Cutaneous alternariosis

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Summary

Alternariosis is a fungal infection usually described in immunodeficient patients. We report a case of cutaneous alternariosis in a renal transplant recipient caused by *Alternaria alternata*. The patient was treated with intralesional amphotericin B and surgical excision of one non-responding lesion was performed.

Key words Alternariosis, Cutaneous infection, Kidney transplant

Alternariosis cutánea

Resumen

La alternariosis es una infección fúngica usualmente descrita en pacientes inmunocomprometidos. Se presenta un caso de alternariosis cutánea en un trasplantado renal, causado por *Alternaria alternata*. El enfermo fue tratado con anfotericina B intralesional y excisión quirúrgica de una de las lesiones que no ha respondido a la terapeutica intralesional.

Alternariosis, Infección cutánea, Trasplante renal

An increasing incidence of cutaneous infections caused by opportunistic fungi have been reported in immunocompromised and, more rarely, in healthy hosts. Members of the genus *Alternaria* are ubiquitous molds, that are frequently isolated from the air, soil and decaying vegetation. Although generally recognized as nonpathogenic for man, several cases of human infection have, however, been reported [1,2]. We describe a new case of this disease representing, as we know, the first observation of this form of phaeohyphomycosis in Portugal.

We report the case of a 43 year old female, housewife, born and resident in Pombal, a rural area of Portugal. In 1962 she had a chronic glomerulonephritis that rapidly evolved into renal insufficiency. Her condition deteriorated and she required hemodialysis twice a week. In 1972 a diagnosis of systemic lupus erytematosus (SLE) was made. In 1987 the patient was submitted to kidney transplant, after which therapy with cyclosporine and prednisone was initiated. In 1988 she had pulmonary tuberculosis.

In October 1995 the patient was admitted to the Dermatology Department of Curry Cabral Hospital with a three month history of painless subcutaneous nodules on the right knee measuring between 1-2 cm in diameter, of firm consistency. The overlaying skin was erythematous, but without erosion or ulceration (Figure 1). Laboratory evaluation revealed normal renal function and inactive SLE and tests for antibodies anti HIV 1 and 2 presence were negative.

A biopsy specimen was collected aseptically into a sterile Petri dish containing normal saline and immediately transported for processing. It was cut into two pieces, one for histopathologic and the other for mycologic examinations.

For histopathologic studies the biopsy specimen was fixed in formalin and mounted in paraffin. Sections were stained with haematoxylin-eosin and periodic acid-Schiff´s stain (PAS). Histopathologic examination of the lesion showed an hyperplastic epidermis. The dermis had an inflammatory infiltrate with lymphocytes and histiocytes. The inflammatory tissue showed fungal elements of round and oval spore-like bodies. In PAS stained sections, these structures stained intensely purple exhibited some protrusions suggesting the budding of yeasts (Figure 2).

A part of the biopsy specimen was homogenized for direct microscopic examination with 20% potassium hydroxide (KOH) and revealed several septate hyphae.

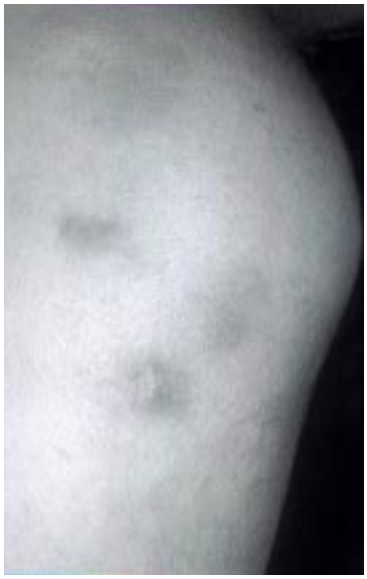

Figure 1. Subcutaneous nodules of the right knee.

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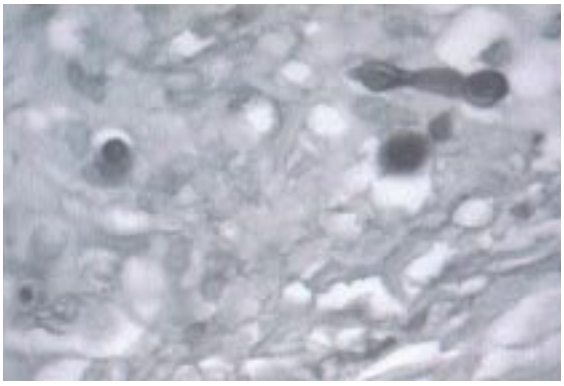

Figure 2. Round and oval spore-like bodies in the dermis (PAS x 400).

The remainder was inoculated onto Sabouraud glucose agar with and without cycloheximide (0.5mg ml^{-1}) and chloramphenicol (0.05mg ml^{-1}), brain-heart-infusion agar and malt agar, and incubated at 24° and 37°C for the isolation of the etiologic agent.

After 5 days at 24°C in all the media, except those with cycloheximide, colonies with white to pale gray aerial mycelia developed. The surface of the colony was initially gray white and cottony in appearance, later becoming brownish with a white border covered by a short gray aerial mycelia. The reverse was dark-brown.

Slide cultures in corn-meal agar were made. Within two weeks we observed simple and branched dark septate conidiophores and several darkly pigmented muriform, obclavate conidia with a beak, in groups and in acropetal chains (Figure 3). On the basis of these findings, a diagnosis of cutaneous alternariosis caused by *Alternaria alternata* was made.

Figure 3. Microscopic morphology of *Alternaria alternata* in corn-meal with two weeks-conidia obclavate to elipsoidal with a short cylindrical beak brown with muriform septation, arising in unbranched chains (x 600).

In our patient two of three lesions had already been excised and daily occlusive local application of ketoconazol in the third lesion was done. One month later three new lesions appeared near to this original site. Because of the risks eventually associated with systemic amphotericin B or imidazole compounds that would increase the cyclosporine blood levels and seriously affect the renal function, we decided to treat the lesions with intralesional amphotericin B according to the following schedule: 50mg of amphotericin B was dissolved in 10ml of distilled water and stored at 4°C. For application, this solution was diluted with four volumes of 0.5% procaine hydrochloride to give a final amphotericin B concentration of 1mg/ml and one milliliter was injected directly into the lesions twice a week for five weeks. The injections were well tolerated, in spite of moderate pain in the local of the injection. No systemic reaction was reported.

After the treatment most of the lesions appeared to be resolved. One remained stable and was surgically excised. The patient is well on a follow-up period of three months.

Alternaria is a saprophytic fungus, now recognized as the cause of a clinical spectrum of infections in both normal hosts [6,8] and immunocompromised patients. Most of the affected are immunodepressed due to Cushing disease [13], kidney transplants [2,3,12], haematologic malignant diseases [14] and AIDS [10]. Rural environment and local traumas facilitating penetration of the agent are important factors, operating mainly in non immunodepressed patients [5].

Cutaneous lesions have been characterized as either localized eruptions of ulcerated, crusted plaques and papules, or as papulonodular ulcerative and vegetative lesions, occurring singly or as multiple lesions on exposed sites [4]. Due to their frequent occurrence as laboratory contaminants, *Alternaria* spp. involvement in human infection must be demonstrated, not only by isolation in culture, but by histologic evidence of its presence in tissues [14].

The organism is readily grown in cultures, allowing the isolation of a dematiaceous mold characterized by simple conidiophores, and by the production of muriform, obclavate or ovoid dark brown conidia in chains [14]. Histopathological examination reveals the presence of fungal elements extending from the stratum corneum downwards, or more often, in the dermis. The inflammatory response may be diffuse or nodular [4]. This case report confirms these findings.

The aim of the treatment is, whenever possible, the correction of predisposing factors. Multiple therapeutics have been used, mainly because the optimum treatment has not yet been established [8].

In the epidermal type topical natamycin was reported to be effective [7]. In another case of dermal alternariosis in a patient who received a renal allograft, daily occlusive local applications of ketoconazol resulted in cure [2].

Excision of multiple lesions [13], oral ketoconazol [3,14] or itraconazol, intralesional infiltration with miconazol [5] or amphotericin B [8] have been advocated by several authors. In our case we used a combined treatment with intralesional amphotericin B and surgical excision of one non-responding lesion.

The incidence of this disease may still grow, due to an increasing number of suspects exposed. Biopsy and culture of the suspected lesions are essential for the diagnosis and adequate treatment of these patients.

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