandemic. *Mycobacterium avium-intracellulare* complex is the cause of 95% of these infections. Disseminated MAC is considered a defining criterion for AIDS and typically occurs late in the course of the disease when the CD4 count is less than 0.05 × 10⁹/L. The infection can be definitively diagnosed by special blood culture techniques, the BACTEC 460³ system (Becton Dickinson Diagnostic Instrument Systems, Spark, Md) or the Dupont isolator (Isolator 10, Wampole Laboratories, Cranbury, NJ), as well as by DNA probes and DNA amplification techniques through polymerase chain reaction.

*Mycobacterium avium-intracellularare* complex may exist in humans as commensal organisms in respiratory secretions, urine, and stool. Although positive cultures from these sites alone are of questionable diagnostic value without the supporting evidence of positive blood cultures, detection of MAC at these sites may herald impending MAC dissemination in patients with end-stage AIDS.

Despite the absence of a confirmatory positive blood culture, our patient was considered to have disseminated MAC based on the clinical and laboratory findings. She had simultaneous endophthalmitis, septic arthritis, and cutaneous ulcerations; cytologic examination of these sites revealed an abundance of AFB. Although cultures from these sites were negative, the sputum and urine cultures grew AFB and the sputum organisms were later identified as MAC by DNA probing. Since the cultures failed to grow *M tuberculosis*, *M marinum*, or *M haemophilum*, the other mycobacteria that commonly cause simultaneous skin and joint infections,³⁶ we concluded that MAC was not simply a commensal organism but the infective agent.

The elevated alkaline phosphatase level and the leukopenia, both common findings in patients infected with MAC,¹ lend additional support for MAC infection in this case. The patient had a relapse after a 4-drug course of systemic antituberculous therapy and subsequently failed to respond to a 6-drug regimen, including ethambutol, amikacin, and rifampin, all of which are known to inhibit most strains of MAC.¹ Unfortunately, relapses commonly occur in patients with disseminated MAC. Because an optimal therapeutic regimen for

Figure 3. Left, Gross appearance of the enucleated right eye. Note the scleral necrosis and the perilimbal scleral rupture (arrowhead) located interiorly. The limbal conjunctiva covers a dome-shaped, brown mass. Right, Histopathologic appearance of the enucleated right eye with a subconjunctival necrotic and inflammatory mass. There is necrosis of the iris and the anterior chamber contains necrotic debris (arrowheads) (hematoxylin-eosin, original magnification × 5).

Figure 4. Left, High-power light microscopy of the perilimbal anterior segment demonstrates the presence of numerous acid-fast bacilli (arrowheads) (original magnification × 200). Right, Ultrastructurally, the bacilli are often intracellular, within phagosomes (arrowheads). Transmission electron micrograph (uranyl acetate-lead citrate, original magnification × 24,000).
disseminated MAC has not been definitively determined, our patient was treated with an empirical formulation.

Large areas of necrosis associated with chronic inflammatory cells and free and macrophage-ingested AFB are typical reactions to MAC. Results of histopathologic examination failed to demonstrate granulomas in the enucleation specimen, a common finding. In a study of 12 patients with MAC, Klaft et al found that only one third of cases had well-formed granulomas, while the remainder lacked the typical features of granulomatous inflammations, including the following: circumscribed necrosis, lymphocytic infiltration, and epithelioid and Langhans giant cells. Caseation has been described but is rare in immunocompromised hosts.

While iris nodules are a common manifestation of granulomatous inflammations of various origins, they rarely occur in mycobacterial infections. In tuberculosis, granulomas may be found throughout the uvea, most commonly in the choroid in the distribution of the posterior ciliary arteries, and only infrequently in the iris. Ocular infection results from hematicogenous spread in patients with miliary tuberculosis. In patients with iris involvement, the choroid is usually similarly affected. In contrast, MAC rarely causes endophthalmitis, even when disseminated, and to our knowledge, has not been reported with iris nodules.

Two cases of MAC endophthalmitis in immunocompromised patients with disseminated MAC have been reported. One patient positive for the human immunodeficiency virus who had undergone a prior trabeculectomy had M avium endophthalmitis that primarily affected the anterior segment. The filtration procedure was believed to have predisposed this patient to subsequent endophthalmitis. The other patient had reticulum cell sarcoma and a predominantly posterior segment infection. Both of these patients’ cases primarily involved the uveal tract and neither developed iris nodules. Our patient is unique for iris nodules in MAC endophthalmitis and the subsequent development of a localized anterior panophthalmitis.

With the increasing incidence and prevalence of AIDS, MAC has become an epidemic problem and ophthalmologists can expect to encounter patients with ocular MAC involvement. When endophthalmitis occurs in patients with end-stage AIDS, with or without iris nodules, the diagnosis of disseminated MAC should be considered.

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REFERENCES


A look at the past . . .

Ocular Changes Associated with Scrub Typhus

The eyes of 451 patients with scrub typhus were studied weekly for evidence of disease. The following external changes were seen: (1) conjunctival injection, 38 per cent; (2) subconjunctival hemorrhages, 6.4 per cent; (3) ecchymosis of the eyelids, 1.0 per cent; (4) eschar on the eyelid, 0.5 per cent; (5) fixation nystagmus, 0.5 per cent.

The following ocular changes were seen: (1) engorgement of veins, 67 per cent; (2) retinal edema, 36 per cent; (3) retinal hemorrhages, 6.6 per cent; (4) exudates, 4.9 per cent; (5) uveitis, 1.3 per cent; (6) vitreous opacities, 4.6 per cent.

Pathologic studies of eyes obtained at autopsy revealed that a subacute diffuse choroiditis was the basic lesion.