Infection and Drug Resistance

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CASE REPORT

Necrotizing Fasciitis Caused by *Aspergillus flavus* in an Immunocompetent Young Patient: A Case Report and Literature Review

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Background: Necrotizing fasciitis caused by *Aspergillus flavus* is extraordinarily rare, with most cases observed in immunocompromised patients. We report a case in an immunocompetent young patient and review the literature.

Methods: We present a case of limb-necrotizing fasciitis caused by *Aspergillus flavus* and conducted a systematic PubMed search using keywords related to "Aspergillus flavus", "soft tissue infection" and "necrotizing fasciitis" to identify previously reported cases.

Results: A 26-year-old man presented with progressive swelling and numbness of the right forearm originating from a minor abrasion. Surgical debridement and fungal cultures confirmed *Aspergillus flavus* infection. The patient was successfully treated with voriconazole. Notably, severe local signs contrasted with nearly normal systemic inflammatory indices throughout the disease course. Literature review identified 8 reports encompassing 10 patients; 7 were immunocompromised. Non-facial *Aspergillus flavus* soft tissue infections were exceedingly rare, with only two cases in immunocompromised hosts and one in an immunocompetent patient following trauma.

Conclusion: We report the youngest immunocompetent patient with limb necrotizing fasciitis caused by *Aspergillus flavus*. This case highlights the discrepancy between local signs and systemic response. Timely intervention is crucial for favorable prognosis.

Keywords: necrotizing fasciitis, soft tissue infection, *Aspergillus flavus*, voriconazole, fasciotomy

Introduction

Necrotizing fasciitis is a necrotizing soft tissue infection that can cause rapid destruction of the superficial fascia, muscle necrosis, and life-threatening sepsis. Necrotizing fasciitis could be secondary to major trauma as well as minor breaches of the skin or mucosa.[1] Gram-positive organisms and mixed flora are the most common pathogens.[2,3] The genus *Aspergillus* is one of the largest groups of filamentous fungi pathogenic to humans. These fungi exhibit remarkable adaptability and are easily transmitted. *Aspergillus fumigatus* is the predominant etiological agent of aspergillosis, responsible for approximately 70–80% of cases.[4,5] Non-*fumigatus* aspergillosis is infrequently described, which include *Aspergillus flavus, Aspergillus niger, Aspergillus terreus*, and *Aspergillus versicolor. Aspergillus flavus*, the second most frequently isolated *Aspergillus* species from clinical samples globally, is notably higher in regions such as Asia, the Middle East, and Africa, likely due to its enhanced tolerance to hot and arid climates. Clinically, it is the predominant fungal pathogen in sinu-orbital and cerebral invasive fungal diseases, particularly among immunosuppressed patients.[6] Necrotizing fasciitis secondary to *Aspergillus flavus* infection is extraordinarily rare, with only a handful of published cases in immunocompromised conditions.[7] Herein, we report a rare case of necrotizing fasciitis caused by *Aspergillus flavus* in a young, immunocompetent patient without comorbidities. This case is documented with detailed occupational exposure history, epidemiological investigation, treatment course, and clinical outcomes. We present this report to

https://doi.org/10.2147/IDR.S587862
Received: 21 December 2025
Accepted: 17 March 2026
Published: 22 April 2026

contribute to the broader understanding of the pathogenesis, clinical spectrum, and management of Aspergillus flavus infections in atypical host populations.

Case Presentation

A 26-year-old man with no medical history presented to the emergency department of a local hospital with swelling in the right forearm. The patient had no history of smoking, alcohol consumption, or drug use. He worked as a feeder at a local chicken farm. He reported superficial abrasion on the back of the right elbow 10 days prior to when work. The wound was scarbed after self-disinfection with iodophor. He had manually removed part of the scab 3 days prior (Figure 1A) and subsequently noticed slight swelling around the wound, accompanied by oozing from the wound surface the next day (Figure 1B). On arrival, he complained of progressive swelling and numbness in the right forearm with no fever or chills. Physical examinations revealed oozing of the wound and erythema around the skin of the elbow, with increased skin tension and multiple tense bullae. Movement of the elbow joint was restricted. Vital signs were as follows: blood pressure, 113/62 mmHg; pulse rate, 72 beats/min; respiratory rate, 15 breaths/min; temperature, 36.7 °C. Routine blood tests revealed a normal white blood cell (WBC) of 6.02 x 10^9/L with 63% neutrophils and a normal lymphocyte count of 1.57 x 10^9/L. Inflammatory biomarkers showed that the C-reactive protein (CRP) level was slightly increased (9.43 mg/L, normal range <8.200 mg/L). All other laboratory values were within the reference ranges. Empirical cephalosporin antibiotics were administered intravenously and the patient underwent emergent fasciotomy. The initial treatment was left open with a sterile dressing (Figure 2A). The tense bullae subsided after fasciotomy (Figure 2B). Wound samples and multiple secretion cultures were negative for bacteria. Six days later, the patient underwent a second debridement and negative-pressure wound therapy was applied to promote healing (Figure 2C). The wound samples were sent for bacterial and fungal detection. Fungal cultures and tissue specimen smear examinations were positive for *Aspergillus flavus* but negative for bacteria (Figure 3). This result was confirmed in subsequent cultures. Oral voriconazole (200 mg twice daily) and intravenous cephalosporin were administered. Finally, the wound was closed on the 11th day (Figure 2D), and he was discharged with oral voriconazole on the 14th day after admission. The patient had no fever or other vital signs that fluctuated throughout the disease course. During hospitalization, infection and inflammation

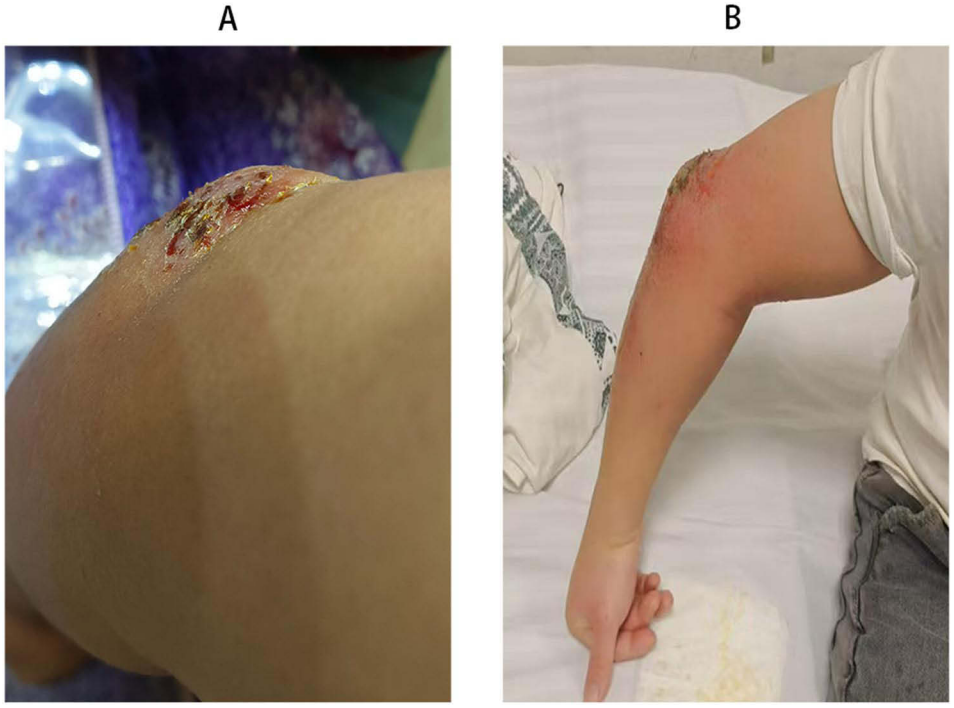

Figure 1 Wound pictures provided by the patient prior to fasciotomy. (**A**) 3 days prior to fasciotomy when the patient manually removed part of the scab. (**B**) Oozing from the wound, erythema around the skin of elbow, and swelling of the forearm 1 day prior to fasciotomy.

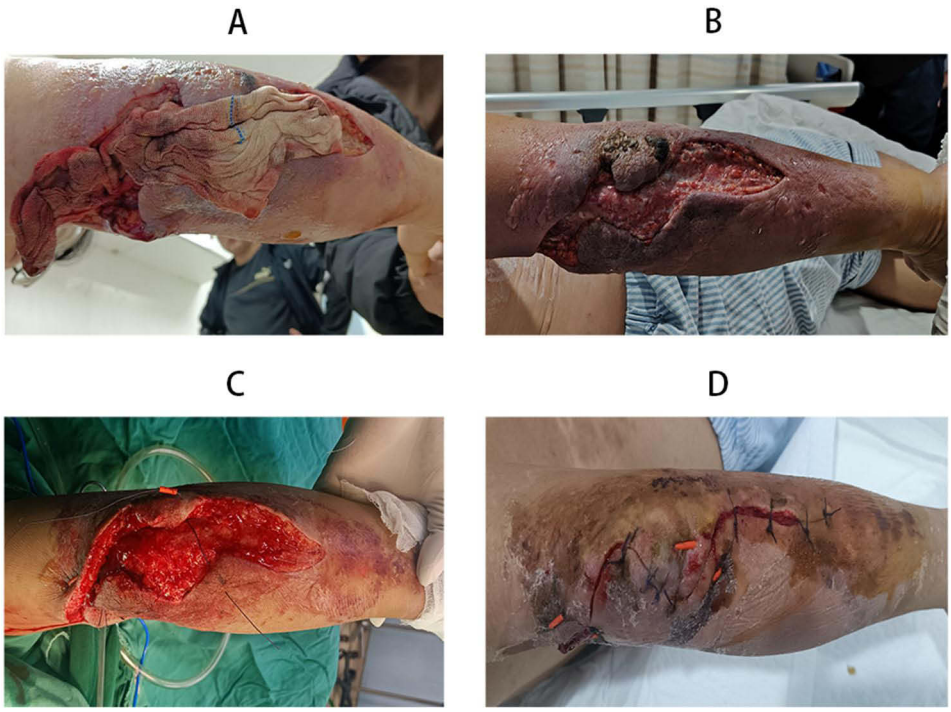

Figure 2 Wound pictures after fasciotomy. (**A**) 1 day after fasciotomy, the wound open with a sterile dressing; multiple tense bullae scattered on the edematous skin. (**B**) 3 days after fasciotomy, the tense bullae subsided; skin, subcutaneous tissue, and fascia were necrotic but muscles and tendons were healthy. (**C**) 6 days after fasciotomy (the second debridement), fresh muscle and fascia were exposed after scraping off the superficial necrotic tissues and inflammatory granulation. (**D**) 11 days after fasciotomy, the wound was closed.

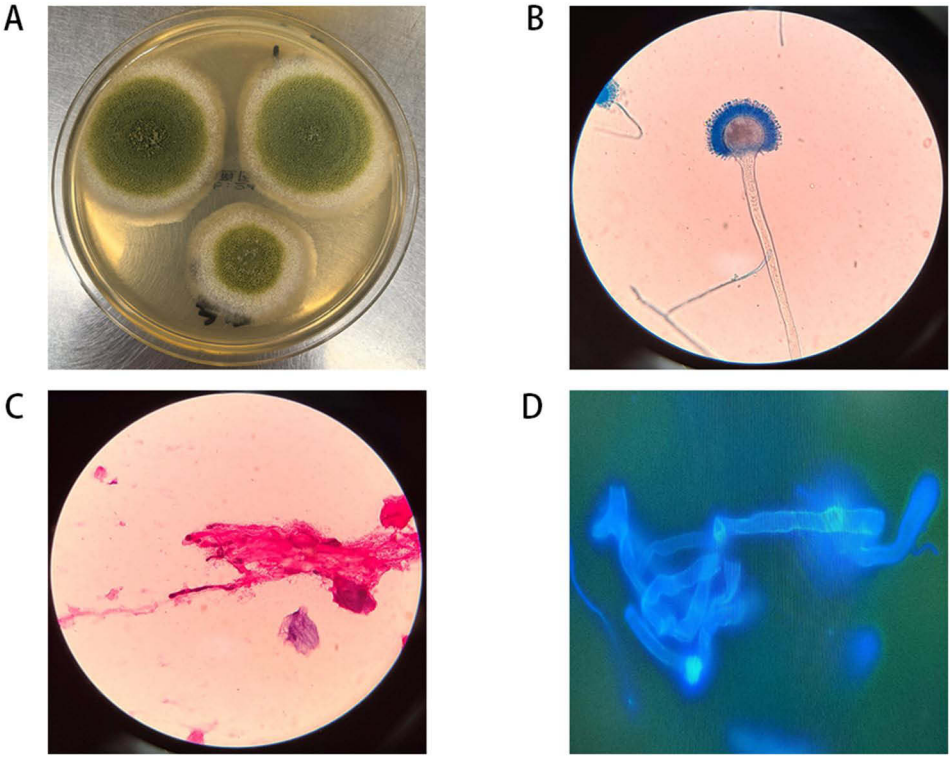

Figure 3 (**A**) *Aspergillus flavus* grow rapidly on Sabouraud Dextrose Agar (SDA) plate, yielding woolly, yellowish-green colonies within a 72-hour incubation period. (**B**) Lactophenol Cotton Blue (LPCB) staining of *Aspergillus flavus*. (**C**) Microscopic examination showed septate hyphae were observed in the patient's tissue specimen using Gram staining. (**D**) Fluorescence microscopic examination showed septate hyphae exhibiting 45-degree angle branching under fluorescent brightener staining.

https://doi.org/10.2147/IDR.S587862

Table 1 Infection and Inflammation Indicators from the Day After Admission

Item	Normal Range	1st (Fasciotomy)	2nd	4th	7th
White blood cell count	3.5–9.5 x 10^9/L	6.02	7.78	6.18	5.17
Neutrophils%	40-75%	63	81↑	59	49
Lymphocyte count	1.1–3.2 x 10^9/L	1.57	0.86↓	1.59	1.64
C reactive protein	< 8.20 mg/L	9.43↑	–	10.95↑	3.54
Interleukin-6	< 7.0 pg/mL	–	6.4	11.19↑	9.47↑
Procalcitonin	< 0.046 ng/mL	–	–	0.030	0.020

Notes: ↑ indicates values above the upper limit of normal; ↓ indicates values below the lower limit of normal.

indicators such as WBC, CRP, interleukin-6 (IL-6), and procalcitonin (PCT) levels were normal or showed only mild abnormalities (Table 1). Serum (1-3)-β-D-glucan (G) and galactomannan (GM) assays were negative.

Discussion

Necrotizing fasciitis is a life-threatening infection characterized by subcutaneous tissue, fascia, or muscle necrosis, and is associated with high morbidity and mortality. Early surgical debridement of necrotic tissues and prompt initiation of broad-spectrum antibiotics are the mainstay of treatment. In this case, the local signs of swelling, erythema, and pain progressed rapidly, but the lack of obvious systemic inflammatory reactions usually seen in a bacterial etiology should raise suspicion of atypical organisms.

Necrotizing fasciitis caused by *Aspergillus flavus* is rare, especially in immunocompetent adults. We systematically searched the PubMed database using the keywords "Aspergillus flavus" in combination with "soft tissue infection" or "necrotizing fasciitis". A total of 8 case reports, including 10 patients were identified,[8–15] which shows that the disease is rare. Of the 10 patients, 7 had immunosuppressed status such as transplant, hematologic malignancies or long term use of corticosteroids. Notably, primary *Aspergillus flavus* soft tissue infections originating from non-facial sites are even rarer. Among seven patients with immunosuppressed status, only two had soft tissue infections occurring in non-facial regions: one involved the chest wall, and the other involved the gluteal muscles.[11,12] Among the remaining three immunocompetent patients, one report described two patients with sino-orbital infections—the most commonly reported site of *Aspergillus flavus* infection.[14] One report describes a 50-year-old female suffered foot cutaneous *Aspergillus flavus* infection after an open fracture caused by a motorcycle accident.[15] Particularly noteworthy in our case was the extremely severe outcome despite the extremely minor initial injury in a young immunocompetent adult.

Gram staining and morphological histopathological identification of surgically obtained tissue have critical roles and remain the gold standard for establishing a proven diagnosis of invasive aspergillosis. Clinical specimens should be inoculated onto a combination of multiple culture media, including Sabouraud dextrose agar (SDA), potato dextrose agar (PDA), cornmeal agar (CMA), Czapek medium, and malt extract agar (MEA). Incubation should be carried out at 25–30°C for a period of 7–10 days. However, this approach suffers from low sensitivity, and is often infeasible in critically ill patients who cannot tolerate invasive procedures. Non-culture based biomarker assays, particularly the galactomannan (GM) testing, are widely used for early diagnosis. According to the revised 2020 EORTC/MSGERC criteria, the GM positivity cut-off values are defined as ≥0.7 for single serum/plasma, ≥0.8 for bronchoalveolar lavage fluid, and ≥1.0 for cerebrospinal fluid.[16] Although simple and quantitative, GM testing is hampered by false-positive results. The 1,3-β-D-glucan assay, while suggestive, lacks specificity for *Aspergillus* and is not recommended as a definitive diagnostic tool. Nucleic acid amplification-based methods, including polymerase chain reaction (PCR) assays and metagenomic next-generation sequencing (mNGS) assays, have been incorporated into the EORTC/MSGERC diagnostic definitions for plasma, serum, whole blood, and bronchoalveolar lavage fluid. Despite these advances, unfortunately, challenges remain including limited standardization of blood PCR, the need for more specialized reference databases, and high costs.[17]

To our knowledge, this is the youngest immunocompetent patient reported with limb necrotizing fasciitis caused by *Aspergillus flavus*. Discrepancies between the local signs and systemic indices should raise caution regarding this atypical organism. Moreover, this patient's occupation indicated that he had the opportunity to contact contaminated agricultural

crops.[18] It is crucial to consider the possibility of *Aspergillus flavus* infection, especially if there is a history of skin wounds that came into direct contact with soil, decaying vegetation, or stored crops. The proper management of fungal necrotizing fasciitis should include early recognition, surgical debridement, and proper antifungal therapy. Of course, it is worth noting this is a single-case report, which by its nature limits the generalizability of our findings. The unique occupational exposure of our patient may not be representative of other populations.

Conclusion

This is the youngest-reported case of limb-necrotizing fasciitis caused by *Aspergillus flavus* in an immunocompetent patient. It is characterized by a discrepancy between the local sign and systemic index. Based on our experience and review of the literature, we offer the following recommendations for clinicians: (1) Maintain a high index of suspicion for fungal etiology in necrotizing soft tissue infections in patients with skin wounds contacting soil, decaying vegetation, or agricultural products; (2) Obtain deep tissue specimens early for both bacterial and fungal cultures; and (3) Timely antifungal therapy combined with aggressive surgical debridement is associated with favorable outcomes. Early recognition and intervention remain the cornerstones of successful management.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

Ethics approval was not required by the local ethics committee as this was a case report with anonymized details. Written informed consent for the publication of clinical details and images was obtained from the patient. A copy of the written consent will be available for review by the Editor-in-Chief when needed.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work is supported by the National Key Research and Development Program (NO. 2025YFC3408403) and The New Chongqing Youth Innovation Talent Project, CSTB2025YITP-QCRCX0026.

Disclosure

The authors declare that they have no competing interests in this work.

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