A 42-year-old white man with a past medical history of intravenous (IV) drug abuse, hypertension, diabetes mellitus, and chronic kidney disease presented to the emergency department with headache of 2 weeks’ duration accompanied by blurred vision, nausea, and frequent vomiting. His initial blood pressure (BP) was 259/152. Examinations of the heart, lungs, and abdomen were normal. The skin over the anterior chest showed a 2-cm × 2-cm indurated erythematous area with purulent drainage along with 2 smaller areas of induration over the right hemithorax that showed no surrounding erythema but had slight tenderness on palpation (Figure 1). Similar areas of induration were found over the scalp, which were found to be retroauricular lymphadenopathy. “Track marks” over flexor areas of both elbows also were found. Neurologic examination revealed a lethargic man, oriented in time, place, and person. No focal deficits were found. There was no papilledema. Because of his initial BP and lethargy the patient had been admitted initially to the intensive care unit with the presumptive diagnosis of hypertensive encephalopathy. Once his BP was controlled he was transferred to the floor.

A computed tomography scan of the chest revealed several focal lytic lesions in the cartilage of the rib cage anterior to the costochondral junction, which was associated with focal soft-tissue swelling. Blood and fungal cultures were negative. A fine-needle aspiration (FNA) of one of the chest nodules was performed and showed no evidence of malignancy. The culture of the aspirate grew Candida albicans. A second FNA of a different lesion reconfirmed the organism. Because of the patient’s complaints of blurred vision, the ophthalmology department was consulted and serial funduscopics were performed; evidence of choroidal lesions compatible with Candida endophthalmitis were found (Figure 2). A transesophageal echocardiogram did not show any evidence of vegetations. The patient tested negative for HIV.

**DISCUSSION**

**Epidemiology and Etiology**

Disseminated candidiasis in IV drug users is a distinctive syndrome, characterized by easily recognizable skin, eye, and osteoarticular lesions that are attributed mainly to C. Dr Rondon-Berrios is an internal medicine resident; Dr Khilnani is Program Director and Assistant Professor, Combined Internal Medicine-Pediatrics Residency Program; and Dr Trevejo-Nunez is an internal medicine resident, Department of Medicine, University of Texas Medical Branch, Galveston, Texas. Dr Rouan is Richard W. and Sue Vitter Professor of Clinical Medicine and Associate Chairman of Education, Department of Internal Medicine, School of Medicine, University of Cincinnati, Cincinnati, Ohio.
CLINICAL VIGNETTE

albicans. The exact prevalence of this condition, as well as the presence of regional variation, is unknown. Prior to 1980, infections due to Candida species in IV drug abusers fell into 3 clinical pictures. The first consisted of heroin users who presented with infective endocarditis caused mainly by Candida parapsilosis, which was first described in 1940. The second consisted of IV drug users with Candida endophthalmitis, first described in 1971 and thereafter reported more frequently in ophthalmologic journals. Finally, the third group showed osteoarticular infections by Candida nonalbicans, first described in 1971. It is important to recognize that the clinical picture of disseminated candidiasis in “immunocompetent” IV drug users is completely different from that of “classical” disseminated candidiasis in immunocompromised patients. The latter may be accompanied by an eruption of macules and papules, with or without petechia, and dissemination may be followed by endocarditis, meningitis, pylonephritis, and cutaneous gastrointestinal and pulmonary abscesses. The original focus from which the subsequent candidal seeding occurs in “classical” Candida sepsis may be endogenous (ie, oral, digestive, or respiratory) or exogenous (ie, from catheters or surgery).

In 1981, French authors reported an outbreak of C. albicans infections in drug users in and around Paris; these infections were characterized by skin, ophthalmologic, and osteoarticular manifestations. Three similar cases had been described in Italy in 1979 and in other European countries, as well as in Australia. Epidemiologically, the outbreak was related to the use of brown (Iranian) heroin, which, because of its poor water solubility, had to be dissolved in lemon juice or another acidic solvent. Some postulated that the origin of these cases of disseminated candidiasis in heroin addicts was directly endogenous. However, other investigations demonstrated that the source of infection was exogenous and that such cases were due to contamination of the lemon juice with C. albicans (either from fresh lemons or from the plastic lemon juice containers used to dissolve the heroin) that was carried on the skin and/or in the oropharynx of the heroin users. C. albicans, however, has been isolated neither from pure heroin samples nor from samples confiscated from street dealers, and pure heroin inhibits the growth of C. albicans. Conversely, C. albicans has been isolated from fresh lemons, the lemon juice in plastic lemon juice containers used by heroin addicts, and from the injection paraphernalia. Newton-John et al demonstrated that lemon juice is an excellent medium for growing C. albicans and, along with other researchers, has suggested that a lemon could be contaminated by C. albicans during its manipulation by heroin users. The latter was demonstrated by Miro in another study.

CLINICAL PRESENTATION

Disseminated candidiasis in its initial (acute) phase presents similarly in most patients: high fever with shivering, general discomfort, and asthenia. These symptoms generally appear within a few hours—but sometimes a few days—following the last injection. Patients may complain of fatigue, arthralgias, myalgias, and generalized malaise, reflecting the systemic nature of the illness. Cutaneous lesions are a common reason to seek medical care and appear about 1 week after the onset of the acute phase (range between 1 to 21 days); nodular subcutaneous lesions, folliculitis, or pustules may be seen. The lesions are tender and often involve the hair follicles of the head and neck. In few cases, this initial phase is accompanied by cholestasis. (However, in one such case, a liver biopsy revealed no specific lesion.) In addition, heroin abusers with disseminated candidiasis frequently have regional lymphadenopathy.

In most cases, the fever regresses spontaneously within 1 to 4 weeks. These signs are not always of concern to patients because they resemble those of the self-healing syndrome known as “dust” that is frequent among addicted persons.

After the acute phase several complications may occur, corresponding to metastatic localizations of Candida, and may involve up to 4 organs. In more than 80% of cases, the involved organ is the skin; the eyes are affected in more than 50% of cases, and the osteoarticular system in 15% to 20% of cases. Rarer is involvement of the lung and pleura (in about 5% of cases). Interestingly, in more than 50% of reported cases, cutaneous and ocular lesions coexist.

DIAGNOSIS

The diagnosis of this distinctive syndrome in IV drug users is based on the epidemiologic antecedent of having used brown heroin diluted with lemon juice; the characteristic clinical pattern with sequential development of cutaneous, ocular, and costochondral lesions; and, most reliably, isolation of C. albicans from blood or from samples taken from skin, eye, or costochondral lesions. The literature reports that isolation of C. albicans from blood cultures is very rare and usually occurs during the acute phase of the disease. Other laboratory tests, including a complete blood count, liver function tests, and a urinalysis, may be normal. In the acute phase (range between 1 to 21 days) of the disease, the white blood cell count is at the upper normal limits or slightly increased. The platelet count is normal or decreased. A mild elevation of the serum transaminases is common. Diabetic Retinopathy in a Background of Candida Endophthalmitis
tests, and chemistries, may not be of much diagnostic value as normal results do not exclude the possibility of disease. Biopsies of subcutaneous nodules, which can help confirm the diagnosis, reveal a variable amount of mycotic filaments within a polymorphous infiltrate.\(^2\) In the case of this patient, he admitted using brown heroin on few occasions but more frequently used the lemon juice to inject himself with crack cocaine.

**Clinical Course**

The cutaneous lesions of disseminated candidiasis usually are self-limited and spontaneously resolve. Ocular lesions account for the severity of the illness. Three forms have been described: chorioretinitis, endophthalmitis, and episcleritis. Characteristically, osteoarticular affection consists of firm costochondral painful tumors of varying size, as seen in this patient. In addition to costochondral involvement, the literature also documents cases of spondylitis, arthritis of the knee, arthritis of the wrist, and sacroiliitis. Costochondral lesions in immunocompromised hosts with disseminated candidiasis also have been reported, though spondylitis and arthritis of the knees are the more frequent localizations. When an isolated costochondral tumor is present in an IV drug user, the knees are the more frequent localizations. When an isolated candidiasis in IV drug users have not been defined.\(^15\) Small disseminated candidiasis in both immunocompetent and immunocompromised hosts are less common and typically involve the trunk and proximal extremities. Another difference between the 2 different types of disseminated candidiasis lies in the microbiology. The organism isolated from the cutaneous lesions of heroin abusers usually is *C. albicans*, whereas most of the cases of cutaneous lesions associated with disseminated candidiasis in immunocompromised hosts are due to *Candida tropicalis*. The differences in microbiology also are evident in the ocular manifestations of the disease. As with disseminated candidiasis in IV drug users, *C. albicans* is the species that causes endophthalmitis in most cases of disseminated candidiasis in immunocompromised hosts, whereas other *Candida* species rarely do. For joint lesions, *C. albicans* is the *Candida* species isolated in most cases of osteoarticular lesions associated with disseminated candidiasis in both immunocompetent and immunocompromised hosts, and in the latter group other *Candida* species (*C. tropicalis*, *Candida parapsilosis*, and *Candida guilliermondii*) also have been isolated.

**Treatment**

Optimal regimens of antifungal treatment for disseminated cutaneous lesions. Although it may prevent the development of ocular or osteoarticular lesions, ketoconazole can now be replaced by the new azoles (eg, fluconazole).\(^4\) When chorioretinitis is present, IV therapy with amphotericin B with or without flucytosine is effective in eradicating infection. When extension of the chorioretinal lesions into the vitreous occurs, producing endophthalmitis, pars plana vitrectomy with local instillation of amphotericin B plus IV amphotericin B therapy is appropriate. This procedure, although curative, may be complicated by intravitreal hemorrhage and persistence of poor visual acuity.\(^3\)

This patient was started on fluconazole 400 mg IV during his hospital stay and he was discharged on fluconazole 400 mg/day taken orally. Despite having evidence of chorioretinitis, he was never initiated in amphotericin B owing to poor renal function. However, he was closely followed by Ophthalmology with fundoscopies performed each month. Four months after therapy, his ocular lesions resolved. After that, the patient was lost to follow up.

**Prognosis**

The prognosis of the syndrome of disseminated candidiasis secondary to IV brown heroin use depends on the immune status of the host, the various organs that are involved, and compliance with treatment. Ocular lesions carry risks of permanent damage to the retina and optic nerve resulting in blindness if not treated aggressively. Localized skin lesions, on the other hand, may resolve without treatment.

Survival in cases of disseminated candidiasis has been shown to be longest when tissue burdens of the organism are reduced with early treatment, reinforcing clinical recommendations for the earliest possible initiation of antifungal therapy.\(^22\) IV drug abusers who receive adequate treatment for the disease and have documented resolution of their symptoms should be admonished that reinfection is possible if drug injection/sterilization habits are not changed. It is worthy to note that the rate of morbidity and mortality secondary to disseminated candidiasis is still significant despite attempts to develop better diagnostic techniques and more effective means of treatment. New antifungal agents and special preparations of amphotericin B are being evaluated with the aim of improving the prognosis of disseminated candidiasis, especially in immunocompromised hosts.\(^23\)

**Conclusion**

Disseminated candidiasis in immunocompetent IV drug users is a distinctive syndrome, the hallmarks of which include: sequential development of skin, eye, and osteoarticular lesions; use of brown heroin diluted with lemon juice; and the etiologic agent, which almost always is *C. albicans*.

**References**