Cutaneous Cryptococcosis Mimicking Basal Cell Carcinoma in a Patient with Sézary Syndrome

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Cryptococcosis is an opportunistic yeast infection that is the most common systemic fungal infection in immuno-compromised patients. Skin involvement is a feature in 10–20% of cases of disseminated cryptococcal infection (1). We report here a case of a 63-year-old woman with Sézary syndrome (T4, N3, M0, B1) with an ulcerated preauricular tumour that developed during photopheresis with a combination of methotrexate and steroid treatment. We highlight the importance of differential diagnosis of cryptococcosis in the case of any atypical or non-healing lesions observed in an immunosuppressed patient.

CASE REPORT

A 63-year-old Caucasian woman who had breast cancer and underwent mastectomy in 1989 followed by chemotherapy was diagnosed in 1998 with parapsoriasis through clinical signs and histological examination in the County Hospital. In 2001 she presented with generalized pruritus and erythroderma at our clinic. She responded poorly to oral psoralen and ultraviolet A (pUV A) therapy. In 2002 clinical signs (weakness, general condition, intermittent fever) were suspicious for Sézary syndrome or Cutaneous Cryptococcosis Mimicking Basal Cell Carcinoma in a Patient with Sézary Syndrome

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In October 2007 the patient started receiving intravenous amphotericin B and fluconazole. Despite all our efforts Cryptococcus antigenaemia was still detected. The patient died 6 weeks later from acute cardiac and renal failure. Autopsy revealed cutaneous cryptococcal infection in the skin of the submammary region of the thorax and in the lungs.

DISCUSSION

Cryptococcal species are yeast-like fungi. Based on their virulence they are classified as pathogenic or non-pathogenic. Classically, *C. neoformans* is the only pathogenic cryptococcal species present in high concentrations in pigeon faeces, but also in soil, fruit, and other sources in nature, such as eucalypt reservoirs. It includes four distinguishable serotypes: A (*C. neoformans var. grubii*) has a worldwide distribution; B (*C. neoformans var. neoformans*) found mostly in Europe; and B and C (*C. neoformans var. gattii*), which are limited to tropical and subtropical areas (2, 3).

Cryptococcal infection is acquired by inhalation and resides in the lung, mostly in the immunocompromised host, as was the case in our patient, due to Sezary syndrome and continuous steroid immunosuppressive treatment with photopheresis extended with a combination of methotrexate. Infection can also involve patients with intact immune systems who are predominantly infected with *C. neoformans var. gattii* (4). The infection can resolve or disseminate, mostly spreading to the meninges, but bones, visceras and the skin can also be involved. In the diagnoses of Cryptococcus infection, culture from smears of body fluids, secretions, exudates, or other specimens is definitive, but X-ray and serological examination are also of importance.

Involvement of the skin can result in a great variety of lesions, most commonly affecting the face and neck, from papules, nodules, acneiform lesions, granulomas, herpetiform vesicles, abscesses, and ulcers, resembling other cutaneous disease, such as molluscum contagiosum, varicella, basal cell carcinoma, cellulitis, cutaneous ulceration, atypical mycobacteriosis and whitlow (5–8). The two forms of histological manifestation are gelatinous and granulomatous reactions. While the granulomatous type results in pronounced tissue reaction, with histiocytes, giant cells, lymphocytes, and fibroblasts, with a low number of yeasts, that vary in size from 2 to 20 μm, in the gelatinous type, masses of organisms occur, with the accumulation of cryptococcal capsular polysaccharide causing mucoid degeneration of the invaded tissue, with only minimal signs of inflammation (6).

Treatment of the systemic infection includes appropriate antifungal drugs, in which the mainstay is intravenous amphotericin B in combination with fluconazole, which is often followed by fluconazole for many months or, depending on the patient’s immune status, even life-long. If fluconazole is not available or is contraindicated, acceptable alternatives include itraconazole, or extended-spectrum azoles (voriconazole and posaconazole). Occasionally, localized cryptococcal infections of the lung not responding to medical therapy may require surgical resection for cure (9). In the case of cutaneous Cryptococcus infection successful treatment with oral fluconazole alone has also been reported, and incision, with local irrigation and debridement, topical application of anti-inflammatory agents and antifungal agents was also recommended (8, 10).

Our case illustrates the importance of serological tests with histological examination, and pathogen-culturing from any atypical or non-healing lesions observed in immunocompromised patients for an accurate diagnosis of opportunistic infection. Importantly, a primary infection of the lung and disseminated infection involving the central nervous system may be present with dermatological rather than pulmonary or neurological manifestations (11).

The authors declare no conflicts of interest.

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