

Soft Tissue Abscess Caused by *Aspergillus Fumigatus* in an Immunosuppressive Patient



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ABSTRACT

Aspergillosis is a definition including a wide variety of diseases caused by fungi in the genus *Aspergillus*. *Aspergillosis* that occurs especially in neutropenic and immunosuppressive patient is an opportunistic infection with a very high mortality rate. In this study, we presented a case of primary cutaneous aspergillosis that caused in a heart transplant recipient. Thirty-nine-years-old male patient with the complaints of high fever lasting for ten days, redness of the right thigh, swelling, and pain, was admitted to our hospital. By the tissue ultrasonography of right thigh, 3x12 cm in size of septated intensive fluid collection (abscess?) in muscle tissue at a depth of 1.5 cm to the skin surface was reported. The biopsy specimens that were taken from the lesion sent to microbiology and pathology laboratories. The branching septate hyphae were observed in Hematoxylin-Eosin and Gram stained preparations. *Aspergillus fumigatus* was isolated and identified from the biopsy specimen. The patient's symptoms were regressed rapidly and the lesion was improved by surgical debridement and antifungal agent (amphotericin B) therapy. In the light of this case report, we were emphasized that microbiologic examination and culture have an important role for diagnosis of cutaneous aspergillosis.

Key words: *Aspergillosis*, cutaneous, *Aspergillus fumigatus*, immunosuppressive, heart transplant

İmmünsüpresif Bir Hastada *Aspergillus Fumigatus*'un Neden Olduğu Yumuşak Doku Apsesi

ÖZET

Asperjiloz; *Aspergillus* genusunda yer alan mantarların meydana getirdiği çok geniş hastalıkları kapsayan bir tanımdır. Özellikle nötropenik ve immünsüpresif hastalarda gelişen aspergillozis çok yüksek mortalite oranına sahip fırsatçı bir enfeksiyondür. Bu makalede kalp nakli yapılan bir hastada meydana gelen primer kütanöz aspergillozis olgusunu sunduk. On günden uzun süren yüksek ateş, sağ uyluğunda şişlik, kızarıklık ve ağrı şikayetleri olan otuz dokuz yaşındaki erkek hasta hastanemize başvurdu. Sağ uyluk ultrasonografi incelemesinde; deri yüzeyinden 1.5 cm derinde kas dokusu içerisinde 3x12 cm boyutlarında septalı yoğun sıvı birikimi (abse?) rapor edildi. Lezyondan alınan biyopsi materyalleri mikrobiyoloji ve patoloji laboratuvarlarına gönderildi. Hematoksilen-Eozin ve Gram boyalı preparatlarda dallanmış septalı hifler görüldü. Biyopsi materyalinden *Aspergillus fumigatus* izole ve tanıya edildi. Cerrahi olarak debride edilen ve amfoterisin B tedavisi başlanan hastanın semptomları hızla geriledi ve lezyonları iyileşti. Bu olgu sunumunun ışığında; aspergillozisin tanısında mikrobiyolojik inceleme ve kültürün önemli bir role sahip olduğunu vurguladık.

Anahtar kelimeler: Asperjiloz, kütanöz, *Aspergillus fumigatus*, immünsüpresif, kalp nakli

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INTRODUCTION

Aspergillus infections are one of the significant causes of morbidity and mortality especially in neutropenic and immunosuppressive patients. A wide variety of diseases caused by fungi in the genus *Aspergillus* is referred to as Aspergillosis. Aspergillosis is an opportunistic infection with a very high mortality rate and occurs especially in neutropenic and immunosuppressive patients. The most common forms of aspergillosis are allergic bronchopulmonary aspergillosis, pulmonary aspergilloma, and invasive aspergillosis. The cutaneous aspergillosis is a rarely encountered form of aspergillosis. Among *Aspergillus* species, the most common causative agent of opportunistic infections in humans is *Aspergillus fumigatus*. It is a filamentous saprophytic fungus that grows in multicellular filaments called hyaline, septate hyphae (1).

Invasive aspergillosis is seen in the presence of risk factors include neutropenia, glucocorticoid therapy, advanced acquired immunodeficiency syndrome, chronic granulomatous disease, hematopoietic stem cell or solid-organ transplantation (2).

Cutaneous lesions of aspergillosis are usually develop secondary to haematogenous dissemination from an underlying infected organ (3-5). In some cases cutaneous lesions can occur as a primary cutaneous infection. Primary cutaneous aspergillosis is caused by direct implantation of *Aspergillus* species following trauma. Cutaneous manifestations are non-specific and can be presented with erythematoviolaceous patches that have a central necrotic ulcer, subcutaneous abscesses and vegetative papules and patches (6).

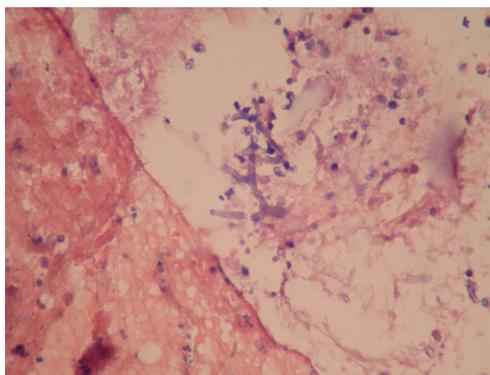


Figure 1. Microscopic appearance of branching septate hyphae (H&E stain, x400).

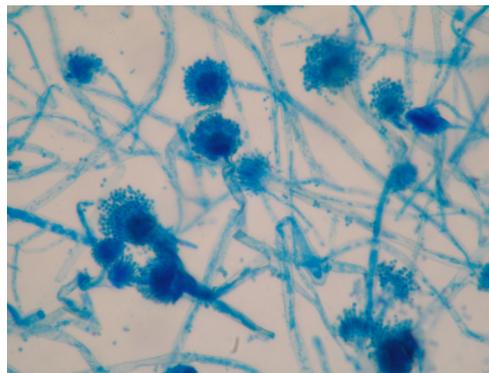


Figure 2. Microscopic appearance of vesicles, filid, conidia forms of the mold (Lactophenol cotton blue stain, x400).

The first case with cutaneous aspergillosis in a renal transplant recipient from Montreal was reported by Langlois et al (7). In the following years cutaneous aspergillosis cases with renal transplantation, heart transplantation, pancreatic transplantation were published. To our knowledge there was a limited number of primary cutaneous aspergillosis cases in solid organ transplant patients (6,8-11). We presented a primary cutaneous aspergillosis case report with heart transplant recipient in this article.

CASE

Thirty-nine-years-old male patient with the complaints of high fever lasting for ten days, redness of the right thigh, swelling, and pain, was admitted to Dicle University Hospital Infectious Diseases Clinic. Vital signs of the patient at the time of admission were as follows: blood pressure 110/60 mmHg, pulse rate 92 beats/min, respiratory rate 18 breaths/min, and body temperature 39.1°C. The patient was awake, alert, oriented, and appears generally well. The other physical examination findings of the patient were normal except swelling and redness in right thigh. In the performed laboratory tests upon admission, the white blood cell count, hemoglobin, platelet count, erythrocyte sedimentation rate and C-reactive protein was 12,000/mm³, 11 g/dL, 465,000/mm³, 55 mm/hr, and 24 mg/dL (normal range 0-5), respectively. The patient was treated empirically with 6 g/day dose ampicillin-sulbactam. By the tissue ultrasound of right thigh, 3x12 cm in size of septated intensive

fluid collection (abscess?) in muscle tissue at a depth of 1.5 cm to the skin surface in postero-lateral part of the proximal right thigh was reported. The contents of the fluid collection were drained as surgical. The biopsy specimens that were taken from the lesion during the surgical operation sent to microbiology and pathology laboratories. In microbiology laboratory the branching septate hyphae observed in Gram stained preparations that were performed from biopsy specimens. In addition the specimen was inoculated onto Sabouraud's Dextrose agar (SDA) (Oxoid Ltd., Basingstoke, United Kingdom) medium plates. One of the SDA medium plates was incubated at 25°C for 20-25 days and the other 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 media plates. Vesicles, filial, conidia forms of the mold were compatible with *Aspergillus fumigatus* by lactophenol cotton blue stained preparations (Figure 1). During the pathological examination the branching septate hyphae were observed in the tissue with hematoxylin-eosin stain (Figure 2). According to result of pathology report, the patient was treated with 5 mg/kg/day IV amphotericin B with the diagnosis of aspergillosis for 14 days. There were no pathological findings in the patient's chest and abdomen, by computed tomography performed for screening a focus. As a result of treatment, the patient's symptoms were regressed rapidly and lesions were improved and the patient was discharged.

DISCUSSION

Cutaneous aspergillosis usually is encountered in immunosuppressive patients but it is rare and usually develops secondary to haematogenous dissemination from an underlying infected organ. However primer cutaneous aspergillosis is more rarely. In Table 1, we presented some of the primary cutaneous aspergillosis in immunosuppressive patients, according to the literature, in chronological order. We searched articles in the English language literature, as well as English-language translations of other language articles were with the combination of key words "cutaneous aspergillosis, *Aspergillus fumigatus*, immunosuppressive patient, transplant recipient", on data base of "Pubmed and Web of Knowledge" from 1980 through the end of 2011. And so we wanted to have an opinion the frequency of primer cutaneous aspergillosis in solid organ transplant recipients, especially in heart transplant recipients.

Fungal infections that occurred by *Aspergillus* species are one of the significant cause of morbidity and mortality in immunosuppressive patients. Risk factors for invasive aspergillosis include neutropenia, glucocorticoid therapy, advanced acquired immunodeficiency syndrome, chronic granulomatous disease, hematopoietic stem cell or solid-organ transplantation (7-19). *Aspergillus* infections are also common in premature and newborn infants hospitalized in intensive care according to the literature (20,21). Our presented case is a heart transplant recipient consistent with the literature.

In transplant recipients skin manifestations are non-

Table 1. Primary cutaneous aspergillosis cases with immunosuppression in the literature by chronological order.

References	Number of case	Age	Gender	Underlying disease	Microorganism
Langlois et al.	1	39	female	Transplantation	<i>A. fumigatus</i>
Hunt et al.	2	-	male	AIDS	<i>A. fumigatus</i>
Papouli et al.	1	25 weeks	-	Prematurite	<i>A. fumigatus</i>
Arikan et al.	1	57	male	HIV positivity	<i>A. fumigatus</i>
	2	38	male	HIV positivity	<i>A. fumigatus</i>
Chakrabarti et al.	7	-	-	Burn wounds, transplantation	<i>A. flavus</i>
Galimberti et al.	1	60	male	Transplantation	<i>A. fumigatus</i>
Barbujo et al.	1	30	male		<i>A. fumigatus</i>
Murakawa et al.	11	32-58	males	AIDS	<i>A. fumigatus</i>
D'Antonio et al.	5	13-37	male	Haematological malignancy	<i>A. flavus</i> , <i>A. fumigatus</i> , <i>Aspergillus</i> spp.
Miele et al.	4	28-60	male	Transplantation	<i>A. fumigatus</i> , <i>Pseudallescheria boydii</i>
			female		<i>Alternaria</i> species, <i>Acoelomycete</i> in the <i>Coniothyrium Microsphaeropsis</i> complex of dark molds.
Park et al.	1	51	male	Transplantation	<i>Aspergillus</i> spp.
Thomas et al.	1	-	-	Transplantation	<i>A. niger</i>
Zhu Yuanjie et al.	1	41	female	Cutaneous T-cell lymphoma	<i>A. terreus</i>
Etienne et al.	1	24 weeks	male	Pneumothorax	<i>A. fumigatus</i>
	2	23 weeks	male	Metabolic disorders	<i>A. fumigatus</i>
	3	24 weeks	male	Sepsis	<i>A. fumigatus</i>

specific and the extent of disease (localized primary cutaneous etc. disseminated systemic disease) is often unclear. The cutaneous aspergillosis may manifest with papules, multiple nodules sometimes purplish in colour, plaques which may ulcerate forming a central eschar or haemorrhagic bullae (13). Our case has also a non-specific cutaneous lesion and soft tissue abscess presented by swelling and redness in right thigh.

In recent year increasing of solid-organ transplant recipients led to increased incidence of invasive or cutaneous aspergillus infections. In solid organ transplant recipients, the cutaneous aspergillosis can be presented as a secondary or primary infection. The cutaneous lesions related to *Aspergillus* species usually develop secondary to haematogenous dissemination from an underlying infected organ. More rarely, the cutaneous lesions are encountered as a primary cutaneous lesion. Primary cutaneous aspergillosis is caused by direct implantation of *Aspergillus* species following the trauma. The cutaneous aspergillosis among solid-organ transplant recipients usually occurs as primary infection directly in the surgical wound or as nodules near a site of a break in the integument, such as catheter insertion site and pressure sore (13). The diagnosis of cutaneous aspergillosis is performed by microbiologic examination, culture, and histopathologic examination. It requires receiving the biopsy of skin lesions for these studies. The skin biopsy specimen for a suspected fungal lesion should be taken from the center of the lesion and should reach the subcutaneous fat tissue because of *Aspergillus* species tend to invade blood vessels of the dermis and subcutis, resulting in an ischemic cone above it. The skin biopsy specimens should be sent in sterile saline to the microbiology laboratory and in formalin to the pathology laboratory (12). If aspergillosis is diagnosed, subsequent efforts should be directed at determining whether the patient has a primary infection or secondary dissemination from a primary focus such as the lung (12,13). The workup should begin with an assessment of risk factors (neutropenia, recent or concurrent presence of a central venous access catheter, the presence of adhesive or occlusive dressings, or other local skin injury). It should be noted that the cutaneous lesions occur in 5-10% of the patients with invasive aspergillosis and, on rare occasions, can be the presenting sign of systemic infection. Lungs are the most frequent focus of secondary cutaneous aspergillosis. Brinca et al. presented a case report of cutaneous aspergillosis in 2011, in this

study they found a pulmonary primary focus of infection (13). Cho et al. were also presented a case report of tracheobronchial aspergillosis following primary cutaneous aspergillosis in a lung-transplant recipient (22). Special attention to pulmonary symptoms and/or signs may determine whether an evaluation for pulmonary aspergillosis is needed. If there are indications of pulmonary infection, a computed tomographic scan of the chest would be the best first diagnostic test. If that test is abnormal, evaluation by bronchoscopy should follow. Our patient is probably a case of primer aspergillosis due to direct inoculation of fungus (13). Our approach to treatment was in this direction due to we did not detect any focus by screening methods.

Aspergillus infections in immunosuppressive individuals are often seen as invasive fatal infections. However, soft-tissue aspergillosis related to cutaneous aspergillosis is also encountered in immunosuppressive individuals. Early diagnosis and appropriate surgical debridement and antifungal agent therapy significantly reduced mortality and morbidity in these patients. For this reason, in the presence of soft-tissue abscesses and other cutaneous lesions with immunosuppressive patient, *Aspergillus* infections should be considered as a reason. In recent years, increase in solid-organ transplantation, and graft survival led to growing reports of *Aspergillus* infections. For this reason treatment of these infections has become more important. *Aspergillus* infections are treated with surgical debridement and/or antifungal therapy. Amphotericin B has been the classical antifungal drug of choice in aspergillosis. However voriconazole, itraconazole and caspofungin are among the other alternative treatment options. Treatment issues, such as the choice of antifungal agent, duration of therapy and role of surgical debridement, are often controversial and can be complicated by the patient's immunosuppressive therapy and graft function (13).

We conclude that primary cutaneous aspergillosis may occur in immunosuppressive patients and also in transplant recipients as an unusual manifestation. The case shows that appropriate biopsy and microbiological examination, and early aggressive therapy have important role in the diagnosis of aspergillosis.

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