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.

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

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. 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...
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/mm\(^3\), 11 g/dl, 463,000/mm\(^3\), 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, phialid 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 (EZK) staining preparation was made to the rest of the biopsy specimen. The patient’s blood culture, mycobacterial culture and EZK 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.\textsuperscript{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.\textsuperscript{1} Our patient has underlying risk factors such as diabetes mellitus and elderly.

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.\textsuperscript{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.\textsuperscript{9} We also treated our patient’s infection with voriconazole, successfully.

The genus Aspergillus is commonly cause infections in lungs, sinuses, and brain.\textsuperscript{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.

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