

hasta un 80% con insuficiencia cardíaca<sup>2,4,8</sup>, y hasta un tercio de estos enfermos tienen erisipeloide cutáneo<sup>1,2,7</sup>. Aunque las complicaciones son similares a otros tipos de endocarditis, pueden conllevar mayor mortalidad, que llega a alcanzar el 38–40%<sup>2,6,9</sup>, estos datos se basan en publicaciones de los años ochenta, con una reducida casuística; tiene predilección por las válvulas nativas normales (60%), preferentemente la aórtica (70%), y requiere cirugía con reemplazo valvular en el 36% de los casos<sup>1,2</sup>. El género *Erysipelothrix* se puede distinguir de otros bacilos grampositivos, como *Lactobacillus*, *Listeria* y otros, por la morfología celular y su capacidad de producir H<sub>2</sub>S en agar TSI. El método de identificación en nuestro caso se ha basado en la morfología de las colonias, tinción de Gram, pruebas de catalasa y oxidasa negativas, producción de H<sub>2</sub>S en agar Kligler y mediante el sistema de identificación API<sup>®</sup> Coryne (BioMérieux, France). Asimismo, se confirmó en el Centro Nacional de Microbiología (Majadahonda, Madrid) por métodos de secuenciación. Este microorganismo generalmente es sensible a penicilina y resistente a vancomicina y a aminoglucósidos<sup>5,10</sup>. El tratamiento con penicilina o con quinolonas en el caso de alergia a betalactámicos debe mantenerse 4–6 semanas. Como conclusión, creemos que debe realizarse una cuidadosa historia epidemiológica y sospecharse esta infección en pacientes con factores y profesiones de riesgo, y más aún cuando se aislen bacilos grampositivos, siendo crucial la identificación correcta de este microorganismo para poder pautar una antibioterapia precoz y adecuada.

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doi:10.1016/j.eimc.2008.02.009

## Cerebral aspergillosis in an HIV-infected patient: Unsuccessful outcome despite combined antifungal therapy

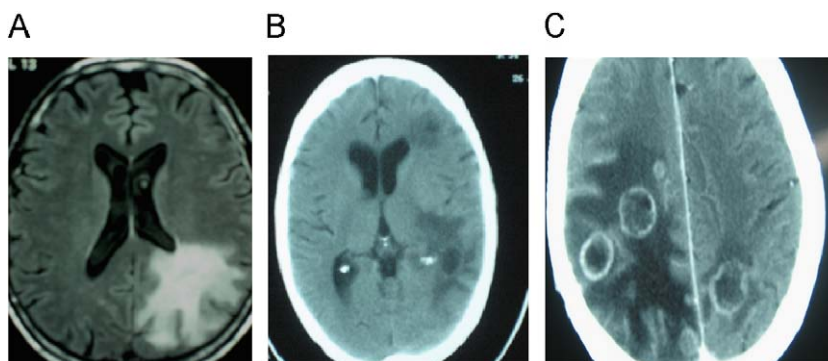
**Aspergilosis cerebral en un paciente con infección por el VIH: evolución desfavorable a pesar de tratamiento antifúngico combinado**

Dear Editor:

Central nervous system (CNS) aspergillosis is the most serious clinical form of invasive aspergillosis and results in substantial mortality, approaching 100% of affected persons<sup>1</sup>. The introduction of new antifungal agents, such as voriconazole, a novel triazole, and echinocandins, a new family of antifungals, has generated new treatment expectancies for invasive aspergillosis. Here we report a fatal case of CNS aspergillosis in an AIDS patient treated unsuccessfully with a combination of systemic voriconazole and caspofungin, as well as intrathecal amphotericin B.

A 47-year-old HIV-seropositive man, former intravenous drug-user, was admitted for bilateral cavitated pneumonia. He had been treated with combined antiretroviral therapy (cART) for the previous 6 months (emtricitabine, tenofovir and lopinavir/ritonavir). Six weeks earlier he had been diagnosed with progressive multifocal leukoencephalopathy (PML) as an expression of immune reconstitution inflammatory syndrome (IRIS) (Figure 1A). High-dose corticosteroid treatment was initiated. After 4 weeks of treatment with tapered doses of corticosteroids,

chest pain, shortness of breath, and bradypsychia developed. Physical examination on admission revealed temperature 38.3 °C, respiratory rate of 32 per min, lethargy, global aphasia and slight upper right limb paresis. A chest radiograph showed bilateral cavitated pulmonary consolidations. The patient's CD4 count was 22 cells/μl. Unenhanced brain CT study showed no changes with respect to a scan carried out at previous admission. Levofloxacin (500mg/day IV) and ceftriaxone (1g/day IV) were given empirically. Blood cultures and pneumococcal and legionella antigen testing in urine were negative. Three days later the patient presented seizures. A new contrast-enhanced CT scan revealed a ring-enhancing lesion with perifocal edema in the left parieto-occipital lobe (Figure 1B). CT-guided needle puncture of one pulmonary lesion was performed, but pathology and cultures of the specimen yielded no positive results. A specimen obtained by CT-guided stereotaxic biopsy of the cerebral abscess revealed septated hyphae on KOH stain; *Aspergillus fumigatus* grew in culture. A diagnosis of necrotizing bilateral pneumonia with CNS involvement by *A. fumigatus* was established. The paraventricular location of the abscess precluded surgical excision; voriconazole and caspofungin at doses of 400mg/12 h and 70mg/24h, respectively, were started. A new CT scan performed 11 days after starting treatment showed new lesions, and *A. fumigatus* was recovered from the aspirated material. One ml (0.5mg) of amphotericin B deoxycholate was instilled into the two largest lesions, but the patient's condition deteriorated and new lesions were seen in another CT scan (Figure 1C). Thus, treatment was



**Fig. 1.** Evolution. A: RMI at PML+IRIS diagnosis. B: CT scan showing one ring-enhancing lesion with perifocal edema in the left parieto-occipital lobe. C: multiple lesions illustrating therapeutic failure.

finally withdrawn and the patient died 78 days after the diagnosis. An autopsy was not performed.

The results of treatment for CNS aspergillosis are usually discouraging, and short-term outcome is fatal<sup>1</sup>. In a retrospective review of invasive aspergillosis, only 9% of patients with CNS involvement achieved partial or complete response with amphotericin B- or itraconazole-based therapy<sup>2</sup>.

Voriconazole is a new broad-spectrum triazole with good in vitro activity against *Aspergillus* species<sup>3,4</sup>. The favorable CNS penetration in humans makes voriconazole a promising option for the treatment of aspergillosis affecting the CNS<sup>5</sup>. The largest study of voriconazole for CNS aspergillosis reported to date is a retrospective study of 81 patients from clinical trials and compassionate-use programs<sup>6</sup>. Overall, partial or complete response was achieved in 35% of patients. The prognosis of CNS aspergillosis among AIDS patients seems to be even worse. Thirty-six cases, including ours, have been reported to date in the English literature<sup>7–9</sup>. Antifungal treatment failed in all but one case. Three patients were treated with voriconazole: 2 did not respond, and although the other did, he ultimately died of invasive cytomegalovirus infection. Our patient was treated with a combination of voriconazole and caspofungin, based on favorable published data<sup>10</sup>; despite this combined treatment, the disease progressed and the patient's clinical condition deteriorated. There were no overt factors, such as under-dosage, drug interactions, or poor gastrointestinal absorption that might have compromised the response to treatment. Unfortunately, plasma and CSF voriconazole concentrations, which might have been of value in evaluating this case, were not available.

In summary, the case reported illustrates the dismal prognosis of CNS aspergillosis. Despite the promising results reported with the newest antifungal agents, treatment of CNS aspergillosis remains ineffective in the majority of cases. Lastly, it is important to underline the limitations of case reports to gather medical evidence; cohort series or randomized clinical trials should be designed for this purpose, although in the case of cerebral aspergillosis, these studies are difficult to perform.

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