Onchocerciasis (River Blindness)

Capt Lance H. Borup, USAF, MC; MAJ John S. Peters, MC, USA; Lt Col Christopher R. Sartori, USAF, MC

GOAL

To gain a thorough understanding of onchocerciasis

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Explain the cutaneous and systemic manifestations of onchocerciasis.
2. Discuss the infection process of onchocerciasis.
3. Describe the treatment for onchocerciasis.

CME Test on page 296.

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A 37-year-old African man presented for excision of a dermal nodule after a diagnosis of ocular onchocerciasis (river blindness). A nodule from the patient's left buttock contained several adult filarial worms, and results from adjacent skin biopsy specimens revealed numerous dermal microfilariae. The patient was admitted to the hospital and treated with one dose of ivermectin. Recommendations were made for ivermectin treatments every 6 months for up to 10 years. The history, clinical presentation, diagnosis, and treatment of onchocerciasis are discussed.

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Dr. Borup is a resident at Osteopathic Medical Center of Texas, Fort Worth. Dr. Peters is Chief of the Dermatology Clinic, Martin Army Community Hospital, Fort Benning, Georgia. Dr. Sartori is Associate Clinical Professor of Dermatology at the University of Colorado School of Medicine, Denver, and Chief of the Dermatology Clinic, United States Air Force Academy Hospital, Colorado Springs, Colorado.

The opinions expressed are those of the authors and do not necessarily state or reflect those of the US military.

Reprints: Capt Lance H. Borup, USAF, MC, 7341 Moon Ridge Ct, Fort Worth, TX 76133 (e-mail: drlanceb@charter.net).

Onchocerciasis (river blindness) is an infectious disease common in west and central Africa, Central and South America, and the Arabian Peninsula. Onchocerciasis is the second leading infectious cause of blindness worldwide. Approximately 18 million people are infected with *Onchocerca volvulus*, of which 99% are in Africa.[1] *O volvulus* is a filarial nematode, the etiologic agent of onchocerciasis. The most common cutaneous manifestations of onchocerciasis

are intense pruritus, subcutaneous nodules, and localized erythematous papules and plaques with induration. Ocular pathology in onchocerciasis manifests as uveitis, punctate keratitis, and glaucoma. Diagnosis is made through slitlamp examination, as well as by demonstration of filarial worms on wet mount and hematoxylin-eosin (H&E) stained sections. Patients are treated with oral or intravenous ivermectin at a dose of 150 mg/kg once every 6 months for up to 10 years.[2]

We present the case of a US Army soldier originally from west Africa who was initially treated over a period of 2 years for conjunctivitis, uveitis, and a labile refractory glaucoma. After referral to ophthalmology and dermatology, a diagnosis of onchocerciasis was made.

Case Report

A 37-year-old African man presented to the glaucoma clinic for evaluation of refractory glaucoma in his right eye and for possible trabeculectomy. Numerous microfilariae were noted in the anterior chamber of both eyes on slitlamp examination. The diagnosis of onchocerciasis was made, and the patient was referred to the infectious diseases clinic, where further examination revealed subcutaneous nodules in his left buttock and left axilla. He then was referred to dermatology.

The patient was a poor historian and spoke limited English. His medical history was significant for ongoing flares of bilateral conjunctivitis and chronic uveitis. Originally from Sierra Leone, west Africa, he emigrated to the United States with his family 3 years previously and thereafter enlisted in the US Army. The patient reported intermittent blurred vision for many years and episodes of severely irritated watery eyes. He had no current complaints of rash or pruritus, but as a younger man he remembered having intermittent pruritus in his left inguinal area and in both eyes. He denied ever having a rash or other skin discoloration. His wife also complained of visual problems. He also recalled that in his village of Sierra Leone, most elderly people were blind. His 2 children, who were born in Sierra Leone, also reported a history of pruritic skin and blurry vision but were currently asymptomatic.

Two years before presentation, the patient was diagnosed with primary open-angle glaucoma. He had experienced atypical exacerbations and remissions. He reported right temporal field visual loss and cloudy vision bilaterally for 5 years. In addition, he had a history of hepatitis B, malaria, and a positive purified protein derivative (tuberculin) skin test, for which he was treated with isoniazid for 6 months. The patient denied any history of surgery. He had no known drug allergies, and his only medications were ophthalmic timolol, latanoprost, and dorzolamide. The remainder of his review of systems was unremarkable.

The patient was of normal height and weight, alert and oriented, and in no acute distress. Bilateral conjunctival injection without drainage or exudate was noted. Results of a cutaneous examination revealed 2 soft, mobile, nontender masses. One mass in the left axilla was superficial and measured 1.5 cm in diameter, while the other in the left buttock was deeper in the dermis and measured 3.0 cm in diameter. No lymphadenopathy or edema was detected. No acute or chronic papular dermatitis, excoriations, lichenifications, fine wrinkles, or depigmentation characteristic of onchocerciasis were appreciated.

Laboratory test results for liver function, prothrombin time, international normalized ratio, partial thromboplastin time, and chemistry panel were within normal limits. The complete blood count demonstrated a mild eosinophilia of 8.6%. Hepatitis panel was consistent with a chronic carrier state for subdeterminants of hepatitis B surface antigen (+), hepatitis B surface antibodies (−), and hepatitis B e antigen (−). Thick and thin peripheral blood smears performed in the afternoon and at midnight showed no other parasitic infections.

Excisional biopsy of the nodule in his buttock was performed and yielded a 1×2-cm diameter mass of fatty tissue with intertwined, white, hairlike worms encased in a thick fibrous capsule (Figure 1). The number of worms in the nodule and their lengths were not determined. Excisional biopsy of the axillary mass was performed, and results revealed a steatocystoma on standard H&E sections. Perilesional skin snips also were obtained.

Paraffin sections of an adult worm were prepared, placed on glass slides, and viewed at ×100 magnification (Figure 2). Histopathology was typical of subcutaneous nodules, with outer walls of dense fibrous tissue extending between the worms. Skin biopsy specimens extending just into the dermis were obtained from the left buttock, embedded into paraffin, and stained with H&E (Figure 3). Eosinophils were present around degenerating microfilariae. Progressive fibrosis of the dermis was present, and the epidermis showed acanthosis and hyperkeratosis.

The patient was admitted to the hospital, treated intravenously with one dose of ivermectin 10,000 mg (150 mg/kg), and monitored overnight. To prevent a hypersensitivity reaction secondary to massive microfilarial death, he was treated orally with both 25 mg of diphenhydramine every 6 hours

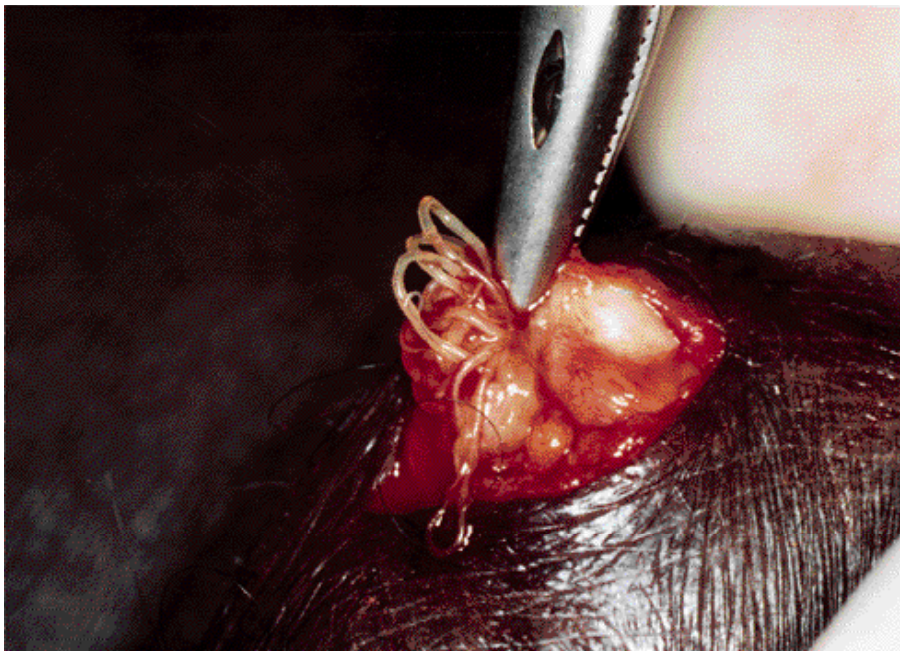

Figure 1. Buttock nodule (onchocercoma) containing fatty tissue with intertwined, white, hairlike worms.

and 25 mg of hydroxyzine, as needed, for itching. The patient tolerated the treatment well and was told he should be treated with ivermectin biannually for the next several years. He was discharged the following day.

Comment

O volvulus is 1 of 8 filarial nematodes that can infect humans and is endemic to west and central Africa, Central and South America, and the Arabian Peninsula (Figure 4). It is estimated that 17.7 million people are infected with *O volvulus*. More than 99% of these infections occur in sub-Saharan Africa. Nearly 1 million people today can attribute their blindness or severe visual impairment to onchocerciasis.[2,3] In areas near fast-moving water where the incidence of river blindness is high, villages cease to be economically viable and are deserted for less productive land, further away from the *Simulium* breeding sites.[4]

The parasite is spread among humans by the bite of an infected female *Simulium* blackfly, which breeds in fast-moving rivers. Once inside the human host, *O volvulus* larvae mature into adult worms (macrofilariae) and become encased in a soft tissue fibrotic nodule (onchocercoma). Inside the nodule, adult pairs mate and release 1300 to 1900 microfilariae per day for up to 9 to 11 years.[5] These tiny offspring (250–300 mm long) migrate through the dermis and commonly invade the anterior chamber and uvea of the eye, as was observed in our patient.

Subcutaneous microfilariae live 6 to 24 months, then die and cause a cutaneous host inflammatory response, which is responsible for the majority of clinical symptoms.[6] The initial dermatologic presentation includes intense pruritus, subcutaneous nodules, and localized discrete papules or plaques with erythema and induration. Chronic skin changes include areas of hyperpigmentation and hypopigmentation ("leopard skin") and lichenification. The cutaneous inflammatory response to the microfilariae leads to breakdown of dermal collagen and elastic tissue. The skin becomes progressively atrophic and wrinkled, leading to gross disfigurement and skin laxity (eg, "hanging groin").[7]

The common name for onchocerciasis, river blindness, is well deserved because of its potential for causing blindness in nearly one half of men and one third of women in some untreated, endemic areas.[3] It is the fourth leading cause of blindness worldwide.[8] Ocular pathology in onchocerciasis is caused by an intense eosinophilic and granulomatous response to dead and dying microfilariae. Frequently, this inflammatory process causes uveitis, which leads to glaucoma. Punctate keratitis is often present and, if left untreated, leads to sclerosing keratitis. Posterior segment lesions such as chorioretinitis and optic atrophy also have been observed.[9] Our patient's history of numerous episodes of conjunctivitis was related to irritation by microfilariae that were migrating to the cornea and the anterior chamber of the eye.[3,6]

Although our patient's condition was discovered by slitlamp examination, cutaneous biopsies known as *skin snips* are the most common diagnostic tool because they are simple and provide definitive

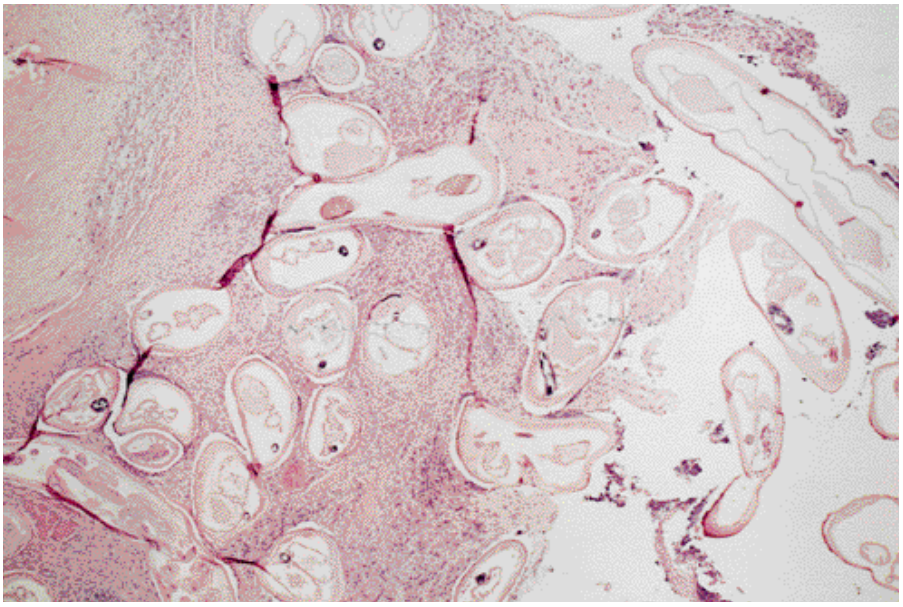

Figure 2. Adult worms within buttock onchocercoma prepared in paraffin sections reveals outer walls of dense fibrous tissue extending between the worms (H&E, original magnification ×100).

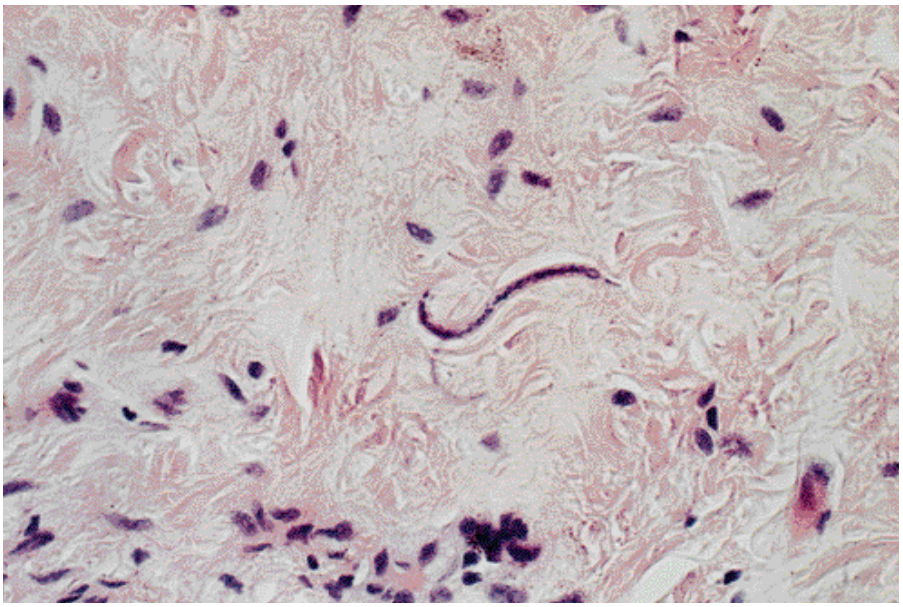

Figure 3. Microfilaria in profile, with numerous eosinophils in close proximity (H&E, original magnification ×400).

diagnosis. A razor blade is used to slice down to the dermal papillae to obtain a bloodless skin sample of 2 to 4 areas from the iliac crest or below.[10,11] After placing the specimens in warm saline for 10 to 60 minutes, motile microfilariae are visualized on a wet mount, using low-power microscopy. Fixed and stained specimens, blood examination, excised nodules, and DNA amplification with polymerase chain reaction also can be used if diagnosis is still questionable.[2,12]

Histologically, onchocercal microfilariae are characterized by a cephalic free space, followed by anterior nuclei that are side by side, a caudal space free of nuclei, and a tail tapered to a fine point (Figure 3). These features readily differentiate *O volvulus* from *Dipetalonema streptocerca*, which are the only other microfilariae that live in dermal collagen throughout the body.[13]

Onchocercomas measure on average 0.5 to 2 cm in diameter and often can be visualized or palpated.[14] These nodules can be misdiagnosed up to 5% of the time by physicians in endemic areas. Most commonly, they are confused with lymph nodes, lipomas, intradermal cysts, cancer, and foreign body granulomas. Our patient demonstrated an onchocercoma *deep* in his left buttock. Cutaneous incision

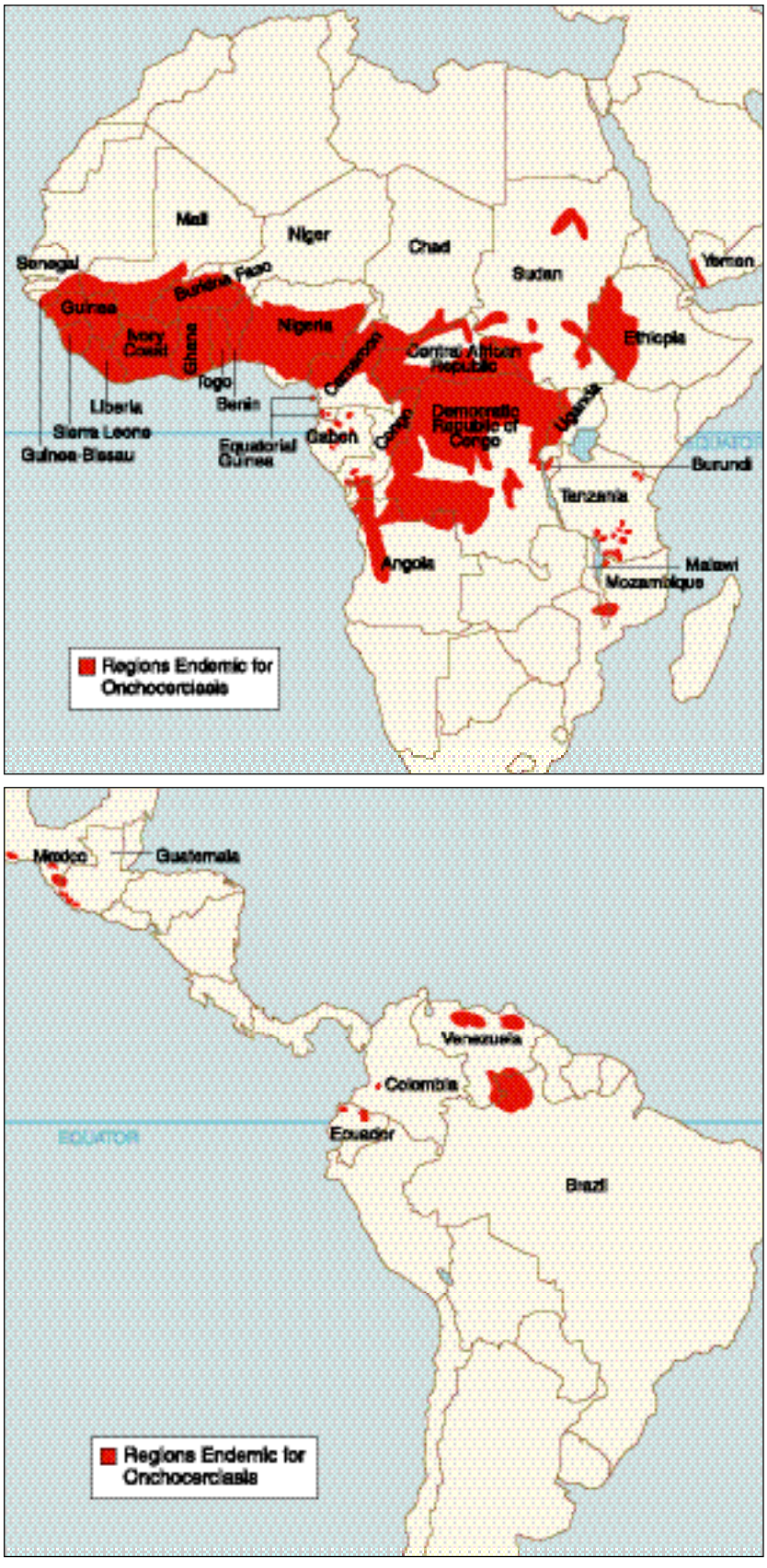

Figure 4. Distribution of onchocerciasis in Central and South America, west and central Africa, and the Arabian Peninsula.

and blunt dissection of an additional subcutaneous mass of the left axilla of our patient demonstrated a steatocystoma. Because some onchocercomas are deep in tissue around bones and in muscle and cannot be detected, nodulectomy of all palpable nodules does not always cure the patient. Nevertheless, nodulectomy should always be considered in patients who live outside endemic areas, as they have a low risk of reinfection, and might be cured if they do not have occult nodules.[5] Ultrasound has been effective in discovering nonpalpable lesions but only when technicians are trained in distinguishing onchocercoma morphology.[15]

The treatment of choice for onchocerciasis is one dose of oral ivermectin 150 mg/kg every 6 months for up to 10 years.[16-18] The drug works at the γ-aminobutyric acid receptors, impairing the neuromuscular function of the microfilariae, which leads to paralysis and death of most of the microfilariae 2 to 3 days after the first dose. The most common adverse effects of the medication are myalgia, rash, node tenderness and swelling, pruritus, fever, chills, and localized edema. These result from a hypersensitivity reaction to massive microfilariae death. Most side effects are usually mild to moderate and occur in 9% of patients.[19] Patients are treated semiannually, which is the lifespan of microfilariae. This optimizes the therapeutic benefit of the drug.[16]

Unfortunately, ivermectin does not kill adult worms that can continue to reproduce for many years. This is why nodulectomy is performed as an adjunct therapy semiannually. It is also why treatment may need to continue for up to 10 years—the lifespan of the adult worm.

In vitro research on potential macrofilaricidal compounds has given some promising leads.[20]

Because onchocerciasis has a devastating impact on millions of impoverished people worldwide, Merck & Co., Inc., established the Mectizan Donation Program in 1987, providing ivermectin treatments free of charge to all endemic areas. Since then, more than 250 million doses of ivermectin have been administered.[21] There is still no adequate vaccine. Only through continuous surveillance and treatment can this preventable cause of blindness be reduced or eliminated.

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