

BRIEF REPORT

Primary cutaneous aspergillosis, mimicking malignancy, a rare presentation in an immunocompetent patient

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Aspergillus species are ubiquitous opportunistic molds that cause both allergic and invasive syndromes. A 65-year-old female, farmer by occupation, presented with left upper limb and trunk swelling for one year, associated with pain, tightening of skin, and vesicles with watery discharge. Local examination showed a diffuse swelling extending from left arm to forearm and lateral chest wall associated with edema, induration, and raised temperature. The swelling was firm to hard with superficial skin ulcers and black eschar. Hematological investigations of the patient showed raised total WBC count and peripheral blood eosinophilia. Patient had no history suggesting immunosuppression. Clinico-radiological impression was left breast carcinoma with secondary skin involvement. Fine-needle aspiration cytology (FNAC) from the swelling showed inflammatory cells, necrosis, epithelioid cell granulomas, and giant cells along with branching hyphae of variable thickness, confirmed on Gomori Methenamine Silver stain as fungal hyphae. Culture was advised which identified the species as *Aspergillus fumigatus*. Primary cutaneous infection by *A. fumigatus* in an immunocompetent patient is unheard of. FNAC has an important role in resolving diagnostic dilemma in primary cutaneous aspergillosis, which may mimic malignancy as in our case.

KEYWORDS

A. fumigatus, cutaneous aspergillosis, immunocompetent, mimicks malignancy

1 | BACKGROUND

Aspergillus species is a saprophytic mold, which is found in decaying organic matter. Infection occurs by inhalation of spores or by direct entry of organisms into body tissue through wounds or during surgery and is more common in immunocompromised patients.¹ Invasive aspergillosis mainly causes infection in lung while skin is the second most common site.¹

Cutaneous aspergillosis may occur as either primary or secondary infection. Secondary cutaneous aspergillosis is more frequent, commonly occurs due to *Aspergillus fumigatus* infection and is almost always seen in immunocompromised patients. The skin involvement occurs due to hematogenous dissemination from a primary focus such as the lungs or contiguous spread from underlying infected tissues.²

Primary cutaneous aspergillosis is uncommon and usually occurs due to *A. flavus* which can be seen in immunocompetent host due to

its high virulence. The skin involvement occurs as a result of direct inoculation of *Aspergillus* spores at the site of injury following intravenous catheterization, trauma, occlusive dressings and tapes, burns, or surgery.^{2,3} Lesions are generally seen on extremities where they first appear as erythematous papules and pustules which ulcerate to form black eschar.² Certain occupational groups such as gardeners, agricultural workers, brick manufacturers, etc, who remain in direct contact with the soil are at a greater risk of acquiring such fungal infections.⁴ However, primary cutaneous infection by *A. fumigatus* in an immunocompetent patient is unheard of.

Here we report a case of primary cutaneous aspergillosis, diagnosed on fine-needle aspiration cytology (FNAC), in a 65-year-old immunocompetent female with an unusual clinical presentation. She presented with left arm and chest swelling and was clinically suspected of having skin involvement from underlying breast carcinoma. Fine-needle aspiration cytology showed fungal hyphae and culture showed growth of *A. fumigatus*.

Patient's consent has been taken.

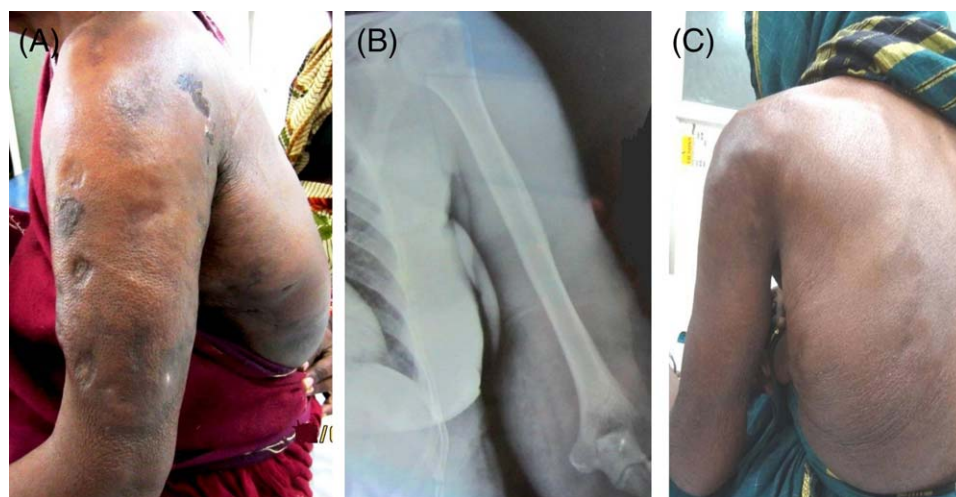


FIGURE 1 A, Clinical photograph showing local edema, induration, firm to hard swelling with superficial skin ulcers and black eschar. B, X ray right arm shows that the swelling does not involve the bone. C, Clinical photograph showing that the swelling subsided post treatment. [Color figure can be viewed at wileyonlinelibrary.com]

2 | CASE

A 65-year-old female, farmer by occupation, presented with left upper limb and trunk swelling for one year, associated with pain, tightening of skin, and vesicles with watery discharge. There was a past history of Ayurvedic medication taken for the above and history of myocardial infarction

2 years back due to right coronary artery blockage. There was no history of diabetes, tuberculosis, or any other major medical or surgical illness.

Hematological investigations of the patient showed raised total WBC count and peripheral blood eosinophilia. Biochemical investigations were within normal limits and patient was HIV negative. On X-ray, swelling did not seem to involve the underlying bone and lung

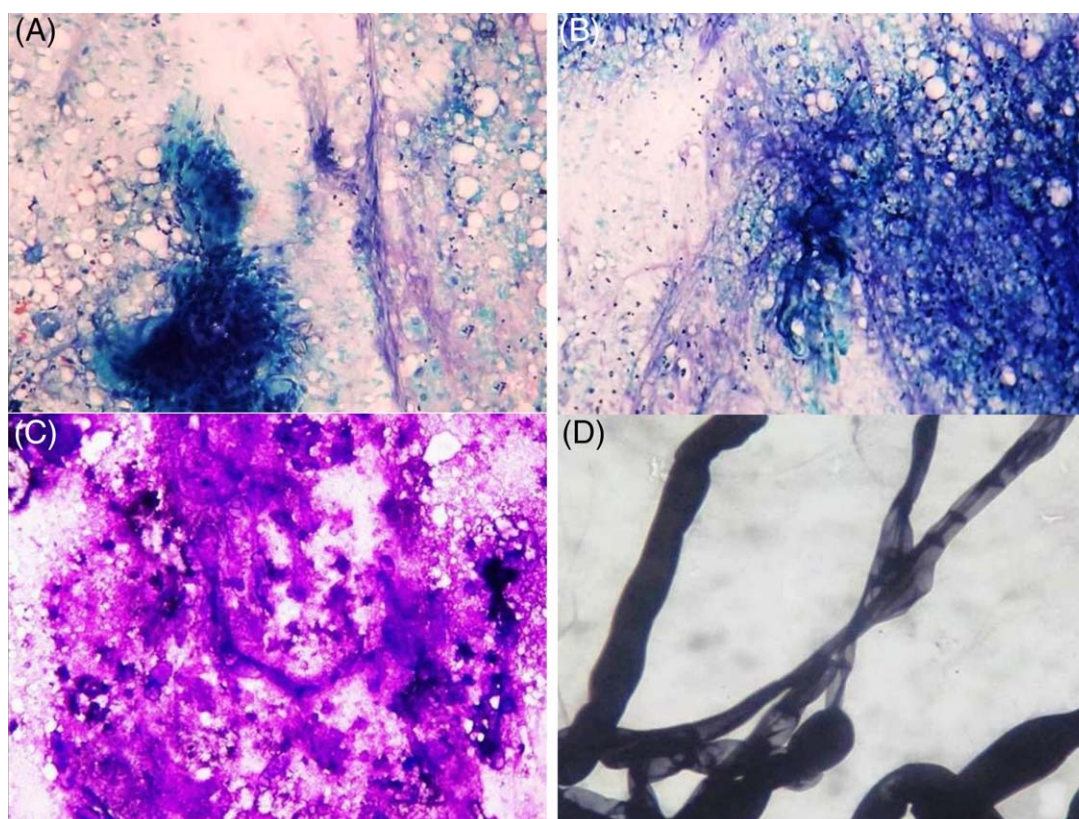


FIGURE 2 A, Giemsa stain, 100×, Necrosis and inflammatory cells and epitheloid cell granulomas. B, Giemsa stain, 100×, Necrosis and inflammatory cells admixed with fungal hyphae. C, Pap stain, 100×, Necrosis and inflammatory cells admixed with fungal hyphae. D, Gomori Methenamine Silver stain, 400×, showing branching fungal hyphae, with few septations. [Color figure can be viewed at wileyonlinelibrary.com]

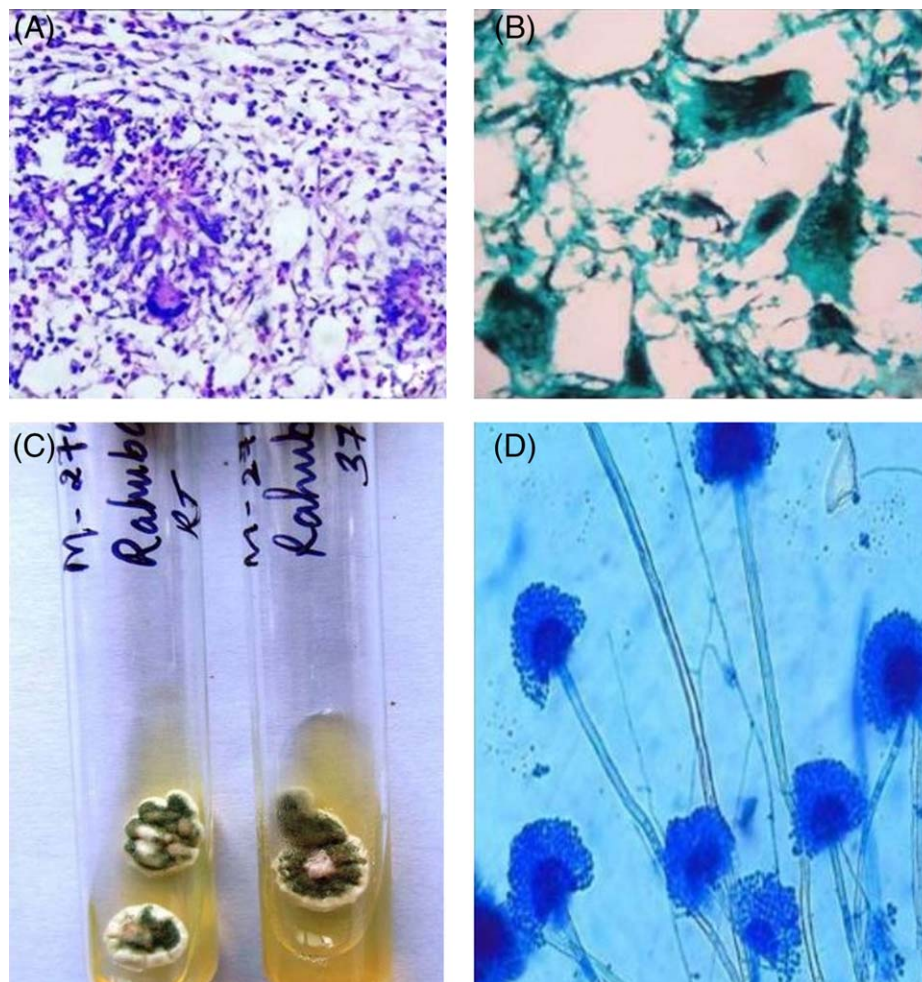


FIGURE 3 A, H&E, 100 $\times$, histopathology showed well formed epithelioid cell granulomas with giant cells. B, Gomori Methenamine Silver, 100 $\times$, fungal hyphae within giant cells. C, SDA shows velvety, smokey green colonies. D, LPCB mount-uniseriate phialides, blue green conidia. [Color figure can be viewed at wileyonlinelibrary.com]

fields (Figure 1B). Ultrasonography showed extensive subcutaneous edema associated with thrombosis of brachial vein. CT scan suggested possibility of left breast carcinoma with secondary skin involvement.

Patient was then referred for aspiration cytology. Local examination showed diffuse swelling involving left arm, extending to the forearm and lateral chest wall, accompanied with edema, induration, and raised temperature. The swelling was firm to hard with superficial skin ulcers and black eschar (Figure 1A). Left axilla and adjacent breast were firm and edematous without any definite lump or lymphadenopathy. The contralateral breast and axilla appeared unremarkable. Fine-needle aspiration (FNA) from the swelling yielded a bloody aspirate. Giemsa and Pap (Papanicolaou) stained smears showed inflammatory cells, necrosis (Figure 2B,C), epithelioid cell granulomas (Figure 2A), and giant cells along with branching hyphae of variable thickness with focal septations. These structures were confirmed on Gomori Methenamine Silver (Gomori Methenamine Silver) stain as fungal hyphae (Figure 2D). Smears were negative for Acid fast bacilli. Thus, a diagnosis of necrotizing granulomatous inflammation secondary to fungal infection was

rendered and microbiologic culture was recommended for confirmation of the fungal organisms. Subsequently, a biopsy was performed and the tissue was submitted for histopathological and microbiological examination.

Histopathology showed eosinophilic microabscesses, giant cells, and epithelioid granulomas on H&E stain (Figure 3A) and fungal hyphae were identified on Gomori Methenamine Silver (Figure 3B). On microbiological examination, KOH (Potassium hydroxide) mount showed hyaline septate hyphae. Primary and subcultures on Sabouraud dextrose agar with antibiotics at 37°C showed velvety, smokey green colonies within a week (Figure 3C). These on repeated subculture showed similar colonies. Lacto Phenol Cotton Blue (LPCB) wet mount showed uniseriate conidial head and columnar conidia in chains (Figure 3D). Thus the species was identified as *A. fumigatus*.⁵

Patient was then started on Itraconazol for one month and she responded very well with 80%–90% reduction in the swelling. The swelling completely subsided following Itraconazol therapy for an additional two months (Figure 1C).

3 | DISCUSSION

Cutaneous aspergillosis occurs in 5%–10% of cases of invasive aspergillosis, making skin the second most frequently involved site after lung. It is mainly caused by *A. fumigatus* and *A. flavus* and rarely by *A. terreus*.⁶

Alessandro in 2009 explained that the size of *A. fumigatus* conidia ranges from 2 to 3.5 μm , while *A. flavus* produces conidia ranging from 3 to 6 μm . This difference in size explains why *A. fumigatus* conidia reach the pulmonary alveoli easily and causes chronic cavitary aspergillosis or lung fungal balls while *A. flavus* is an important etiological agent for *Aspergillus* sinusitis and primary cutaneous aspergillosis. This study also proved *A. flavus* as more virulent species than *A. fumigatus*, based on experimental models of disseminated infection.⁷

A. fumigatus does not need human host to complete its life cycle, indeed, encountering an immunocompetent human host generally results in the death of the fungus. *A. fumigatus* is a true saprophytic fungus, which becomes pathogenic only in an immunosuppressed host.⁸ Reports have described primary cutaneous infection in immunocompetent patients in association with agricultural trauma.⁹ In our patient, it was a primary cutaneous infection by *A. fumigatus*, which is very rare and was possibly due to direct inoculation as patient was a farmer by occupation. Moreover, patient was immunocompetent as there was no history suggesting immunosuppression.

Hope et al. in 2005 have mentioned in their study that Gomori Methenamine Silver stain on histopathology sections and cytology smears is more sensitive for detecting fungal hyphal elements than routine stains.⁸ Early on in our case also, Pap and Giemsa stains, mostly showed scant filamentous structures against necrotic background which were reported as suspicious for fungal organisms and the biopsy was merely signed out as granulomatous inflammation. On Gomori Methenamine Silver stain septate fungal hyphae with occasional dichotomous branching were identified. A classical morphology of *Aspergillus* usually shows uniform narrow tubular and regularly septate, hyaline hyphae with acute angle branching.¹⁰ In our case, the hyphae showed variable thickness with focal septations. This would have occurred possibly due to degenerative changes as reported in the literature.¹¹ However, subsequent microbiological cultures confirmed the species as *Aspergillus* (Sp. *A. fumigatus*). Serological tests such as serum Galactomannan were not available at our institute for further confirmation.⁸

According to the current literature cutaneous aspergillosis in immunocompetent patients has a favorable outcome.¹⁰ In accordance with the above, our patient was also symptom free with complete resolution of the upper trunk swelling within three months of therapy.

To summarize, we present the case of an elderly immunocompetent patient with left arm and lateral chest wall swelling, which was first diagnosed on FNAC and later the diagnosis was confirmed by microbiological cultures as primary cutaneous aspergillosis due to *A. fumigatus*, which is extremely rare in an immunocompetent individual. Expedited diagnosis could help in initiating an early antifungal treatment before the infection disseminates, thereby reducing the morbidity

and mortality. As seen in our case, the initial presentation of primary cutaneous aspergillosis may mimic as malignancy. FNAC can play an important role in resolving such diagnostic dilemma. Thus, FNAC along with special histochemical stains and fungal cultures play an important role in diagnosis and speciation of fungal infections, which incidentally also played an important role in the management of our case.

CONFLICTS OF INTEREST

Nil

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