CLINICAL REPORT

Chronic Infection Due to *Fusarium oxysporum* Mimicking Lupus Vulgaris: Case Report and Review of Cutaneous Involvement in Fusariosis

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A 67-year-old female presented with a 20-year-old lesion involving the right ear and preauricular area mimicking tuberculous lupus. *Fusarium oxysporum* infection was confirmed by biopsy studies and cultures. The biopsy specimen showed an unusually extensive dermal invasion with fungal hyphae. This is an uncommon clinical presentation for *Fusarium* infection in a healthy patient. When referred to us, the patient had received antifungal therapy with itraconazole without any benefit. Improvement was obtained with fluconazole therapy. The spectrum of cutaneous involvement related to *Fusarium* spp. includes toxic reactions, colonization, superficial indolent infection, deep cutaneous or subcutaneous infections and disseminated infection.

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*Fusarium* spp. are soil and plant saprophytes commonly associated with human and animal mycotoxicosis. However, species in this genus play an emerging role as pathogens in human infections. *F. solani*, *F. oxysporum* and *F. verticilloides* are the species most frequently reported as human pathogens in localized and disseminated infections (1).

Reports on localized *Fusarium* infections have mainly described therapeutic and diagnostic difficulties in onychomycosis and keratitis and other extra-cutaneous involvement. There have been few reports of atypical cutaneous fusariosis. We report a well-documented case of long-standing localized cutaneous fusariosis mimicking lupus vulgaris that responded well to fluconazole therapy. Cutaneous diseases related to *Fusarium* spp. infections are reviewed.

CASE REPORT

A 67-year-old female with a history of type II diabetes, which had been treated orally, was referred to our hospital for diagnosis and management of a 20-year-old lesion in the right ear. The patient did not recall any previous traumatic injury in the affected area. In 1980 she was diagnosed with infectious granuloma caused by fungi or mycobacteria. At that time, all complementary tests for mycobacteriosis were negative. No mycological cultures were carried out. However, based on clinical and histological findings she then received treatment with rifampicin, isoniazid and ethambutol for 2 months, followed by rifampicin and isoniazid for 7 months. In 1982 she received tentative cryotherapy. In 1990, as a result of the presence of fungal elements in biopsy specimens, she was diagnosed with cutaneous mycosis and received treatment with itraconazole 200 mg/day for 6 months followed by terbinafine 250 mg/day for 2 months, without any benefit.

In January 2000 she was referred to us, presenting with an infiltrated, soft plaque involving the whole helix, slight pruriginous, resembling lupus vulgaris (Fig. 1). Routine tests, including blood cell count, biochemistry and X-ray examination were normal. A standard multi-test for cellular immunity (tetanus, diphtheria, Streptococci, proteus, tuberculin, glycerol, Candidin, trichophytin) gave normal results. All laboratory tests for mycobacteria, including cultures and PCR detection, were negative. A biopsy specimen was taken for histological examination. Hematoxylin–eosin staining showed a chronic inflammatory response produced by epithelioid cells, eosinophils and numerous giant foreign body cells. Inside the foreign

Fig. 1. Infiltrated plaque with erythematous areas, covered by slight scaling and scars and with badly defined margin in the right ear.
body cells, pale structures resembling fungal hyphae were observed. Periodic acid–Schiff (PAS) staining showed numerous hyphae sparsely distributed in the dermis and also inside giant cells (Fig. 2).

A new biopsy specimen for mycological identification was sampled onto chloramphenicol–gentamicin–Sabouraud’s agar and cyclohexamide–Sabouraud’s agar at 25°C and 37°C. Chloramphenicol–gentamicin–Sabouraud’s agar cultures yielded velvety colonies, white to pale gray in color at 25°C and orange at 37°C. Old cultures developed violet areas at both 25°C and 37°C. Subcultures and slide cultures were prepared for species identification onto oatmeal agar, potato sucrose and potato dextrose agar. Microscopic examination revealed wide vegetative aerial mycelium with septate, branched hyphae, saccate fusiform, 3–5-celled, slightly curved, macroconidia, pointed at the tip, numerous, single-celled, oval/ellipsoid, non-chain microconidia developed on short lateral conidiophores and intercalary, single or paired, hyaline, smooth-walled chlamydospores (Fig. 3).

On the basis of these data we identified the colony as *F. oxysporum* Schlecht.:Fr. (2), and started treatment with oral fluconazole 150 mg/day. After 3 months the patient showed a marked improvement.

**DISCUSSION**

Cutaneous diseases related to *Fusarium* spp. can appear in both immunocompromised and healthy hosts and include toxic reactions, colonization, superficial infection, deep cutaneous or subcutaneous infections and disseminated infection.

Exposure to the toxin deoxynivalenol caused lesions of the skin and mucous membranes, suggesting a toxic reaction, in grass planters in The Netherlands (3). Chronic indolent superficial fusariosis limited to the skin appendages or corneal layer, namely onychomycosis and intertrigo, is frequent (4). *F. oxysporum* was reported as causing distal subungual, proximal subungual (5) and superficial white toenail mycosis in a patient who presented with a low extremity temperature after cranial trauma (6). Colonization in surgical wounds, severe burns, venous and arterial leg ulcers is a common finding (1, 7, 8) and was related to diabetes in one case (7). However, *F. oxysporum* was also reported as being the only causative agent of a large foot ulcer (9). When fungal hyphae reach the dermis and subcutaneous tissue, subcutaneous nodules (10, 11), sporotrichoid nodules (12), panniculitis (13), mycetoma (14, 15) or chronic granuloma (16, 17) can be observed in both immunocompromised and healthy hosts.

In healthy hosts, localized papular and pustular lesions that developed after trauma were reported (18, 19). A case presenting with extensive chronic granulomatous lesions involving the 2 arms, in which the authors could not demonstrate any known immune defect, was caused by *F. oxysporum* (20). Our case report described a diabetic patient who denied any trauma at the onset of the process. However, over the years she had received several treatments, including tentative cryotherapy. This cryotherapy injury possibly facilitated the deep invasion and later clinical appearance, as well as further antifungal resistance.

Host responses in localized cutaneous chronic *Fusarium* infections have included granuloma (16), pseudocarcinomatous hyperplasia (15), sometimes with carcinomatous changes (21), and eccrine syringofibroadenomatous hyperplasia (22). Despite the long evolution time, granuloma without carcinomatous changes was observed in the present case.

The first case of systemic infection by *Fusarium* spp. was published in 1973 (23). Since then, a number of systemic infections caused by *Fusarium* spp. alone (24, 25) or in association with other agents (26) have been published. Neutropenia is probably the most important predisposing factor for disseminated infections in immunocompromised hosts. The clinical picture is characterized by fever and muscular pain refractory to treatment. Cutaneous involvement is common, including painful erythematous maculce, palpable or non-palpable purpura, flaccid pustules and necrosis on the trunk, face, scalp, extremities, palms and soles (1, 23–26).

There is no agreement between the *in vitro* and *in vivo* results in the reports describing the management of *Fusarium* infections and therefore none of the therapeutic regimens reported can be considered ideal (1). The gold standard for the treatment of disseminated infection continues to be amphotericin B, either alone or in combination with 5-fluorocytosine, rifampicin or azole derivatives (1, 23–26). In deeply located infections, good results were obtained by
combining surgical excision with antifungal treatment (27). However, reported treatments have produced contradictory results depending on the patient’s condition (3, 6—27). In the case reported here the patient’s history, which revealed itraconazole resistance, and the benign condition of a 20-year-old infection caused us to reject the use of a more aggressive therapy. Fluconazole has little activity on intra-cellular fungi (28), but does enhance the killing activity of neutrophils, monocytes and macrophages (29). In our case clinical improvement was obtained after 3 months of fluconazole therapy.

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REFERENCES

1. Guarro J, Gené J. Opportunistic fusarial infections in humans. Eur J Clin Microbiol Infect Dis 1995; 14: 741—754.
2. Guarro J, de Hoog GS, Figueras MJ, Gene J. Rare opportunistic fungi. In: de Hoog GS, Guarro J, eds. Atlas of clinical fungi, Part 2. Baarn: Centralbureau voor Schimmelcultures, 1995: 528—529.
3. Snijders CH, Samson RA, Hoekstra ES, Ouellet T, Miller JD, de Rooij-van der Goes PC, et al. Analysis of Fusarium causing dermal toxicosis in marram grass planters. Mycopathologia 1996; 135: 119—128.
4. Bordain-Bidot ML, Baran R, Baixench MT, Bazex J. Fusarium onychomycoses. Ann Dermatol Venereol 1996; 123: 191—193.
5. Romano C, Presenti L, Massai L. Interdigital intertrigo of the feet due to therapy-resistant Fusarium solani. Dermatology 1999; 199: 177—179.
6. Pereiro Jr. M, Pereiro E, Toribio J, Pereiro-Miguens M. Superficial white toenail onychomycosis due to Fusarium oxysporum. A case report and review of the literature. J Mycol Méd 1997; 7: 219—222.
7. Dijk E, Berg WH, Landwehr AJ. Fusarium solani infection of a hypertensive leg ulcer in a diabetic. Mykosen 1980; 23: 603—606.
8. Willemsen MJ, Cosinck AL, Coremans-Pelsener JE, Marichal-Pipeleers MA, Roseeuw DI. Parasitic invasion of Fusarium oxysporum in an arterial ulcer in an otherwise healthy patient. Mykosen 1986; 29: 248—252.
9. Landau M, Srebnik A, Wolf R, Bashi E, Brenner S. Systemic ketoconazole treatment for Fusarium solani leg ulcers. Int J Dermatol 1992; 31: 511—512.
10. Young C, Meyers AM. Opportunistic fungal infection by Fusarium oxysporum in a renal transplant patient. Sabouraudia 1979; 17: 219—223.
11. Datry A, Leblond V, Feger C, Gabarre J, Guheo E, Lecoo G, et al. A propos de trois cas de mycoses à Fusarium sp. Bull Soc Fr Mycol Méd 1988; 17: 137—142.
12. Watsky KL. Sporotrichoid nodules in an immunocompromised host. Cutaneous emboli of Fusarium. Arch Dermatol 1995; 13: 1329—1330.
13. Patterson JW, Brown PC, Broecker AH. Infection-induced panniculitis. J Cutan Pathol 1989; 16: 183—193.
14. Resnik BI, Burdick AE. Improvement of eumycetoma with itraconazole. J Am Acad Dermatol 1995; 33: 917—919.
15. Baudraz-Rosselet F, Monod M, Borradori L, Ginalskey JM, Vion B, Boccard C, et al. Mycetoma of the foot to Fusarium sp. Treated with oral ketoconazole. Dermatology 1992; 184: 303—305.
16. Soo-Pin O, Tein-Tai C, Tse-Hsun H, Hong-Sing C, Hsu-Yung H. Granuloma annulare-like lesion due to Fusarium roseum: therapy with ketoconazole. Arch Dermatol 1987; 123: 167—168.
17. Benjamin RP, Callaway JL, Conant NF. Facial granuloma associated with Fusarium infection. Arch Dermatol 1960; 101: 598—600.
18. Collins MS, Rinaldi MG. Cutaneous infection in man caused by Fusarium moniliforme. Sabouraudia 1977; 15: 151—160.
19. Hiemenz JW, Kennedy B, Kwon-Chung KJ. Invasive fusariosis associated with an injury by a stingray barb. J Med Vet Mycol 1990; 28: 209—213.
20. Attappattu MC, Anandakrishnan C. Extensive subcutaneous hyphomycosis caused by Fusarium oxysporum. J Med Vet Mycol 1986; 24: 105—111.
21. Sayama K, Ohtsuka H, Shiraishi S, Miki Y, Tada M, Matsumoto T. Squamous cell carcinoma arising in long-standing granulomatous hyalohyphomycosis caused by Fusarium solani. Arch Dermatol 1991; 127: 1735—1737.
22. Pereiro Jr. M, Labandeira J, Toribio J. Planter hyperkeratosis due to Fusarium verticilloides in a patient with malignancy. Clin Exp Dermatol 1999; 24: 175—178.
23. Cho CT, Vats TS, Lowman JT, Bransberg JW, Tosh FE. Fusarium solani infection during treatment for acute leukemia. J Pediatr 1973; 83: 1028—1031.
24. Sander A, Beyer U, Amberg R. Systemic Fusarium oxysporum infection in a immunocompetent patient with an adult respiratory distress syndrome (ARDS) and extracorporeal membrane oxygenation (ECMO). Mycoses 1998; 41: 109—111.
25. Guinvarc’h A, Guilbert L, Marmorat-Khuong A, Lavarde V, Chevalier P, Amrein C, et al. Disseminated Fusarium solani infection with endocarditis in a lung transplant recipient. Mycoses 1998; 41: 59—61.
26. Vasiloudes P, Morelli JG, Weston WL. Painful skin papules caused by concomitant Acremonium and Fusarium infection in a neutropenic child. J Am Acad Dermatol 1997; 37: 1006—1008.
27. Freidank H. Hyalohyphomycoses due to Fusarium spp.—Two case reports and review of the literature. Mycoses 1995; 38: 69—74.
28. Van’t Wout JW, Meynaar I, Linde I, Poell R, Mattie H, Furth R. Effects of amphotericin B, fluconazole and itraconazole on intracellular Candida albicans and germ tube development in macrophages. J Antimicrob Chemother 1990; 25: 803—811.
29. Natarajan U, Randhawa N, Brummer E, Stevens DA. Effect of granulocyte-macrophage colony-stimulating factor on candidacidal activity of neutrophils, monocytes or monocyte-derived macrophages and synergy with fluconazole. J Med Microbiol 1998; 47: 359—363.