

CASE REPORT

Septic arthritis caused by *Aspergillus fumigatus* in an immunosuppressive patient: A case report and review of the literature

Tuba Dal¹, Alicem Tekin¹, Özcan Deveci², Mehmet Bulut³, Uğur Fırat⁴, Mahmut Mete¹

¹ Dicle University Faculty of Medicine, Department of Medical Microbiology, Diyarbakır

² Dicle University Faculty of Medicine, Department of Infectious Diseases, Diyarbakır

³ Dicle University Faculty of Medicine, Department of Orthopedic Surgery, Diyarbakır

⁴ Dicle University Faculty of Medicine, Department of Pathology, Diyarbakır

ABSTRACT

Septic arthritis is a serious medical problem that causes rapidly chronic and irreversible joint damage when diagnosis and treatment are delayed. Although, the bacteria are the most frequent cause of septic arthritis, rarely fungi may be responsible for this disease. We presented here a case of septic arthritis caused by *Aspergillus fumigatus*, developed in a 65 years-old-male patient with diabetes mellitus. The patient admitted to our hospital with complaints of pain, swelling, redness in the right knee and high fever, which are not exceeding despite using vancomycin and ceftriaxone for 18 days. Imipenem was started to the patient in our hospital. At the end of 7 days because of no regression of patient's complaints, arthroscopic synovectomy and lavage were performed for the patient's right knee. *Aspergillus fumigatus* was isolated from the aspiration biopsy specimen that received during the surgical operation and patient was treated with voriconazole, successfully. *J Microbiol Infect Dis* 2012; 2(1): 29-32

Key words: *Aspergillus fumigatus*, aspergillosis, septic arthritis, immunosuppressive patient, diabetic patient.

İmmünsüpresif bir hastada *Aspergillus fumigatus*'un neden olduğu septik artrit: Olgu sunumu ve literatürün gözden geçirilmesi

ÖZET

Septik artrit; tanı ve tedavisi geciktiğinde hızlı bir şekilde kronik ve geri dönüşümsüz eklem hasarına neden olan ciddi bir problemdir. Septik artrit en sık nedeni bakteriler olmasına rağmen nadiren mantarlar da bu hastalığa yol açabilmektedir. Biz bu makalede diabetes mellituslu 65 yaşındaki erkek hastada gelişen *Aspergillus fumigatus*'un neden olduğu septik artrit olgusunu sunduk. Hasta onsekiz gündür vankomisin ve seftriakson kullanmasına rağmen gerileme göstermeyen yüksek ateş ve sağ dizinde ağrı, şişlik, kızarıklık şikayetleri ile hastanemize başvurdu. Hastaya hemen imipenem tedavisi başlandı. Hastanın şikayetlerinde herhangi bir azalma olmadığı için yedinci günün sonunda tedavi sonlandırıldı ve hastanın sağ dizine artroskopik sinovektomi ve lavaj yapıldı. Cerrahi operasyon sırasında alınan aspirasyon biyopsi materyalinden *Aspergillus fumigatus* izole edildi ve hasta vorikonazol ile başarılı bir şekilde tedavi edildi.

Anahtar kelimeler: *Aspergillus fumigatus*, aspergilozis, septik artrit, immünsüpresif hasta, diabetik hasta.

INTRODUCTION

Septic arthritis, also known as infectious arthritis, may represent a direct invasion of joint space by various microorganisms. It is a rheumatologic emergency that can lead to chronic and irreversible joint damage, when not treated early. Typically, septic arthritis affects a single large joint, such as the knee or hip, but it is possible for several joints to be infected. Septic arthritis is developed by hematologic route, infected contiguous

foci, neighboring route and by direct inoculation due to trauma or an iatrogenic event, such as arthrocentesis, joint surgery and intra-articular corticosteroid injection.¹ *Staphylococcus aureus* is the most frequent microorganism responsible for septic arthritis in all ages and risk groups, with the exception of children younger than two years. *Streptococcus* species and the other bacteria also cause septic arthritis. However fungi, especially *Candida* species and *Aspergillus* species

Correspondence: Dr. Alicem Tekin, Dicle University Faculty of Medicine, Department of Medical Microbiology, 21280 Yenişehir, Diyarbakır-Turkey E-mail: alicemtekin@gmail.com

Received: 12 February, 2012, Accepted: 16 March, 2012

Copyright © Journal of Microbiology and Infectious Diseases 2012, All rights reserved

can be responsible from the septic arthritis in immunosuppressive and diabetic patients.^{2,3}

Aspergillus species are opportunistic pathogens that include more than 35 species of saprophytic molds. *Aspergillus fumigatus* is the most common encountered microorganism among the *Aspergillus* species.⁴ Aspergillosis includes a wide variety of diseases caused by fungi of the *Aspergillus* genus. Aspergillosis may occur, especially in neutropenic and immunosuppressive and diabetic patients by a very high mortality rate of opportunistic infection.^{5,6} The most common forms of aspergillosis are allergic bronchopulmonary aspergillosis, pulmonary aspergilloma, sinonasal and brain infections. Due to increase in the number of immunocompromised patients from chemotherapy and use of steroids, solid organ transplant recipients and also the aging of the population in recent years, incidence of aspergillosis increased, dramatically.⁴ Articular aspergillosis is a rare form of septic arthritis and it is a significant medical emergency associated with high morbidity and mortality.⁷

We presented here a case of septic articular aspergillosis in a patient with diabetes mellitus and we reviewed cases of septic arthritis caused by *Aspergillus* species, previously was reported in the literature.

CASE REPORT

A 65-years-old-male with diabetes mellitus admitted to our hospital with complaints of pain, swelling, redness of right knee and high fever despite no history of trauma. The patient had received vancomycin and ceftriaxone therapy in another station for 18 days. The patient admitted to Dicle University Hospital Infectious Diseases Clinic, due to persistence of complaints. The first and second phalanges in the fourth toe of his right foot had been amputated as a result of diabetic foot infections, one year ago.

Vital signs of the patient during the admission were as follows: blood pressure 120/80 mmHg, pulse rate 95 beat/min, respiratory rate 14 breath/min, and body temperature 39.2°C. The patient was awake, alert, oriented and appears generally well. The physical examination of the patient was no another abnormal finding except severe swelling, redness, local thermal sensations of right knee and discharge. In the performed laboratory

tests upon admission, the white blood cell count, amount of hemoglobin, platelet count, erythrocyte sedimentation rate and C-reactive protein was 20,400/mm³, 11 g/dl, 463,000/mm³, 58 mm/hr and 1.1 mg/dl, respectively. Minor narrowing of joint space was observed in the medial compartment of the right knee but no another abnormal finding was noted on the plain radiographs. The computerized tomography of the right knee revealed an enhancing fluid collection, suggestive of a septic joint. Imipenem was started to patient because of suspicion of septic arthritis based on these diagnostic findings. Arthroscopic synovectomy and lavage was planned after receiving blood cultures. Aspiration biopsy specimen received during the surgical operation was sent to pathology and microbiology laboratories. In microbiology laboratory the biopsy specimen was inoculated onto Sabouraud's Dextrose agar (SDA), 5% sheep blood agar, Eosin-Methylene Blue (EMB) agar (Oxoid Ltd., Basingstoke, United Kingdom) media. One of the SDA medium plates was incubated at 25°C for 20-25 days and the other medium at 37°C for 48-72 hours. At the end of the second day of incubation, mold colonies of yellow-green pigmentation, grew on the surface of both plates. Vesicles, filid and conidia forms of the mold were compatible with *Aspergillus fumigatus* by lactophenol cotton blue staining preparation. Mycobacterial culture was performed and Ehrlich-Zielh-Neelsen (EZN) staining preparation was made to the rest of the biopsy specimen. The patient's blood culture, mycobacterial culture and EZN staining preparation were negative. Branching septate hyphae were also observed by the pathological examination with hematoxylin-eosin stain. According to microbiological and pathological report, the patient was treated with voriconazole with the diagnosis of aspergillosis for 14 days. As a result of treatment, patient's symptoms were reduced and lesions were improved and the patient was discharged. At follow-up one month after treatment there were no signs of recurrent aspergillosis.

DISCUSSION

Septic arthritis is a rheumatologic emergency that can lead to chronic and irreversible joint damage, if not treated early. Typically, septic arthritis affects a single large joint, such as the knee or hip, but it is possible for several joints to be infected.² Septic arthritis can affect individuals of all ages,

but it is more frequent in children and the elderly, and males are more frequently affected than females.² Diabetes mellitus, joint diseases such as rheumatoid arthritis and osteoarthritis, immunosuppression, trauma and surgical intervention are the reported risk factors for developing septic arthritis.¹ Our patient has underlying risk factors such as diabetes mellitus and elderly.

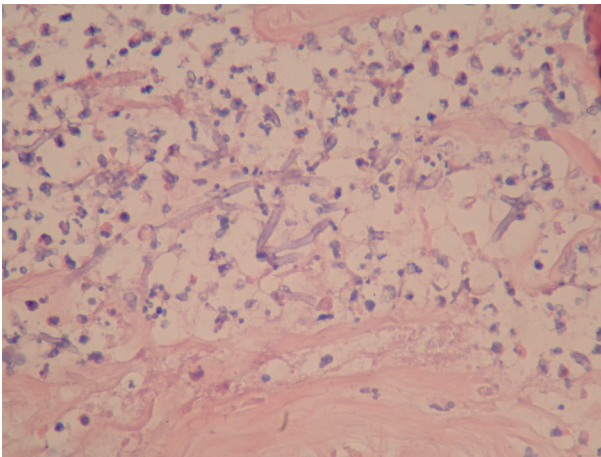


Figure 1. Microscopic appearance of branching septate hyphae (H&E stain, x400).

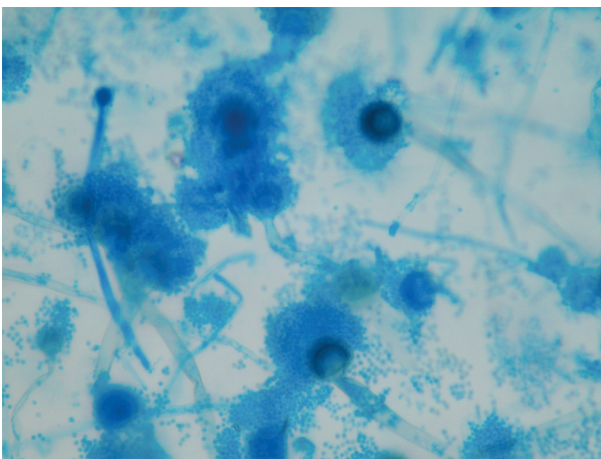


Figure 2. Microscopic appearance of vesicles, filial, conidia forms of the mold (Lactophenol cotton blue stain, x400).

Septic arthritis is developed by hematologic route, infected contiguous foci, neighboring route and by direct inoculation due to trauma or an iatrogenic event, such as arthrocentesis, joint surgery and intra-articular corticosteroid injection.^{1,2,8}

Our patient has a history of amputation surgery however it is not clear the mechanism of septic arthritis developed in our patient.

Species of bacteria are the most frequent microorganisms responsible for septic arthritis in all ages and risk groups, with the exception of children younger than two years. Treatment involves prompt surgical debridement for removal of purulent material and empiric treatment with broad-spectrum antibiotics.² However *Candida* species, *Aspergillus* species, and *Mycobacteria* may also be responsible for septic arthritis. In our case, treating with only broad-spectrum antibiotics, led to a delay in treatment. Delayed or inadequate treatment could result in irreversible joint destruction and death. Therefore in patients with suspected septic arthritis, in the presence of underlying risk factors such as diabetes mellitus, immunosuppression; aspergillosis should also be considered and antifungal drugs should be added to the treatment. In addition, the specimens received during surgical operation should send to microbiology laboratory for microbiological examination and culture for effective treatment of septic arthritis. Amphotericin B is the most preferred antifungal agent for the treatment of invasive aspergillosis. However amphotericin B has not good penetration to the bone and joint tissue. Combination of amphotericin B with a second antifungal agent is recommended for the treatment of articular aspergillosis. Voriconazole is another treatment option of invasive aspergillosis. In many studies it has showed that voriconazole have high-efficiency at the treatment of articular aspergillosis.⁹ We also treated our patient's infection with voriconazole, successfully.

The genus *Aspergillus* is commonly cause infections in lungs, sinuses, and brain.^{5,10} The presented case is an uncommon form of aspergillosis. In addition there is a small number cases of septic arthritis associated with *Aspergillus* species in immunosuppressive patients and in diabetic patients (Table 1).

We conclude that the genus *Aspergillus* should be considered as a causative agent in immunosuppressive and diabetic individuals and appropriate empiric therapy, sampling and microbiological examination have important role for treatment of septic arthritis.

Table 1. Septic arthritis cases caused by *Aspergillus* species in immunosuppressive patient in the literature by chronological order.

References	Age/Sex	Underlying disease	Microorganism	Treatment
1997 Garcia-Porrúa et al. ⁸	58/female	corticosteroid infiltration and leukaemia	<i>A. fumigatus</i>	itraconazole and amphotericin B
1997 Steinfeld et al. ¹¹	51/male	cirrhosis	<i>A. terreus</i>	itraconazole
1997 Steinfeld et al. ¹¹	69/male	vascular graft infection	<i>A. fumigatus</i>	itraconazole
2003 Bodur et al. ¹	17/male	Chronic granulomatous disease	<i>A. fumigatus</i>	itraconazole
2004 Sohail et al. ¹²	88/male	intra-articular corticosteroid injection	<i>A. fumigatus</i>	itraconazole
2004 Mekan et al. ⁴	18/male	immunocompetation	<i>A. fumigatus</i>	itraconazole
2010 Yu et al. ¹³	18/male	febrile neutropenia	<i>A. flavus</i>	voriconazole and caspofungin
2011 Golmia et al. ¹⁴	58/female	stem cell transplantation	<i>A. fumigatus</i>	voriconazole and caspofungin

REFERENCES

- Bodur H, Ozoran K, Colpan A, Balaban N, Tabak Y, Kulacoglu S. Arthritis and osteomyelitis due to *Aspergillus fumigatus*: a 17 years old boy with chronic granulomatous disease. *Ann Clin Microbiol Antimicrob* 2003; 2:2.
- Garcia-Arias M, Balsa A, Mola EM. Septic arthritis. *Best Pract Res Clin Rheumatol* 2011; 25:407-21.
- Sung-Wook C, Tong-Joo L, Myung-Ku K, Moon L, Jae-Ho J. A Case of Fungal Arthritis Ca-used by *Hansenula Anomala*. *Clin Orthop Surg* 2010; 2:59-62.
- Mekan SF, Saeed O, Khan JA. Invasive aspergillosis with polyarthritis. *Mycoses* 2004; 47:518-20.
- Zmeili OS, Soubani AO. Pulmonary aspergillosis: a clinical update. *QJM* 2007; 100:317-34.
- Shahnazi A, Mansouri N, Malek A, Sepehri Z, Mansouri SD. Is Pulmonary Aspergillosis Common in Diabetes Mellitus Patients? *Tanaffos* 2010; 9:69-74.
- Golmia R, Bello I, Marra A, Hamerschlak N, Osawa A, Scheinberg M. *Aspergillus fumigatus* joint infection: a review. *Semin Arthritis Rheum* 2011; 40:580-4.
- Garcia-Porrúa C, Blanco FJ, Atanes A, Torres P, Galdo F. Septic arthritis by *Aspergillus fumigatus*: a complication of corticosteroid infiltration. *Br J Rheumatol* 1997; 36:610-1.
- Denes E, Boumediene A, Durox H, et al. Voriconazole concentrations in synovial fluid and bone tissues. *J Antimicrob Chemother* 2007; 59:818-9.
- Sharada DM, Arunkumar G, Vandana KE, Rao PS. Sin-orbital aspergillosis in a diabetic pa-tient. *Indian Journal of Medical Microbiology* 2006; 24:138-40.
- Steinfeld S, Durez P, Hauzeur JP, Motte S, Appelboom T. Articular aspergillosis: two case reports and review of the literature. *Br J Rheumatol* 1997; 36:1331-4.
- Sohail MR, Smilack JD. *Aspergillus fumigatus* septic arthritis complicating intra-articular corticosteroid injection. *Mayo Clin Proc* 2004; 79:578-9.
- Yu OH, Keet AW, Sheppard DC, Brewer T. Articular aspergillosis: case report and review of the literature. *Int J Infect Dis* 2010; 14:433-5.
- Golmia R, Bello I, Marra A, Hamerschlak N, Osawa A, Scheinberg M. *Aspergillus fumigatus* joint infection: a review. *Semin Arthritis Rheum* 2011; 40:580-4.