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CASE AND RESEARCH LETTERS

Necrotizing Cellulitis as the First Manifestation of Disseminated Cryptococcosis

Celulitis necrotizante como primera manifestación de una criptococosis diseminada

To the Editor:

Cryptococcosis is an opportunistic fungal infection caused by *Cryptococcus neoformans*, an encapsulated yeast of worldwide distribution that is associated with pigeon droppings. The main route of infection is inhalation and in immunocompetent individuals it produces asymptomatic pneumonitis and can very rarely produce primary skin infection.¹⁻³ However, in immunocompromised individuals the infection spreads via the blood to affect other organs: mainly the central nervous system, the skin, and the bones, but any organ or tissue is susceptible to invasion.

We report the case of a 70-year-old woman with chronic autoimmune hepatitis that had progressed to cirrhosis. She had been on treatment with prednisone at a dose of 10 mg per day for the previous 2 years. She was admitted to our hospital for a respiratory infection that had started 4 days earlier and was treated empirically with ciprofloxacin. A week after admission the patient developed high fever and painful skin lesions on her left leg. Physical examination revealed edema of the left leg, together with an indurated, erythematous, and intensely painful plaque in the pretibial region on which numerous vesicular-bullous lesions with necrotic and hemorrhagic content were observed (Figure 1). There was no evidence of arterial ischemia. Histopathology of a lesion revealed edema in the dermis and subcutaneous cell tissue with a predominantly perivascular inflammatory infiltrate. We observed well-defined diffuse dermal microabscesses that extended focally to the subcutaneous cell tissue. The abscesses contained slightly basophilic encapsulated yeast-like structures (Figure 2) that were positive for Alcian blue, periodic acid-Schiff, and methenamine silver. The most relevant laboratory findings were elevated aspartate aminotransferase and alanine aminotransferase levels and

prolongation of the prothrombin time. Serology for hepatitis B and C viruses and human immunodeficiency virus (HIV) was negative. Chest radiograph revealed a bilateral pleural effusion with alveolar infiltrates in the lower lung fields and multiple nodules in the right lung. Latex agglutination of samples from the material aspirated from the vesicular-bullous skin lesions and bronchoalveolar lavage revealed the presence of *C. neoformans* antigens and infection was later confirmed by fungal culture. Treatment was started with liposomal amphotericin B (3 mg/kg/d), low molecular weight heparin, and contact isolation measures. However, the skin lesions progressed rapidly to necrosis and at the same time similar lesions began to appear on the right leg (Figure 3), together with superficial venous thrombosis confirmed by Doppler ultrasound. The clinical course was negative and deterioration of the patient's general condition and the underlying disease ultimately led to death.

Cryptococcosis is a systemic fungal infection that often develops in the context of underlying conditions associated with cellular immunodeficiency, such as transplant, HIV/AIDS, and malignant tumors; in chronic diseases such as rheumatoid arthritis, sarcoidosis, cirrhosis, and systemic lupus erythematosus; and in patients receiving long-term immunosuppressive therapy.⁴⁻⁷



Figure 1 Indurated erythematous plaque consisting of numerous purpuric and vesicular-bullous lesions with necrotic and hemorrhagic content located on the lower and middle thirds of the left pretibial region.

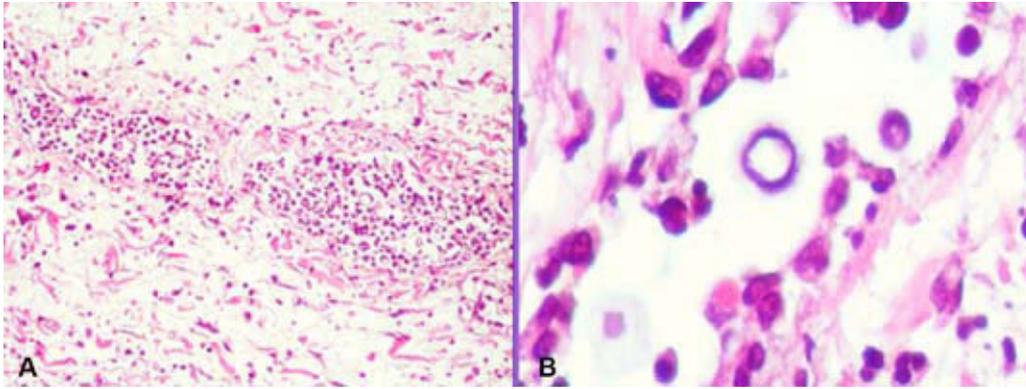


Figure 2 Encapsulated yeast-like structures were observed within the microabscesses (A) and some vascular lumens (B). These structures were round, slightly basophilic, and had a denser peripheral zone surrounded by clear or empty spaces.

Skin involvement in cryptococcosis occurs in 10% to 20% of cases; it is almost always secondary to systemic infection and is therefore considered a sentinel sign of disseminated disease.^{1,4,5} It usually affects the head, scalp, and neck. The lesions may be solitary or multiple, painless or painful, and are characterized by marked clinical polymorphism: papules, ulcers, pustules, granulomas, subcutaneous abscesses, nodules, vesicles, erythematous plaques, pseudoherpetiform lesions, molluscum contagiosum-like lesions, tumor masses, and acneiform lesions.⁸ On rare occasions, necrotizing soft tissue infections (cellulitis and necrotizing fasciitis^{1,4,5}) such as those of the case reported have been found, as have lesions resembling pyoderma gangrenosum, keloid scars, or Kaposi sarcoma.^{9,10}

Cellulitis as the first clinical manifestation of cryptococcal infection, as occurred in our patient, is unusual^{1,5}; it is usually seen only in immunosuppressed patients and, like other necrotizing infections, is associated with a high mortality (80%).¹

Knowledge of the cutaneous manifestations of this infection is important for 2 reasons. First, the lesions may precede other clinical findings that have an insidious onset with few symptoms, such as pulmonary or neurologic involvement. Second, the easy access for skin biopsy, a minimally invasive procedure with a high diagnostic yield, allows samples to be obtained for microbiological culture

and histopathology, diagnostic procedures that are often necessary because of the lack of specificity and clinical polymorphism of the lesions.

The prognosis for these patients is poor because of the close association with immunosuppression, and it depends on an early diagnosis and rapid initiation of effective treatment. It must be remembered that corticosteroids, which are commonly used in daily practice, are potent immunosuppressants of humoral and cellular immunity, leading to increased susceptibility to infection by opportunistic microorganisms; patients receiving corticosteroids must therefore be monitored for any suggestive signs or symptoms, however minor they seem.

In conclusion, cryptococcal infection should be considered in the differential diagnosis of necrotizing cellulitis in immunocompromised patients because rapid diagnosis and treatment will improve the prognosis.^{1,6}

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References

1. Baer S, Baddley JW, Gnann JW, Pappas PG. Cryptococcal disease presenting as necrotizing cellulitis in transplant recipients. *Transpl Infect Dis.* 2009;11:353-8.
2. Posada C, de la Torre C, González-Sixto B, Cruces MJ. Primary cutaneous cryptococcosis presenting with a sporotrichoid pattern in a cancer patient. *Actas Dermosifiliogr.* 2009;100:78-80.
3. Ballesteros M, García I, Daudén E, Sánchez-Pérez J, Iscar T, Fraga J, et al. Criptococosis cutánea primaria asociada a oncotaxia en un paciente inmunodeprimido. *Actas Dermosifiliogr.* 2009;100:77-83.
4. Yoo SS, Tran M, Anhalt G, Barrett T, Vonderheid EC. Disseminated cellulitis cryptococcosis in the setting of prednisone monotherapy for pemphigus vulgaris. *J Dermatol.* 2003;30:405-10.
5. Díaz-Sarrió C, García-Navarro X, Claver-Cercós G, Baucells-Azcona JM, Martín-Plata C, Corcoy-Grabalosa M. Celulitis



Figure 3 Vesicular-bullous lesions with hemorrhagic content on the right leg, associated with firmness of the tissues in the territory of the right saphenous vein.

diseminada como presentación inicial de criptococosis sistémica en un paciente con artritis reumatoide. *Actas Dermosifiliogr.* 2010;101:274-5.

6. Korfel A, Menssen HD, Schwartz S, Thiel E. Cryptococcosis in Hodgkin's disease: description of two cases and review of literature. *Ann Hemat.* 1998;76:283-6.
7. Ramos L, López C, Gómez C, Mathurin S, Mateo A. Cutaneous cryptococcosis in a patient with systemic erythematous lupus. *Mycoses.* 2001;44:419-21.
8. Jones-Caballero M, Fernández-Herrera J, Fernández-Peña P, Fraga-Fernández J, García-Diez A. Criptococosis cutánea imitando a Molluscum contagiosum en paciente con SIDA. *Actas Dermosifiliogr.* 1992;1:24-6.
9. Massa MC, Doyle JA. Cutaneous cryptococcosis simulating pyoderma gangrenosum. *J Am Acad Dermatol.* 1981;5:32-6.
10. Hecker M, Weinberg JM. Cutaneous cryptococcosis mimicking keloid. *Dermatology.* 2001;202:78-9.

M.T. Bordel-Gómez,^{a,*} M.I. Zafra-Cobo,^a
M.E. Cardeñoso-Álvarez,^a J. Sánchez-Estella,^a
M.I. Martín-Arribas^b

^a*Servicio de Dermatología, Hospital Virgen de la Concha, Complejo Asistencial de Zamora, Zamora, Spain*

^b*Servicio de Digestivo, Hospital Virgen de la Concha, Complejo Asistencial de Zamora, Zamora, Spain*

*Corresponding author.

E-mail address: maitebordel@aedv.es,
matebordel@yahoo.es
(M.T. Bordel-Gómez).

Linear Darier Disease

Enfermedad de Darier segmentaria

To the Editor:

Darier disease is an autosomal dominant genodermatosis that usually appears between the ages of 10 and 20 years in seborrheic areas of the trunk and face; it can sometimes present a localized, linear, or zosteriform pattern. The



Figure 1 Patient 1.

presence of these patterns leads to controversy about the most suitable name, as some authors consider it a variant of Darier disease and others consider it an epidermal nevus with special histologic features.

We present 2 cases of linear Darier disease seen in our department. The first case was that of a 42-year-old man with no relevant personal or family history, who had had skin lesions located on the right chest for 25 years. The lesions had remained stable since onset and were asymptomatic, except with exercise, during which the erythema and pruritus increased. The second case was that of a 51-year-old man who was positive for human immunodeficiency virus category A3 and for 17 years had had slightly pruritic skin lesions located on the right abdomen; these lesions had become more apparent in recent months. In both patients we observed several grouped, round papules smaller than 5 mm that were erythematous-orange in color, keratotic, slightly infiltrated, and in some cases excoriated. The lesions had a metameric distribution in the right clavicular fossa and right subpectoral region in case 1 (Figure 1) and on the right abdomen in case 2 (Figure 2). No skin lesions in other areas or mucosal or nail lesions were observed in either of the 2 patients.



Figure 2 Patient 2.