Necrotizing Fasciitis Caused by *Cryptococcus gattii*

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Abstract

Necrotizing fasciitis (NF) is a severe soft-tissue infection that can lead to high morbidity and mortality. The etiology of NF is often polymicrobial. Although rare, fungal organisms have been known to cause NF. Cryptococcus is a fungal infection that may lead to NF.

Here we report the case of a 73-year-old man who had diabetes and presented with pain and swelling in the left hand after being bitten by an insect over the dorsum of the hand. Operative débridement revealed NF caused by *Cryptococcus gattii*. Antifungal medication was started, and the patient underwent multiple débridements of the hand with subsequent skin grafting. Four months later, the hand wound was completely healed.

Authors have reported several cases of NF secondary to *Cryptococcus neoformans* in immunocompromised patients. The emerging *C gattii* pathogen affects immunocompetent patients. Although the transmission route is mainly respiratory, direct inoculation has been described as well.

Ours is the first reported case of NF secondary to *C gattii*. It is important to consider fungal elements as a source of NF. Appropriate treatment includes aggressive surgical débridement and antifungal therapy.

Necrotizing fasciitis (NF) is a severe, rapidly spreading soft-tissue infection with high morbidity and mortality. Bacteriology in NF may be varied, and the etiology is often polymicrobial. It is important to consider the potential for fungal involvement despite its rarity. Cryptococcal NF has been reported in immunocompromised patients, with *Cryptococcus neoformans* being the most common offending organism.[1-4]

C neoformans is a basidiomycotic yeast that was previously considered a homogenous species.[5,6] From the antigenic properties of its polysaccharide capsule, 3 main variants were described: *C neoformans* var. *grubii*, *C neoformans* var. *neoformans*, and *C neoformans* var. *gattii*. Subsequently, *C neoformans* var. *gattii* was found to be genetically and biochemically different from *C neoformans*. This discovery led to the distinction of *C neoformans* var. *gattii* as a separate species and it being renamed *C gattii*.[6]

C gattii was first recognized on Vancouver Island in 2001.[7] Although *C gattii* is predominantly restricted to tropical and subtropical climates, its true epidemiology has been limited by diagnostic methods. *C gattii* can be diagnosed with laboratory culture media such as birdseed agars and L-canavanine-glycine-bromothymol (CGB) agar.[6] However, most reports of *Cryptococcus* NF do not specify the culture media used to isolate *Cryptococcus*. In addition to culture media, molecular genotyping studies also allow for confirmation of the diagnosis of *C gattii* and have the added benefit of enabling identification of the molecular genotype. Nonetheless, in many clinical microbiology laboratories, *Cryptococcus* is not identified to the species level, much less to the molecular genotype.[7] Given these diagnostic limitations and the fact that *C gattii* was only recently identified as a separate species, it is possible that any pre-2006 cases of NF attributed to *C neoformans* could in fact have been caused by *C gattii*.

In this article, we review the literature and report a case of NF of the hand that was caused by *C gattii* in a patient with diabetes. To our knowledge, this is the first reported case of NF caused by *C gattii*. The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 73-year-old man was admitted with a 1-week history of swelling and pain in the dorsum of the left hand. He had been sitting in an outdoor eatery in Singapore when an insect bit the hand over the dorsum. Two days later, he consulted his family physician, who began treatment with oral amoxicillin/clavulanic acid. After 4 days of treatment, there was clinical progression of increased swelling and pain in the hand. Six days after initial injury, the patient presented to the department of orthopedic surgery.

Physical examination revealed diffuse, brawny, nonfluctuant swelling over the entire dorsum of the left hand (**Figure 1**). There was a 1×1-cm ruptured blister with some nonpurulent discharge just distal to the wrist joint. Neurovascular status and the extensor mechanism of the fingers were intact. The wrist

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joint had full range of motion. There was no fever.

Laboratory testing revealed an elevated white blood cell count (16.6×10^9/L), a C-reactive protein (CRP) level of 237 nmol/L, a random blood glucose level of 12.6 mmol/L, and a LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score of 7.[8]

Given the severe swelling, intravenous amoxicillin/clavulanic acid was started. The patient received a total of 3 doses before operative débridement of the left hand. Operative findings were NF of the hand, grayish necrotic fascia, and foul-smelling "dishwater" fluid. A single specimen of fascia from the surgical site was sent for examination. Histopathologic examination of formalin-fixed, paraffin-embedded tissue revealed necrotizing suppurative inflammation with fungal organisms present (**Figures 2, 3**).

Tissue cultures were obtained during surgery. The organism grew as scanty, small, wet-looking colonies on sheep blood agar after 48 hours of incubation. Microscopy revealed an oval yeast. The organism was identified and reported as *C gattii* by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS; Biotyper 2.0.1 software; Bruker Daltonics), with a score of 1.914.[9] All other intraoperative cultures for aerobic and anaerobic bacteria were negative. Molecular genotyping was performed with polymerase chain reaction assay to identify the molecular subtype.[10] *C gattii* genotype VGII was isolated. A cryptococcal serum antigen assay was positive at 1:256.

A series of tests was performed to screen for disseminated disease. Blood cultures were negative for fungus. Chest radiography and computed tomography of the brain did not show any pulmonary or cerebral involvement. Cerebrospinal fluid was not available for examination, as the patient declined lumbar puncture. Blood tests included a negative result for human immunodeficiency virus (HIV). The patient was found to have previously undiagnosed diabetes mellitus (hemoglobin A_{1c}, 7.9%). T-cell counts and ratios were normal.

The patient was started on intravenous amphotericin B 60 mg/d and flucytosine 500 mg every 6 hours for 3 weeks. Oral

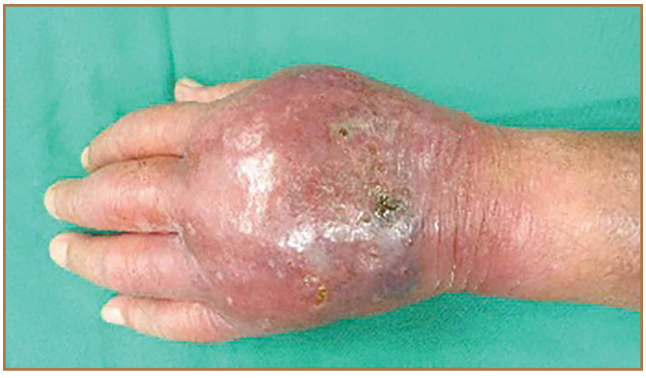

Figure 1. Diffuse, brawny, nonfluctuant swelling over entire dorsum of left hand. Ruptured blister (1×1 cm) with nonpurulent discharge is present.

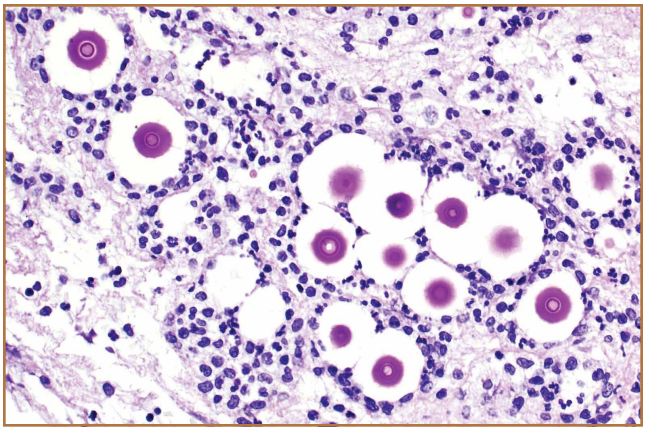

Figure 2. Spherical structures stain positive with periodic acid-Schiff diastase.

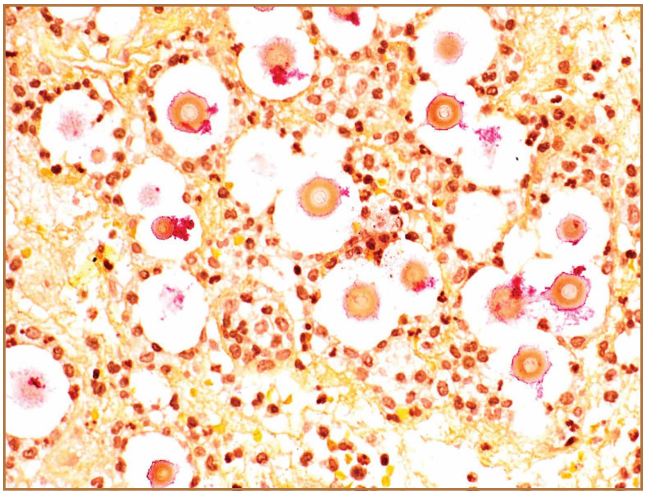

Figure 3. Fungal elements with mucicarmine-positive capsules, consistent with *Cryptococcus*.

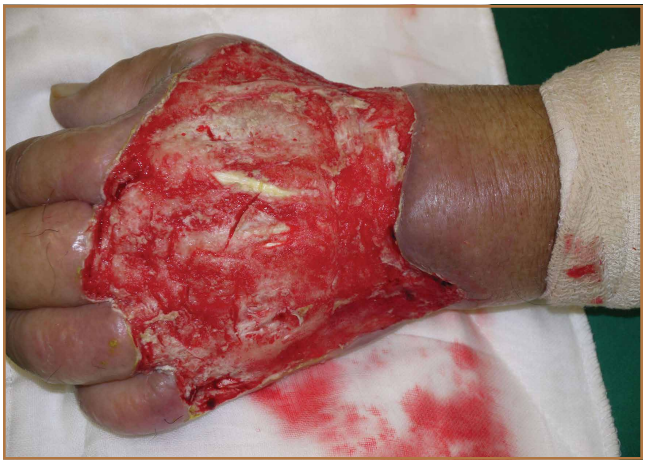

Figure 4. Extensive débridement and reversal of infection before skin grafting.

fluconazole 400 mg every morning was also given (intended duration, 6 mo). Given that diabetes was newly diagnosed, the patient was treated with metformin; his capillary blood glucose level remained stable during his inpatient stay.

Four débridements of the dorsal hand wound were performed—the first on day of admission and the other 3 on hospitalization days 3, 7, and 18 (**Figure 4**). Subsequent wound resurfacing with a split skin graft harvested from the forearm was performed on hospitalization day 22. After surgery, the hand was dressed with a bulky cotton dressing. Five days after the patient was discharged, during review in the outpatient clinic, the skin graft was noted to be taking well. The patient did not attend postoperative physical therapy. He was maintained on metformin and given a follow-up clinic appointment for his diabetes. Four months after surgery, the wound was completely healed, and normal functional use of the hand recovered.

Discussion

NF is a severe soft-tissue infection with potential for rapid progression. Surgical débridement should be performed urgently to reduce the chance of morbidity and mortality.[11] The initial classification by Giuliano and colleagues[12] was based on bacteriology and included type I (anaerobic species in combination with a facultative species) and type II (monomicrobial usually involving group A β-hemolytic *Streptococcus*). This classification was modified by Morgan[13] to include gram-negative organisms as well as fungal organisms (**Table 1**).

Fungal NF is rare, with *Candida*, *Apophysomyces*, and *Cryptococcus* described in the literature.[1,14,15] Fungal infections tend to occur in immunocompromised patients; risk factors are steroid immunosuppression, poorly controlled diabetes, and peripheral vascular disease.[16] Some zygomycetes may also affect immunocompetent patients.[15]

C gattii is an encapsulated yeast organism that is genetically and biochemically distinct from *C neoformans*. It is endemic to tropical parts of Africa and Australia. Its main environmental sources are eucalyptus trees (*Eucalyptus camaldulensis*, *Eucalyptus tereticornis*) and decaying hollows in living trees.[17] In addition, there have been reports of isolation of *C gattii* from insect frass,[18] which would make infection by an insect bite a possible transmission route. Worldwide distribution of this pathogen has increased recently, with outbreaks noted on Vancouver Island and in areas in Canada and the northwest United States.[7]

The true incidence of NF secondary to *C gattii* is difficult to determine. *C gattii* was only recently identified as a separate species, and pre-2006 cases of NF attributed to *C neoformans* may instead have been caused by *C gattii*. Misidentification has been compounded by the fact that the tests required for accurate diagnosis of *C gattii* infection may not be readily available in many clinical microbiology laboratories. *Cryptococcus* can be identified with various methods, including direct microscopy, culturing of tissue or fluid samples, and measurement of cryptococcal serum antigen. However, tests such as specific culture media, mass spectrometry, and molecular typing studies are required to determine cryptococcal species. L-canavanine-glycine-bromothymol blue (CGB) agar is a medium that is often used to differentiate *C gattii* from *C neoformans* because of the ability of *C gattii* to produce a blue appearance.[6] Modern techniques, such as MALDI-TOF MS, have also been used to successfully distinguish between *C gattii* and *C neoformans*.[9] MALDI-TOF MS identifies species on the basis of characteristic protein spectra extracted from whole cells. Using commercial and supplemental reference libraries, the system compares signal matches in the reference spectrum with *Cryptococcus* entries in the library—allowing rapid and accurate identification of cryptococcal species. However, this diagnostic method is limited by availability of adequate *Cryptococcus* entries in the reference library and by the high cost of acquiring the machine.

Serotyping is based on the antigenic property of the capsule and was once used to differentiate *C neoformans* into its 3 main varieties: var. *neoformans*, var. *grubii*, var. *gattii*. However, when it was realized that the antigenic property of the strain can be unstable and that there are hybrids containing more than 1 serotype, serotyping was abandoned as a species-differentiation test.[6] The current gold standard for species differentiation is molecular genotyping. Molecular genotyping studies can confirm the diagnosis of *C gattii* infection and allow differentiation of *C gattii* into its 4 main molecular types: VGI, VGII, VGIII, VGIV. Using methods such as polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis, molecular typing allows for specific epidemiology charting of *C gattii* genotypes.[7]

Although the transmission route for cryptococcal infection is mainly respiratory, direct inoculation has been reported

Table 1. Microorganisms That Cause Necrotizing Fasciitis

NF Type[a]	Clinical Description	Organism(s)
Type I	Most common type of NF[11]	Polymicrobial Synergistic infections with aerobic and anaerobic organisms
Type II	May occur in individuals with no underlying comorbidities[11]	Monomicrobial Most commonly from group A β-hemolytic *Streptococcus* (GAS)[11]
Type III	History of exposure to seawater and marine animals or seafood ingestion Fulminant course and may result in rapid multi-organ failure[13]	*Vibrio* species
Type IV	Usually associated with trauma[13] May affect both immuno-competent[3] and immuno-compromised patients[1,4]	Fungal species *Cryptococcus*[1,3,4] *Candida*[14] Zygomycetes[15]

Abbreviation: NF, necrotizing fasciitis.
[a]Based on Morgan's typing scheme for necrotizing fasciitis.[13]

as well.[19] Cutaneous lesions, which occur in 5% to 20% of cryptococcal infections, often present in the head and neck.[2,20,21] Primary cutaneous infections from cryptococcosis are rare, and cutaneous manifestations are often a sign of disseminated disease. Disseminated disease is defined as the involvement of 2 or more noncontiguous sites or evidence of high fungal burden

Table 2. Characteristics of Reported Patients With Necrotizing Fasciitis From *Cryptococcus*

Reference (Country/Year)	Patient Age, y/ Sex	*Cryptococcus* Variety	Disseminated or Cutaneous	Diagnostic Test	Comorbidities	Immuno-suppressant	Presentation Site	Outcome
Marcus et al[1] (USA/1998)	43/M	*Neoformans*	Disseminated	Histopathology Culture Serum antigen	Renal transplant	Cyclosporine 150 mg twice daily Prednisolone 10 mg daily	Bilateral thighs	Alive Débridement with SSG
Huang et al[2] (Taiwan/2007)	58/M	Unknown	Disseminated	Histopathology Culture Serum antigen	Diabetes mellitus	Nil	Right thigh	Death
Capoor et al[3] (India/2008)	40/M	*Neoformans* var. *grubii*	Disseminated	Culture Serotyping	Chronic alcoholism	Nil	Right gluteus	Alive Débridement with SSG
Adachi et al[4] (Japan/2009)	55/F	*Neoformans*	Unknown	Histopathology Culture Serum antigen	Pemphigus vegetans	4-week history of: Cyclosporine 5 mg/kg/d Methotrexate 6 mg weekly MMF 2 g daily	Right calf	Alive Débridement with SSG
Basaran et al[20] (Turkey/2003)	45/M	*Neoformans*	Cutaneous	Histopathology Culture	Renal transplant	Cyclosporine 200 mg daily Prednisolone 20 mg daily Azathioprine 100 mg daily	Bilateral calves	Alive Débridement with SSG
Baer et al[21] (USA/2009)	61/M	*Neoformans*	Disseminated	Histopathology Culture Serum antigen	Renal transplant	Cyclosporine 50 mg twice daily MMF 750 mg twice daily Prednisolone 10 mg daily	Bilateral calves	Alive Débridement with SSG
	64/M	*Neoformans*	Disseminated	Histopathology Culture Serum antigen	Renal transplant	MMF 750 mg twice daily Tacrolimus 1 mg twice daily Prednisolone 10 mg daily	Left leg	Death
	57/M	*Neoformans*	Disseminated	Histopathology Culture Serum antigen	Heart transplant	MMF 500 mg twice daily Prednisolone 10 or 15 mg daily	Bilateral calves	Death
Gave et al[24] (USA/2004)	84/F	*Neoformans*	Cutaneous	Histopathology Culture	Hemolytic anemia Renal disease Porcine mitral valve	Nil	Bilateral calves	Death
Bégon et al[26] (France/2009)	85/F	*Neoformans*	Cutaneous	Histopathology Culture	Diabetes mellitus Chronic renal failure	Nil	Right hand	Death
Doorenbos-Bot et al[27] (Netherlands/ 1990)	25/M	*Neoformans*	Cutaneous	Histopathology Culture	Nil	Nil	Periorbital	Alive
Yoneda et al[28] (Japan/2014)	50/M	*Neoformans*	Cutaneous	Histopathology Culture Serum antigen	Renal transplant	Doses not available: Basiliximab Tacrolimus MMF Prednisolone	Bilateral lower limbs	Alive Débridement with SSG

Abbreviations: MMF, mycophenolate mofetil; SSG, split skin graft.

based on cryptococcal antigen titer of more than 1:512.[12] It is important to exclude disseminated disease in all cases of cryptococcosis, as it may be fatal.[20] The neural and pulmonary systems should be screened.[22] Cellulitis from cryptococcosis is almost always limited to immunocompromised patients, though there are reports of crytococcal cutaneous disease in immunocompetent patients.[3,15] Interestingly, though *C neoformans* often affects immunocompromised patients, the emerging pathogen of *C gattii* affects immunocompetent patients.[7,17,23] Our patient's undiagnosed diabetes may have been a risk factor for cryptococcal infection. His cryptococcal antigen titer was 1:256, with no evidence of other sites of involvement. We therefore believe this to be a rare case of direct inoculation secondary to an insect bite.

The literature includes 12 reported cases of NF secondary to *Cryptococcus* (**Table 2**), all *C neoformans*. Of these cases, 9 involved immunosuppression, and most of these patients were on long-term steroid treatment after organ transplantation. The most common infection site was the lower extremity. These cases of cryptococcal NF show that immunosuppression, and long-term steroid use in particular, is an important risk factor. The mortality rate for these reviewed cases was 41.6% (5/12). According to the literature, the mortality rates for patients with cryptococcal soft-tissue infections[24] and posttransplant patients with cryptococcal NF[21] were 37.5% and 60%, respectively. We believe the mortality rate in our reviewed cases likely was confounded by the fact that most of the patients were posttransplant patients on long-term immunosuppression.

Of the 12 patients, 5 had primary cutaneous disease. There seems to be no relationship between outcome and dissemination of disease. In addition, there is a paucity of literature on the effect of disseminated disease and cryptococcal soft-tissue infections. Therefore, no firm conclusions can be drawn regarding the effects of disseminated disease on severity of cryptococcal soft-tissue infection.

Treatment of cryptococcal NF involves a combination of surgical débridement and long-term antifungal therapy. Surgical débridement of NF includes delineating the extent of infection with complete surgical excision of the affected tissue.[25] The aims of surgery should be to remove all unhealthy tissue, identify the offending organism, and plan for resurfacing or reconstruction of the afflicted extremity. Intraoperative-tissue histology should be performed to confirm the diagnosis of NF. Histology can be used to demonstrate cryptococcal infection. The diagnosis of cryptococcal infection can be aided with fungal cultures, and therefore we recommend that tissue cultures be sent not only for routine aerobic/anaerobic bacteria but also for mycobacteria and fungal organisms. Laboratory tests that aid in diagnosis include serum cryptococcal antigen titer.

The current treatment recommendation for cryptococcal disease in patients who are not HIV-positive or transplant hosts is amphotericin B deoxycholate 0.7 to 1.0 mg/kg/d plus flucytosine 100 mg/kg/d for at least 4 weeks.[22] The regimen period may be shortened to 14 days for patients at low risk of treatment failure. Fluconazole should be given as maintenance therapy (200 mg/d) for 6 to 12 months. There is no compelling evidence for immunoglobulin therapy for cryptococcal disease.[22]

Conclusion

NF caused by *Cryptococcus* is rare. A high level of suspicion, and intraoperative specimens for histology and fungal microscopy and culture, can help in establishing the diagnosis. Molecular genotyping remains the diagnostic method of choice for NF secondary to *Cryptococcus*. Effective treatment consists of aggressive surgical débridement and antifungal therapy.

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References

1. Marcus JR, Hussong JW, Gonzalez C, Dumanian GA. Risk factors in necrotizing fasciitis: a case involving *Cryptococcus neoformans*. *Ann Plast Surg*. 1998;40(1):80-83.
2. Huang KC, Tu YK, Lee KF, Huang TJ, Wen-Wei Hsu R. Disseminated cryptococcosis presented as necrotizing fasciitis of a limb. *J Trauma*. 2007;63(2):E44-E46.
3. Capoor MR, Khanna G, Malhotra R. Disseminated cryptococcosis with necrotizing fasciitis in an apparently immunocompetent host: a case report. *Med Mycol*. 2008;46:269-273.
4. Adachi M, Tsurata D, Imanishi H, Ishii M, Kobayashi H. Necrotizing fasciitis caused by *Cryptococcus neoformans* in a patient with pemphigus vegetans. *Clin Exp Dermatol*. 2009;34(8):e751-e753.
5. Enache-Angoulvant A, Chandenier J, Symoens F, et al. Molecular identification of *Cryptococcus neoformans* serotypes. *J Clin Microbiol*. 2007;45(4):1261-1265.
6. Kwon-Chung KJ, Varma A. Do major species concepts support one, two or more species within *Cryptococcus neoformans*? *FEMS Yeast Res*. 2006;6(4):657-687.
7. Datta K, Bartlett KH, Baer R, et al; *Cryptococcus gattii* Working Group of the Pacific Northwest. Spread of *Cryptococcus gattii* into Pacific Northwest region of the United States. *Emerg Infect Dis*. 2009;15(8):1185-1191.
8. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med*. 2004;32(7):1535-1541.
9. McTaggart LR, Lei E, Richardson SE, Hoang L, Fothergill A, Zhang SX. Rapid identification of *Cryptococcus neoformans* and *Cryptococcus gattii* by matrix-assisted laser desorption ionization-time of flight mass spectrometry. *J Clin Microbiol*. 2011;49(8):3050-3053.
10. Meyer W, Castañeda A, Jackson S, Huynh M, Castañeda E; IberoAmerican Cryptococcal Study Group. Molecular typing of IberoAmerican *Cryptococcus neoformans* isolates. *Emerg Infect Dis*. 2003;9(2):189-195.
11. Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO. Necrotizing fasciitis: clinical presentation, microbiology and determinants of mortality. *J Bone Joint Surg Am*. 2003;85(8):1454-1460.
12. Giuliano A, Lewis F Jr, Hadley K, Blaisdell FW. Bacteriology of necrotizing fasciitis. *Am J Surg*. 1977;134(1):52-57.
13. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. *J Hosp Infect*. 2010;75(4):249-257.
14. Buchanan PJ, Mast BA, Lottenberg L, Kim T, Efron PA, Ang DN. *Candida albicans* necrotizing soft tissue infection: a case report and literature review

of fungal necrotizing soft tissue infections. *Ann Plastic Surg*. 2013;70(6):739-741.
15. Jain D, Kumar Y, Vasishta RK, Rajesh L, Pattari SK, Chakrabarti A. Zygomycotic necrotizing fasciitis in immunocompetent patients: a series of 18 cases. *Modern Pathol*. 2006;19(9):1221-1226.
16. Fontes RA Jr, Ogilvie CM, Miclau T. Necrotizing soft-tissue infections. *J Am Acad Orthop Surg*. 2000;8(3):151-158.
17. Sorrell TC. *Cryptococcus neoformans* variety *gattii*. *Med Mycol*. 2001;39(2):155-168.
18. Kidd SE, Sorrell TC, Meyer W. Isolation of two molecular types of *Cryptococcus neoformans* var. *gattii* from insect frass. *Med Mycol*. 2003;41(2):171-176.
19. Neuville S, Dromer F, Morin O, Dupont B, Ronin O, Lortholary O; French Cryptococcosis Study Group. Primary cutaneous cryptococcosis: a distinct clinical entity. *Clin Infect Dis*. 2003;36(3):337-347.
20. Basaran O, Emiroglu R, Arikan U, Karakayali H, Haberal M. Cryptococcal necrotizing fasciitis with multiple sites of involvement in the lower extremities. *Dermatol Surg*. 2003;29(11):1158-1160.
21. Baer S, Baddley JW, Gnann JW, Pappas PG. Cryptococcal disease presenting as necrotizing cellulitis in transplant recipients. *Transpl Infect Dis*. 2009;11(4):353-358.
22. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(3):291-322.
23. Chan M, Lye D, Win MK, Chow A, Barkham T. Clinical and microbiological characteristics of cryptococcosis in Singapore: predominance of *Cryptococcus neoformans* compared with *Cryptococcus gattii*. *Int J Infect Dis*. 2014;26:110-115.
24. Gave AA, Torres R, Kaplan L. Cryptococcal myositis and vasculitis: an unusual necrotizing soft tissue infection. *Surg Infect*. 2004;5(3):309-313.
25. Wong CH, Yam AK, Tan AB, Song C. Approach to debridement in necrotizing fasciitis. *Am J Surg*. 2008;196(3):e19-e24.
26. Bégon E, Bachmeyer C, Thibault M, et al. Necrotizing fasciitis due to *Cryptococcus neoformans* in a diabetic patient with chronic renal insufficiency. *Clin Exp Dermatol*. 2009;34(8):935-936.
27. Doorenbos-Bot AC, Hooymans JM, Blanksma LJ. Periorbital necrotising fasciitis due to *Cryptococcus neoformans* in a healthy young man. *Doc Ophthalmol*. 1990;75(3-4):315-320.
28. Yoneda T, Itami Y, Hirayama A, Saka T, Yoshida K, Fujimoto K. Cryptococcal necrotizing fasciitis in a patient after renal transplantation—a case report. *Transplant Proc*. 2014;46(2):620-622.

This paper will be judged for the Resident Writer's Award.