Opportunistic Fungi Often Elude Diagnosis

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SAN DIEGO — The rise in incidence of unusual fungi, especially in immunocompromised individuals, is complicating the diagnosis of cutaneous mycoses, said Dr. Ted Rosen at the American Academy of Dermatology's Academy 2006 conference.

"Fungal illnesses can mimic lots of different things, especially in immunocompromised patients. For example, *Cryptococcus* infection can look like Kaposi's sarcoma, bacterial cellulitis, molluscum, or even herpes," said Dr. Rosen of the department of dermatology, Baylor College of Medicine, Houston. "In HIV-positive patients, all morphologic bets are off."

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Dr. Rosen mentioned a case in which a 41-year-old HIV-positive white man presented with brown-purple papules and plaques, some of which were ulcerated. The referring physicians thought it was Kaposi's sarcoma (KS) with a secondary bacterial infection. Like many HIV-positive patients, the man had a complicated history peppered with opportunistic infections, including *Pneumocystis carinii* pneumonia, herpes zoster, and cytomegalovirus. He'd also had oral KS, so it was reasonable for the referring physician to think about cutaneous KS.

"I saw the lesions and understood right away why they thought it was KS. But the diffuse, brownish ulceration was strange, so I took a biopsy of all the brownish areas, and they came back showing *Cryptococcus neoformans*," Dr. Rosen said. The patient's blood and bone marrow were also positive for *Cryptococcus*.

Unfortunately, the patient committed suicide before Dr. Rosen was able to treat the fungal infection with amphotericin B. He recommends 1 mg/kg for 2 weeks of the standard form of amphotericin B, rather than the lipid-based form. In some cases, it makes sense to add flucytosine, 100 mg/kg per day, and then fluconazole, 400 mg per day for 10 weeks. Some HIV-positive patients should remain on fluconazole maintenance, at a dose in the 200- to 400-mg range, for life.

Dr. Rosen said between 5% and 10% of all HIV-positive individuals get *Cryptococcus*, and nearly 90% of all *Cryptococcus* cases are in HIV-positive people, though it can also affect organ transplant patients and pregnant women.

Fungal infections need not be life threatening to cause major problems for patients. Dr. Rosen described another case involving a 24-year-old, otherwise healthy woman who'd had a chronic eczemalike rash on her cheeks for 13 years. She had been applying steroid creams for years, to no avail.

Biopsy showed pseudoepitheliomatous hyperplasia, granulomata, and small, short budding yeast forms. The culture grew out a thick fungal plaque that turned out to be *Phoma* complex, an aggregate of soil fungi that normally affect celery, beets, tomatoes, potatoes, and peppers.

"We reread the original biopsy specimen from 13 years ago, and we were able to grow out the *Phoma*. For 13 years, this patient was smearing steroids on a plant pathogen." The patient had spent a lot of time as a child on a pig farm, which is where she likely picked up the plant fungus.

"I asked for in vitro testing, to see what [the fungi were] sensitive to. You really need help from a good microbiologist in cases like this." They proved sensitive to ketoconazole and itraconazole, but not to fluconazole or griseofulvin. Dr. Rosen went with ketoconazole, 200 mg, twice daily, which resulted in a clinical and histologic cure within 18 months.

With worldwide travel and immigration come new and unusual fungal infections that mimic other common skin diseases. A case in point is a 47-year-old male construction worker who Dr. Rosen saw for a scaly, horseshoe-shaped plaquelike lesion on his forearm. The presenting lesion was actually a recurrence of the original lesion, which had been excised by a physician who thought it was a skin cancer.

The surface of the lesion was coated with a blackish powdery substance. Dr. Rosen cultured it and grew out *Fonsecaea pedrosoi*, a soil fungus that is rare in the United States and usually seen in Central American agricultural workers. It is also common in Madagascar and parts of South America. The lesions can be dead ringers for skin cancers.

For relatively mild cases of *Fonsecaea* infection, itraconazole is a good choice, said Dr. Rosen. Roughly 60% of U.S. isolates are sensitive to this drug at a dose in the 200- to 400-mg range. For more severe cases, posaconazole is the most promising choice. Cryotherapy or thermotherapy can also help, in conjunction with drug treatment. But large lesions can be hard to clear and often take a year or more of continuous treatment before showing a complete resolution, he warned.

Whenever one sees something that looks a bit unusual, especially in patients who are immunocompromised or taking any medication that might impair the immune system, one should think "fungi," said Dr. Rosen.

Novel "biologics" and anti-TNF drugs can leave patients susceptible to opportunistic fungi such as *Sporothrix*. Clinical conditions such as alcoholism, diabetes, and some forms of cancer can also leave patients vulnerable to odd fungi, he said. ■