



Secondary cutaneous aspergillosis disseminated from the lungs of a patient with asthma on 1 month steroid treatment

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Abstract

Cutaneous aspergillosis is very rare and occurs predominantly in transplant patients. Here, we report a 55-year-old female who underwent steroid treatment for 1 month and developed secondary cutaneous aspergillosis from pulmonary aspergillosis due to *Aspergillus fumigatus*.
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1. Introduction

Fungi of the genus *Aspergillus* are widely distributed in nature, particularly in soil and decomposing vegetation (Larkin et al., 1996). Although exposure to *Aspergillus* occurs frequently, subsequent illness is uncommon. However, in immunocompromised hosts with major risk factors such as prolonged granulocytopenia and long-term steroid treatment, it can develop into invasive infection. Recently, several studies have reported pulmonary aspergillosis in patients with chronic obstructive pulmonary disease (COPD) (Bulpa et al., 2007; Lin et al., 2001; Rodrigues et al., 1992). Cutaneous aspergillosis is a rare form of locally invasive disease (Galimberti et al., 1998). It can occur via hematogenous dissemination or direct contact of traumatized skin with contaminated material (Woodruff and Hebert, 2002). Although rare, a few cases of it have been reported in immunocompromised patients, especially transplant recipi-

ents. However, no prior study has reported secondary cutaneous aspergillosis (SCA) disseminated from a pulmonary focus in a patient with asthma who received short-term steroid therapy for 1 month. We wish to share this complication in the setting of steroid treatment.

2. Case report

A 55-year-old woman, a nonsmoker with bronchial asthma, was admitted due to dyspnea for 2 weeks before admission. She has not been on steroids previously. An initial chest X-ray revealed no active lesions (Fig. 1A). Notable laboratory data included the following: white blood cell count 13.4 cells/L, hematocrit 42.4%, platelets 336,000/L, glucose 168 mg/dL, and creatinine 1.2 mg/dL. Subsequent evaluations included a C-reactive protein of 0.41 mg/dL, human immunodeficiency virus-negative using an enzyme-linked immunosorbent assay, and a negative viral hepatitis panel.

After appropriate cultures were obtained, she was diagnosed with an acute exacerbation of bronchial asthma and was started on oral levofloxacin (500 mg/day) and prednisolone (20 mg/day). As no improvement was observed

Abbreviations: COPD, chronic obstructive pulmonary disease; SCA, secondary cutaneous aspergillosis.

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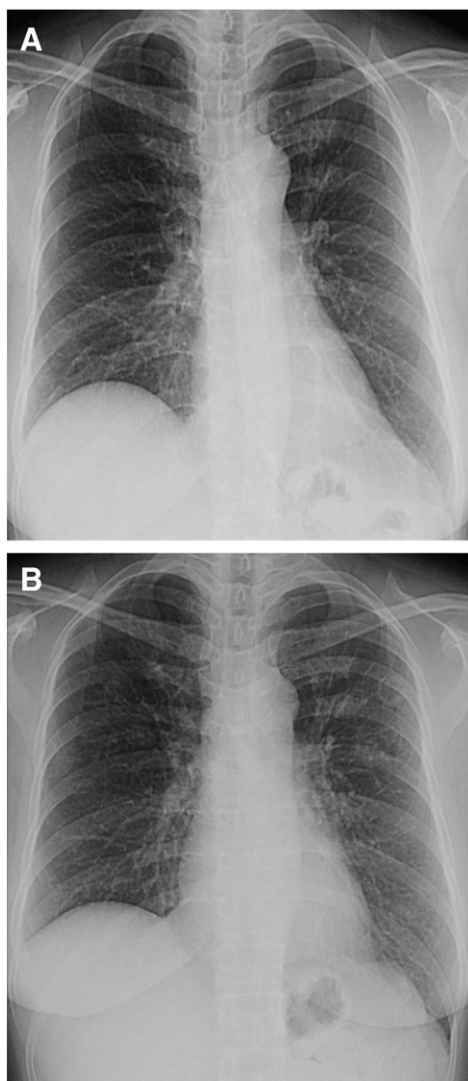


Fig. 1. (A) Plain film of the chest: no remarkable abnormality on admission. (B) Plain film of the chest: multiple cavitary nodules in the both upper lung zone.

for a week, the oral prednisolone was replaced with intravenous methylprednisolone (180 mg/day).

After 3 weeks of intravenous methylprednisolone, her symptoms improved, so we reduced the steroid dose. However, a follow-up chest X-ray on hospital day 28, after reducing the steroid dose, showed multiple cavitary lesions in both lungs (Fig. 1B), and chest computed tomography (CT) revealed peribronchial necrotizing consolidations in both lungs (Fig. 2A and B).

We performed a bronchoscopic examination and a culture of the bronchial washing fluid grew *Aspergillus fumigatus*. The isolates grew on Sabouraud dextrose agar as agranular, green-brown pigmented colonies. Microscopically, a single row of phialides was observed over the top half of a club-shaped vesicle. The conidia were spherical and arranged in long chains.

We started amphotericin B to treat the pulmonary lesions. However, no improvement was observed, and in the 5th day

of antifungal treatment, cutaneous lesions consisting of 8 tender, firm, well-demarcated erythematous subcutaneous nodules 1–1.5 cm in diameter were discovered on her neck, trunk, left inguinal area, and right thigh. The largest measured 2.5×0.8 cm and was in the right lower abdominal quadrant (Fig. 3A and B). A skin biopsy of the largest nodule was performed. Microscopically, the cutaneous nodule contained a dense neutrophilic infiltration in the septae of the subcutaneous fat tissue, resulting in abscess formation. On periodic acid–Schiff (PAS) stain, numerous septate hyphae with acute angle branching were seen (Fig. 4A and B) and fungal cultures grew *A. fumigatus*.

To confirm the chest lesion, we performed a video-assisted thoracic biopsy. This biopsy specimen also showed numerous septate hyphae (Fig. 4C and D). Therefore, we continued with the amphotericin B (30 mg/day) for 7 days, followed by amphotericin deoxycholate (250 mg/day) and caspofungin acetate (50 mg/day). After 3 months of treatment, her general condition improved, along with both the skin and nodular lung lesions.

3. Discussion

Aspergillosis is caused by saprophytic fungus species in the genus *Aspergillus*, of which *A. fumigatus* is the most

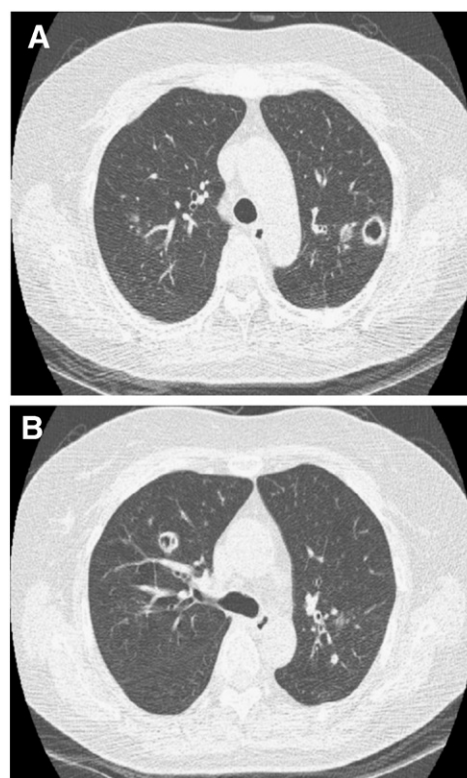


Fig. 2. CT scan of the chest: small ill-defined centrilobular opacities and cavitary nodules with or without internal septation (A, B) in both the upper lobes and bronchial wall thickening of left upper lobe.

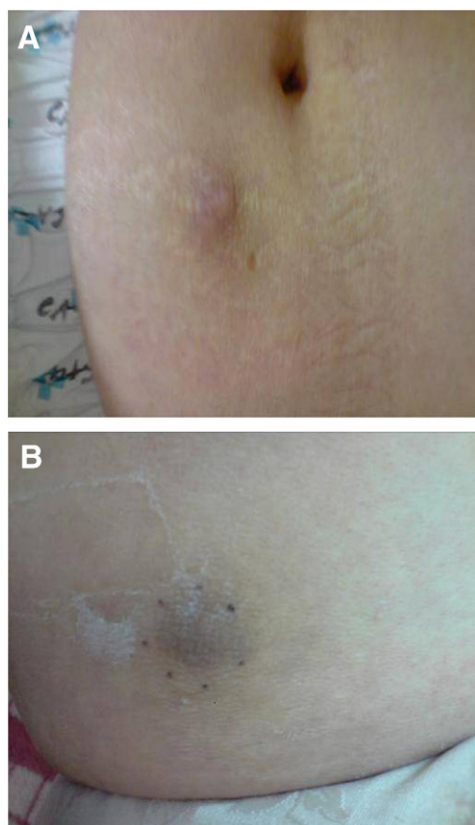


Fig. 3. Skin lesion: firm, tender, erythematous subcutaneous nodules located on the abdomen (A) and right thigh (B).

common. It is a weak pathogen and usually causes opportunistic infections in immunocompromised hosts. It can also develop in patients with COPD, who may have increased susceptibility to fungal invasion for several reasons (Ader et al., 2005; Bulpa et al., 2007; Ng et al., 1994). Our patient was first treated with a diagnosis of bronchial asthma and was given antibiotics and steroids without any improvement.

In the workup of the skin lesions that developed after 1 month, a microscopic examination of the cutaneous lesion revealed findings consistent with aspergillosis, especially the visualization of numerous septate hyphae with acute angle branching in the epidermis and dermis, along with a positive tissue culture for *A. fumigatus*. A definitive diagnosis of cutaneous aspergillosis was made. Chest CT confirmed pulmonary involvement, and the patient was diagnosed with SCA.

Although pulmonary aspergillosis is the most common clinical presentation, involvement of the gastrointestinal system, brain, heart, skin, and kidneys is also possible (Ader et al., 2005). Specifically, cutaneous infection, as in our case, is reported in only 5% of the patients with *Aspergillus* infections, and it can develop either primarily or secondarily (Kramer et al., 1991). Primary cutaneous aspergillosis usually involves sites of skin injury, such as at or near intravenous catheter sites, at sites of traumatic inoculation,

and at sites associated with occlusive dressings, burns, or surgery (Kramer et al., 1991; van Burik et al., 1998). The secondary form results from either contagious extension to the skin from an underlying infected organ or widespread blood-borne seeding of the skin (van Burik et al., 1998). Most of these disseminated infections are caused by *A. fumigatus*, as in our case (Ricci et al., 1998). The cutaneous presentation of this disease in previous reports varies and includes violaceous macules, ulcerative nodules, erythematous plaques with pustules, erythematoviolaceous papulonodules, and hemorrhagic bullae (Galimberti et al., 1998; Grossman et al., 1985; Larkin et al., 1996; Ricci et al., 1998; Woodruff and Hebert, 2002). In our case, the presenting lesions were multiple erythematous subcutaneous nodules. Patients receiving long-term steroid treatment are very susceptible to invasive aspergillosis, which has a mortality rate ranging from 74% to 92% (Singh and Paterson, 2005).

After the initial infection, major risk factors for dissemination are long-term corticosteroid therapy and poor allograft function (Venkatesan et al., 2005). In contrast, our patient developed skin aspergillosis after short-term steroid therapy for 1 month, not long-term steroid treatment, and no evidence was observed of the involvement of other organs, including the brain, kidneys, and liver.

Although the criteria for long-term and short-term steroid therapy are not clear, the dosage and duration of steroid used in this case is considered short-term and is the standard amount given to asthma patients in our outpatient department.

Amphotericin B is the standard therapy for invasive aspergillosis, although the response is suboptimal in severely immunosuppressed patients. Initial therapy with voriconazole is reported to lead to better responses, improved survival, and fewer side effects compared to the standard approach with amphotericin B (Herbrecht et al., 2002). Amphotericin preparations or voriconazole is the preferred initial therapy in cutaneous aspergillosis (Singh and Paterson, 2005). In our patient, sequential therapy with liposomal amphotericin B and caspofungin acetate successfully controlled the disease. As opportunistic fungal infections may be the major cause of morbidity and mortality in immunocompromised patients, early diagnosis and prompt treatment are very important (Venkatesan et al., 2005). Although cutaneous involvement is uncommon in aspergillosis, it may be the only sign leading to the correct diagnosis. Therefore, cutaneous aspergillosis should be considered in the differential diagnosis of cutaneous nodular lesions that arise in patients with asthma during short-term steroid treatment for 1 month.

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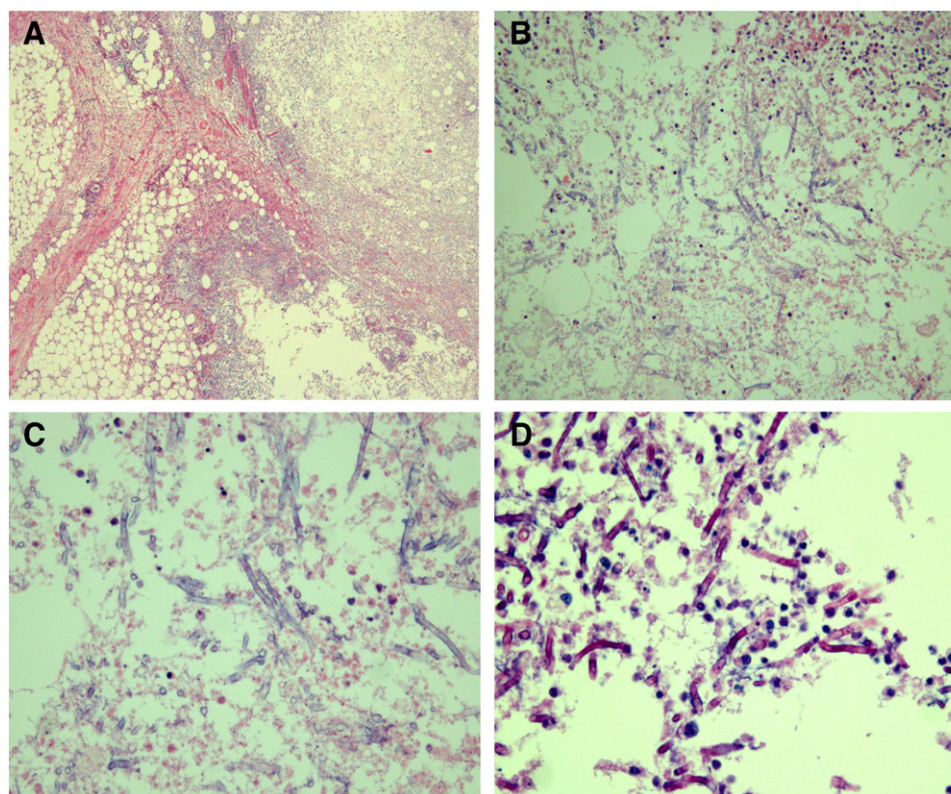


Fig. 4. (A) Skin lesion: dense neutrophilic infiltration in the septae of the subcutaneous fat tissue (hematoxylin–eosin staining; original magnification $\times 40$). (B) High-power view of the skin lesion: numerous fungal hyphae (hematoxylin–eosin staining; original magnification $\times 200$). (C) Lung lesion: septated hyphae with acute angle branching (hematoxylin–eosin staining; original magnification $\times 400$). (D) PAS staining of the fungus: septated and branching hyphae (original magnification $\times 400$).

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