Rheumatol Int (2009) 29:1237–1241
DOI 10.1007/s00296-009-0928-1

SHORT COMMUNICATION

Spondylodiscitis due to an emergent fungal pathogen: *Blastoschizomyces capitatus*, a case report and review of the literature

Aygul Dogan Celik · Resat Ozaras · Serda Kantarcioglu · Ali Mert · Fehmi Tabak · Recep Ozturk

Received: 20 November 2008 / Accepted: 28 March 2009 / Published online: 16 April 2009

Abstract The study includes a case report and a literature review. The main objective of this study is to present a case of spondylodiscitis due to a fungal pathogen, *Blastoschizomyces capitatus* and to review the published literature on this emergent fungus in etiology of spondylodiscitis, and osteomyelitis. Osteoarticular involvement due to *B. capitatus* has been reported in six cases, and vertebral involvement has been seen in five of them. All of these cases had underlying malignancy. Infection is usually advanced at presentation. Case notes and online databases were reviewed. Organism was isolated from bone material in all of the cases and antibiotic treatment by antifungal agents cured the infection. We present another case of infectious spondylodiscitis due to *B. capitaus*, which is reported first in Turkey and tried to attract attendance to this emergent fungal pathogen as an etiologic agent of spine infections in cancer patients.

Keywords Spondylodiscitis · *Blastoschizomyces capitatus* · Fungus

Introduction

Opportunistic fungal infections represent one of the most frequent causes of morbidity, and mortality in immunocompromised patients. The most common fungal pathogens are *Candida, Aspergillus,* and *Rhizomucor* species. *Geotrichum capitatum* (formerly known as *Blastoschizomyces capitatus, Trichosporon capitatus)* is a rare pathogen in immunocompromised host. The mycosis caused by this fungal agent is often associated with multiorgan involvement and fatal outcome [1, 2]. According to the MEDLINE database in English language, 132 cases of *B. capitatus* infection have been reported during 1966–2008 [1–33]. Musculoskeletal involvement has been presented in six of them: mandibular osteomyelitis in one and spondylodiscitis in five patients [1, 3–7] (Table 1). We presented here another case of spondylodiscitis caused by *B. capitatus*, which is documented first in Turkey in a patient with colon adenocarcinoma with liver metastases and reviewed the other cases.

A. D. Celik (✉)
Trakya University School of Medicine, Edirne, Turkey
e-mail: adogancelik@yahoo.com.tr

R. Ozaras · S. Kantarcioglu · A. Mert · F. Tabak · R. Ozturk
Istanbul University Cerrahpaşa School of Medicine,
Istanbul, Turkey

Case report

A 65-year-old man was admitted to our clinic with lumbar pain and weakness on both of his legs in January 2003. Before admission to our clinic, he had undergone sigmoid colon resection and, colostomy operation due to colon adenocarcinoma. His colostomy has surgically been corrected in September 2001. Ileostomy was closed in December 2001 and antineoplastic chemotherapy with 5-fluorouracil for colon adenocarcinoma was started in January 2002.

His complaints of lumbar pain developed in May 2002. At this time, upper abdominal magnetic resonance imaging (MRI) had been performed and hypointense pathologic signals on third and fourth lumbar vertebral bodies at T_2-weighted images were detected. Bone scan revealed compression fracture on fourth lumbar vertebral body; and increased activity on left lateral part of the third lumbar vertebral body. These findings had suggested an adenocarcinoma metastasis to the vertebra, and radiotherapy had been performed. He had been followed up without any complaints until December 2002. At this time, weakness on

Table 1 Features of cases with osteoarticular infection due to *Blastoschizomyces capitatus*

Reference number	Year	Underlying disease	Previous therapy for underlying disease	Site of infection	Sites from which *B. Capitatus* was recovered	Therapy	Duration of therapy	Outcome
1	1994	ALL	NA	Vertebra intervertebral disk	Blood/CVC tip/bone	Amph B, Itraconazole	2 months ND	Cure
3	1998	ALL	BMT	Lungs/vertebra intervertebral disk	Blood/bone	Amph B, Itraconazole	40 days 10 months	Cure
4	1999	AML	Cytarabine, idarubicin, methotrexate	Mandibular bone	Bone	Amph B, Fluconazole	1 month 5 months	Cure
6	2004	ALL	BMT	Costal cartilage/vertebra	Costal cartilage	Itraconazole	ND	Cure
5	2004	ALL	BMT	Vertebra intervertebral disk	Blood/bone	Itraconazole	220 days	Cure
6	2008	AML	Cytarabine, idarubicin	Vertebra intervertebral disk	Bone	Voriconazole, Amph B	6 months	Cure
Present case	2008	Colon adenocarcinoma	Colectomy 5-fluorouracil	Vertebra intervertebral disk	Bone	Amph B, Itraconazole	40 days 4 months	Cure

ALL acute lymphoblastic leukemia, *AML* acute myeloid leukemia, *Amph B* Amphotericin B, *BMT* bone marrow transplantation, *CVC* central venous catheter, *ND* no data

Fig. 1 Sagittal T1-weighted, fat saturated T2-weighted and axial T1-weighted images show pathological signal intensities at the sides of third and fourth lumbar vertebral end-plates. There is also pathological signal in disk space

both of his legs, and lumbar pain has recurred. Lumbar MRI was performed again. Lytic lesions had been detected at the sides of third, and fourth lumbar vertebral bodies and fluid collections had been detected in intervertebral discs (Figs. 1, 2, 3). He had been operated on, all necrotic material was surgically removed, and biopsy materials from disk, and bone tissue had been examined pathologically and microbiologically. Histological examination of the biopsy specimens with hematoxylin–eosin, and periodic acid-Schiff stain revealed mycotic spondylodiscitis. Gram staining of the biopsy specimens had disclosed fungal elements, and culture had grown yeast. After these findings the patient referred to our clinic.

On admission to our clinic, he reported pain on the lumbar area, and general weakness. The leukocyte count was 6,500/mm^3 with 65% neutrophils; the erythrocyte sedimentation rate was 35 mm/h; C-reactive protein was 5 mg/dl (*N* 0–5 mg/dl). Biochemistry was totally normal. Abdomen CT revealed metastatic lesion on the right lobe of the liver, also disclosed soft tissue mass with free air images near to left psoas muscle. Because of the patient's poor general condition surgical drainage of this abscess could not be performed. The patient was treated with amphotericin B for 40 days. A control CT after therapy showed a significant

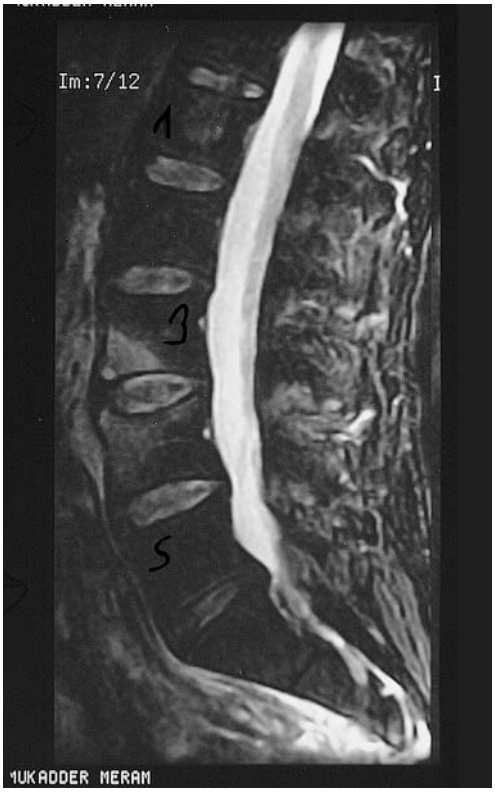

Fig. 2 Sagittal T1-weighted, fat saturated T2-weighted and axial T1-weighted images show pathological signal intensities at the sides of third and fourth lumbar vertebral end-plates. There is also pathological signal in disk space

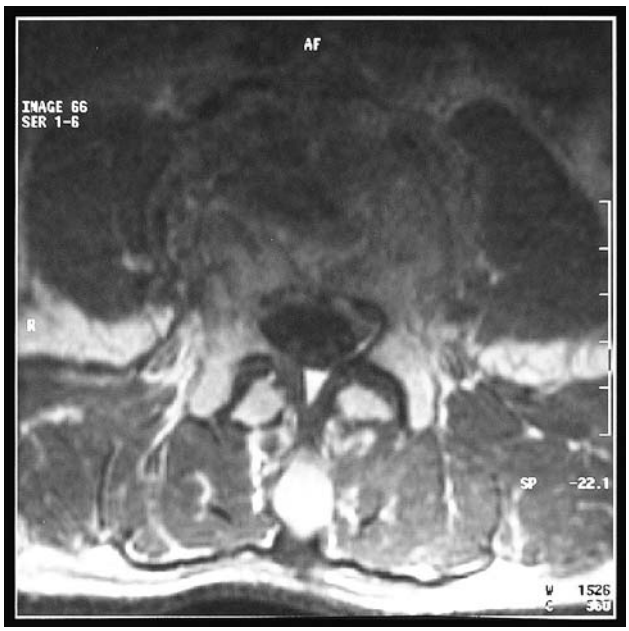

Fig. 3 Sagittal T1-weighted, fat saturated T2-weighted and axial T1-weighted images show pathological signal intensities at the sides of third and fourth lumbar vertebral end-plates. There is also pathological signal in disk space

regression of abscess. The therapy switched to oral itraconazole. After 2 months of itraconazole treatment, he has been doing well but he failed to come following up.

Microbiological studies

Identification of the case isolate was performed in Deep Mycoses Laboratory (Department of Microbiology and Clinical Microbiology, Basic Medical Sciences Section). Minimal inhibitory concentrations of antifungal agents for the isolate were found as follows: Amphotericin 0.25 μ/ml, fluconazole 32 μ/ml, itraconazole 4 μ/ml, ketoconazole 4 μ/ml, terbinafine 0.5 μ/ml.

Discussion

Blastochizomyces capitatus (formerly *T. capitatum, G. capiatatum*) is a normal inhabitant of soil, human skin, digestive and respiratory tract [8, 9]. As far as *Trichosporon* species are concerned *T. capitatum* (*G. capitatum*) has been considered as a separate genus and retained as *B. capitatus* [10–12]. Although it is a frequent cause of superficial mycotic infections such as white piedra, it rarely causes systemic infection in a non-compromised individual [9]. The incidence of invasive fungal infections with *Trichosporon spp.* in patients with hematological malignancies has risen over the last two decades, mainly as a result of the increased use of immunosuppressive therapy. There are also several studies suggesting this species as the most common yeast type after *Candida spp*. causing fungal infection in cancer patients but in these reports *B. capitaus* is the genus that is the least frequent causative agent [13, 14].

B. capitaus is a yeast-like fungus with a low pathogenic potential, which is occasionally isolated from clinical specimens, usually without clinical significance [11]. Neutropenia, cytotoxic agents or corticosteroids administration, use of antibiotics, presence of central venous catheter have been presumed to predispose for infection or colonization with this fungal agent [10, 15]. Opportunistic infections with *B. capitatus* can occur in various types of immunocompromised patients; those with hematological malignancies are by far the most common victims. Underlying condition in all of the reported cases of spondylodiscitis due to this fungal organism is hematologic malignancy [1, 3, 5–7] and all of these local infections are secondary to documented fungemia except for one [6]. In two cases, the infections occurred during a period of neutropenia after cytotoxic chemotherapy [1, 6]. The other two patients had fungemia during the neutropenic phase after undergoing an allogeneic bone marrow transplantation, which was

apparently cured with antifungal therapy [3, 5]. One of these patients developed proven multiple spondylodiscitis due to *B. capitatus* infection 7 months after cure; this second episode was considered to be a reactivation of a latent infection during immunosuppression for treatment of graft-versus-host disease [5]. Blood count had no abnormality in the other patient when spondylodiscitis was detected [3]. The other osteoarticular infection caused by *B. capitatus* reported in the literature is mandibular osteomyelitis. This infection also developed in a patient who had acute myelogenous leukemia and low neutrophil count due to cytotoxic chemotherapy [4]. The case we present here had a solid tumor and his neutrophil count was always in normal value. There was no clinical sign of infection such as fever, and there was no abnormality in laboratory values suggesting any infectious process and we also did not detect fungemia so the findings on vertebral MRI was considered as metastatic process due to colon adenocarcinoma instead of an infectious spondylodiscitis. Although antifungal therapy has been delayed in our patient due to the late diagnosis the clinical course was not so aggressive like the other cases reported in the literature. This dormant course in our case is thought to be due to the absence of neutropenia in any period. This observation also confirms the slow progression of infectious spondylodiscitis even if a fungal agent is present in the etiology like D'Antonio et al. [1] reported in their review. The insidious progression of clinical course, the no specificity of laboratory data, and the inability to recognize the etiologic agent without open biopsy or closed needle aspiration may lead to diagnostic and therapeutic delay like in our case.

B. capitaus is a fungus that is present in the soil, normal human skin, and digestive and respiratory tracts. The lungs, gastrointestinal tract, intravenous catheter sites, oral mucosa are thought to be the likely portals of entry for this agent [16]. We suspect that in our patient the organism was introduced during intraabdominal surgery due to impairment of integrity of the intestinal wall, and caused spondylodiscitis by contagious way.

Most disseminated *B. capitaus* infections in immunosuppressed patients who were severely neutropenic had a fatal outcome [8, 10–12, 17–25]. Besides these cases therapeutic success with amphotericin B [4, 10, 13, 25], ketoconazole, itracaconazole [1], 5-fluorocytosine [26] has been reported. According to the results of in vitro antifungal susceptibility tests of our clinical isolate amphotericin B was convenient agent for therapy. This result correlated with clinical observation of intraabdominal inflammation regression. The therapeutic response of amphotericin B in our case was also due to the absence of severe immunosuppression.

In conclusion, we present another case of infectious spondylodiscitis due to *B. capitaus*, which is reported first in Turkey and tried to attract attendance to this emergent fungal pathogen as an etiologic agent in osteoarticular infections in cancer patients.

References

1. D'Antonio D, Piccolomini R, Fioritoni G, Iacone A, Betti S, Fazii P, Mazzoni A (1994) Osteomyelitis and intervertebral discitis caused by *Blastoschizomyces capitatus* in a patient with acute leukemia. J Clin Microbiol 32(1):224–227
2. Groll AH, Walsh TJ (2001) Uncommon opportunistic fungi: new nosocomial threats. Clin Microbiol Infect 7(Suppl 2):8–24. doi:10.1111/j.1469-0691.2001.tb00005.x
3. Ortiz AM, Sanz-Rodriguez C, Culebras J et al (1998) Multiple spondylodiscitis caused by *Blastoschizomyces capitatus* in an allogeneic bone marrow transplantation recipient. J Rheumatol 25:2276–2278
4. Cheung MY, Chiu NC, Chen SH et al (1999) Mandibular osteomyelitis caused by *Blastoschizomyces capitatus* in a child with acute myelogenous leukemia. J Formos Med Assoc 98:787–789
5. Martino R, Salavert M, Parody R et al (2004) *Blastoschizomyces capitatus* infection in patients with leukemia: report of 26 cases. Clin Infect Dis 38:335–341. doi:10.1086/380643
6. Yoshihara T, Mori K, Nishimura Y et al (2004) Osteocartilaginous involvement in *Blastoschizomyces capitatus* (Trichosporon capitatum) infection in a bone marrow transplant recipient. Br J Haematol 124:405. doi:10.1046/j.1365-2141.2003.04666.x
7. Mejdoubi M, Huynh A, Danho C, Boot B (2008) Cervical spondylodiscitis caused by *Blastoschizomyces capitatus*. Infection. doi:10.1007/s15010-007-7081-0
8. Liu KL, Herbrecht R, Bergerat JP et al (1990) Disseminated *Trichosporon capitatum* infection in a patient with acute leukemia undergoing bone marrow transplantation. Bone Marrow Transplant 6:219–221
9. D'Antonio D, Mazzoni A, Iacone A et al (1996) Emergence of fluconazole-resistant strains of *Blastoschizomyces capitatus* causing nosocomial infections in cancer patients. J Clin Microbiol 34:753–755
10. Martino P, Venditti M, Micozzi A et al (1990) *Blastoschizomyces capitatus*: an emerging cause of invasive fungal disease in leukemia patients. Rev Infect Dis 12:570–582
11. Buchta V, Zak P, Kohout A et al (2001) Case report. Disseminated infection of *Blastoschizomyces capitatus* in a patient with acute myelocytic leukaemia. Mycoses 44:505–512. doi:10.1046/j.1439-0507.2001.00699.x
12. Polacheck I, Salkin IF, Kitzes-Cohen R et al (1992) Endocarditis caused by *Blastoschizomyces capitatus* and taxonomic review of the genus. J Clin Microbiol 30:2318–2322
13. Sanz MA, Lopez F, Martinez ML et al (1996) Disseminated *Blastoschizomyces capitatus* infection in acute myeloblastic leukaemia. Report of three cases. Support Care Cancer 4:291–293. doi:10.1007/BF01358882
14. Al-Hedaithy SS (2003) The yeast species causing fungemia at a university hospital in Riyadh, Saudi Arabia, during a 10-year period. Mycoses 40:293–298
15. Sycova-Mila Z, Sufliarsky J, Trupl J et al (1992) Catheter associated septicemia due to *Trichosporon capitatum*. J Hosp Infect 22:257–258. doi:10.1016/0195-6701(92)90050-V
16. Mahul P, Piens MA, Guyotat D et al (1989) Disseminated *Geotrichum capitatum* infection in a patient with acute myeloid leukemia. Mycoses 32:573–577
17. Ito T, Ishikawa Y, Fujii R et al (1988) Disseminated *Trichosporon capitatum* infection in a patient with acute leukemia. Cancer 61:585–588. doi:10.1002/1097-0142(19880201)61:3<585::AID-CNCR2820610327>3.0.CO;2-#

18. Naficy AB, Murray HW (1990) Isolated meningitis caused by *Blastoschizomyces capitatus*. J Infect Dis 161:1041
19. Baird DR, Harris M, Menon R et al (1985) Systemic infection with *Trichosporon capitatum* in two patients with acute leukaemia. Eur J Clin Microbiol 4:62–64. doi:10.1007/BF02148664
20. Haupt HM, Merz WG, Beschorner WE et al (1983) Colonization and infection with Trichosporon species in the immunosuppressed host. J Infect Dis 147:199–203
21. Winston DJ, Balsley GE, Rhodes J et al (1977) Disseminated *Trichosporon capitatum* infection in an immunosuppressed host. Arch Intern Med 137:1192–1195. doi:10.1001/archinte.137.9.1192
22. Perez-Sanchez I, Anguita J, Martin-Rabadan P et al (2000) *Blastoschizomyces capitatus* infection in acute leukemia patients. Leuk Lymphoma 39:209–212
23. Girmenia C, Micozzi A, Venditti M et al (1991) Fluconazole treatment of *Blastoschizomyces capitatus* meningitis in an allogeneic bone marrow recipient. Eur J Clin Microbiol Infect Dis 10:752–756. doi:10.1007/BF01972503
24. Schiemann R, Glasmacher A, Bailly E et al (1998) Geotrichum capitatum septicaemia in neutropenic patients: case report and review of the literature. Mycoses 41:113–116
25. Amft N, Miadonna A, Viviani MA et al (1996) Disseminated *Geotrichum capitatum* infection with predominant liver involvement in a patient with non Hodgkin's lymphoma. Haematologica 81:352–355
26. Arnold AG, Gribbin B, De Leval M et al (1981) *Trichosporon capitatum* causing recurrent fungal endocarditis. Thorax 36:478–480. doi:10.1136/thx.36.6.478
27. Pimentel JD, Baker M, Woodgyer AJ et al (2005) Fatal disseminated *Blastoschizomyces capitatus* (*Geotrichum capitatum*) in a patient with relapse of acute lymphoblastic leukaemia. Pathology 37:319–321. doi:10.1080/00313020500169222
28. Christakis G, Perlorentzou S, Aslanidou M et al (2005) Fatal *Blastoschizomyces capitatus* sepsis in a neutropenic patient with acute myeloid leukemia: first documented case from Greece. Mycoses 48:216–220. doi:10.1111/j.1439-0507.2005.01098.x
29. Wills TS, Degryse A, Lavina J et al (2004) *Blastoschizomyces capitatus* pneumonia in an immunocompetent male. South Med J 97:702–704. doi:10.1097/00007611-200407000-00019
30. Gadea I, Cuenca-Estrella M, Prieto E et al (2004) Genotyping and antifungal susceptibility profile of *Dipodascus capitatus* isolates causing disseminated infection in seven hematological patients of a tertiary hospital. J Clin Microbiol 42:1832–1836. doi:10.1128/JCM.42.4.1832-1836.2004
31. Girmenia C, Pagano L, Martino B et al (2005) Invasive infections caused by Trichosporon species and *Geotrichum capitatum* in patients with hematological malignancies: a retrospective multicenter study from Italy and review of the literature. J Clin Microbiol 43:1818–1828. doi:10.1128/JCM.43.4.1818-1828.2005
32. De Maio J, Colman L (2000) The use of adjuvant interferon-gamma therapy for hepatosplenic *Blastoschizomyces capitatus* infection in a patient with leukemia. Clin Infect Dis 31:822–824. doi:10.1086/314047
33. Fanci R, Pecile P (2003) *Geotrichum capitatum* fungemia in a patient with acute myeloid leukemia: case report. J Chemother 15:412–413