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Cutaneous phaeohyphomycosis presenting as multiple ecthyma-like skin lesions caused by *Curvularia lunata* in a previously healthy man: A case report☆

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ABSTRACT

Ecthyma grangrenosum is an unusual condition, mostly related to *Pseudomonas* septicemia. Ecthyma-like skin lesions caused by cutaneous phaeohyphomycosis are extremely rare. Here, we report a case of a 20-year-old Thai man, previously healthy, presenting multiple ecthyma-like skin lesions in both arms and both legs for 2 months. Physical examination revealed ill-defined erythematous plaque with central necrotic crust at both arms and both legs. Tissue biopsy showed a neutrophil collection identified by GMS stain revealing septate hyphae organisms in the vascular lumen. The skin culture was positive for *Curvularia lunata*, while the final diagnosis was cutaneous phaeohyphomycosis caused by *Curvularia lunata*. He was empirically treated with amphotericin B and then voriconazole. Itraconazole was administered as a definitive regimen, resulting in complete resolution after 2 months of treatment. Cutaneous phaeohyphomycosis is also an uncommon cause of ecthyma-like lesions and should be considered for investigation when initial results do not demonstrate a bacterial etiology.

Introduction

Ecthyma gangrenosum (EG), a hemorrhagic pustule evolving in necrotic ulcers, typically arises from *Pseudomonas aeruginosa* infection and often occurs in immunocompromised hosts [1]. The cutaneous lesion of EG resembles pyoderma gangrenosum (PG), presenting as a gangrenous lesion with black eschar. However, PG is a noninfectious neutrophilic dermatosis related to several systemic diseases, particularly autoimmune diseases [2]. Various bacterial species have also been reported as causative pathogens of EG, namely, *Escherichia coli*, *Citrobacter freundii*, *Klebsiella pneumonia* and *Morganella morganii* as well as some fungi including *Candida albicans, Fusarium* and others [1,3]. *Curvularia lunata* is a saprophytic dematiaceous mold originally residing in soil, and occasionally reported to contribute to human disease even in an immunocompetent host including endocarditis, brain abscess, keratitis, skin infection and disseminated disease [4,5]. Phaeohyphomycosis is the term used to group infections caused by molds with dark-colored colonies. Cutaneous phaeohyphomycosis typically begins as a single red nodule, usually on the extremities [6]. Thus, ecthyma gangrenosum-like lesions caused by dematiaceous fungi particularly *Curvularia lunata* are extremely rare.

Here, we report a case of a 20-year-old Thai man, previously healthy, presenting multiple ecthyma-like skin lesions in both arms and both legs caused by *Curvularia lunata.*

Patient information

A 20-year-old Thai male noticed red rashes in spots on both legs two months before coming to the hospital. He is an automobile mechanic with an unremarkable medical and family history. The rash was without pain and itching. Afterward, the rash changed to small, black spots, 0.5 to 1 cm, with minimal itching, and gradually increased in quantity over 1 to 2 months. No symptoms were reported of fever, weight loss or loss of appetite, neurological deficit, and the patient could continue to work as

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usual without seeking medical treatment. One month before, a similar rash appeared on the arms, starting from the left arm, and subsequently spread to the right arm. One week before hospital admission, the patient came for military training and was able to participate. Twelve hours before coming to the hospital, the military instructor found the patient lying in bed with his eyes open but unresponsive to commands. Both hands were extended and rigid but not convulsing, so the patient was urgently taken to the hospital. On arrival, the emergency physician noted the patient was comatose (Glasgow Coma Scale E1, V1, M 1) and exhibited a temperature of 42 °C, heart rate of 100 beats per minute, respiratory rate of 28 breaths per minute and high blood pressure of 130/100 mmHg. Oxygen saturation at atmospheric ambience was 96 %. The physician initially diagnosed it as heatstroke. He was immediately intubated and transported to the intensive care unit.

On the admission date, the patient was obese (body mass index 35 kg/m^2). Physical examination revealed multiple ill-defined erythematous plaques with central necrotic crust found on both arms and both legs (Fig. 1). On neurologic examination, the patient was comatose without any stiffness of the neck and other neurologic exams were unremarkable. The initial cerebral computed tomography (CT) of the brain did not reveal any pathology, a lumbar puncture was performed, and the result showed a normal cerebrospinal fluid profile (CSF).

At initial laboratory findings, complete blood count values were as follows: Hb 14 g/dL, HCT 43 %, WBC 14,670 cell/mm^3(neutrophil 78.8 %, lymphocyte 17.5 %) and platelets 127,000 cells/mm^3 and the Anti-HIV Test was nonreactive. The fasting blood glucose was 82 mg/dL, and HbA1C was 4.7 %. A punch biopsy of the skin lesions on the right hand and left leg was performed. Histopathology with hematoxylin and eosin staining identified vascular thrombosis with fibrinoid deposition in the vascular lumens and vascular wall, while sparse perivascular infiltration with neutrophils and lymphocytes was observed. Gomori methenamine silver (GMS) stain and Periodic Acid-Schiff Stain revealed a septate hyphae organism in vascular lumens and ulcers (Fig. 2). A special stain AFB and mAFB were negative for the organism. The fungal culture from the tissue biopsy indicated *Curvularia* spp, and Sabouraud dextrose agar yielded colonies of brown to black fungi from the top and black color from the reverse. Conidia were brown, cylindrical and septated with an enlarged central part, consistent with *Curvularia* spp. (Fig. 3). Molecular analysis was performed on the fungal colony, and 18 s rRNA (fungal genes) also reported *Curvularia lunata* (Accession no. MN540246.1).

Finally, he received a diagnosis of heat stroke and cutaneous phaeohyphomycosis caused by *Curvularia lunata*. The patient was initially treated with amphotericin B deoxycholate (1 mg/kg/day) as the initial histopathology revealed the characteristics of fungus and subsequently changed regimen to voriconazole (4 mg/kg/day) due to amphotericin B toxicity. After the tissue culture was finally reported, we switched the regimen to itraconazole 400 mg/day. After a total course of antifungal for two months, all lesions resolved, but leaving hyperpigmented scars.

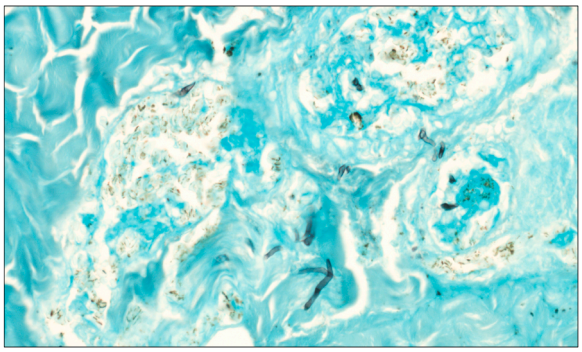

Fig. 2. Skin biopsy of left leg ulcers with GMS stain reveals a septate hyphae organism in the vascular lumen.

Discussion

Phaeohyphomycosis refers to infections caused by dematiaceous fungi that have a worldwide distribution and are found in soil, wood and decaying matter. The disease spectrum is wide and can be present as keratitis, subcutaneous, rhinosinusitis and allergic bronchopulmonary but sometimes also as invasive pulmonary or severe cerebral infections with fungemia, commonly occurring among immunocompetent patients [6]. Clinically important species causing systemic infections belong to the genera *Alternaria, Aureobasidium, Bipolaris, Chaetomium, Cladophialophora, Cladosporium, Curvularia, Exophiala, Exserohilum, Fonsecaea, Helminthosporium, Lomentospora* and *Ochroconis* [6,7].

Cutaneous phaeohyphomycosis usually follows a traumatic injury and typically begins as a single red nodule, usually on the extremities. In an immunocompetent individual, an indolent, painless expansion in the skin and subcutaneous tissue occurs [7,8]. In this case, we present a previously healthy man with skin biopsy and culture-proven extensive cutaneous phaeohyphomycosis, presenting an atypical skin lesion, namely, an ecthyma gangrenosum-like lesion. Dematiaceous fungi skin infection has rarely been reported to present lesions resembling ecthyma gangrenosum. Typically, this presentation is considered pathognomonic for *Pseudomonas aeruginosa* infection. Patients developing ecthyma gangrenosum have a known diagnosis of hematologic malignancy or immunodeficiency such as agammaglobulinemia, hypogammaglobulinemia, aplastic anemia or AIDS. However, among our patients, the presentation was unusual. Ecthyma gangrenous skin lesions were found in multiple locations on the arms and legs, but no fungi were detected in

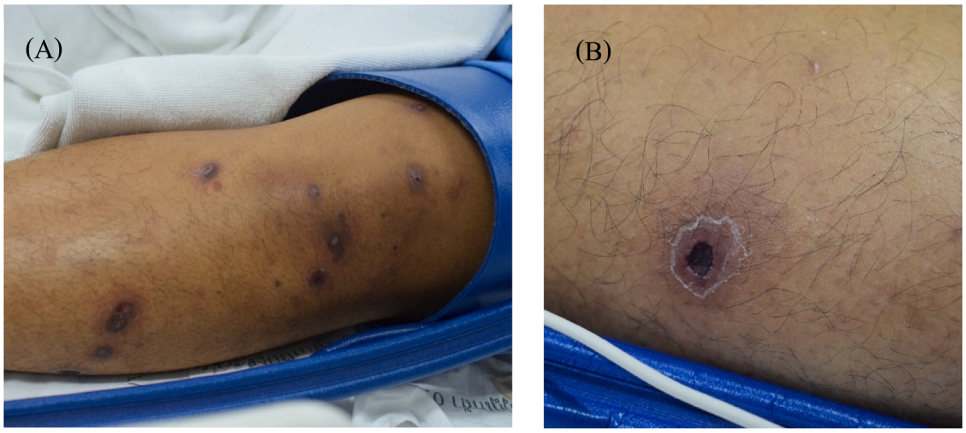

Fig. 1. (A) and (B) The patient's left leg with multiple gangrenous ulcers with erythematous borders.

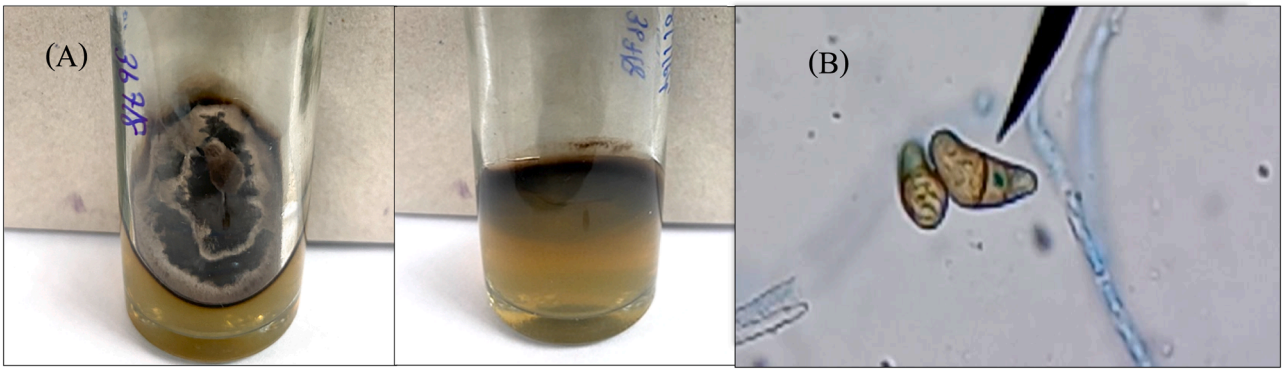

Fig. 3. (A) Culture on Sabouraud dextrose agar showing growth of *Curvularia* greyish brown colonies with pigment on the reverse side. (B) Conidia are brown, cylindrical, septated, with an enlarged central part, consistent with *Curvularia* spp.

the bloodstream. Importantly, the patient did not present any underlying immunodeficiency [1,3]. Only one report demonstrated ecthyma-like phaeohyphomycosis caused by *Cladosporium cladosporioides* in an immunocompetent individual, where the skin lesions resembled those found in this case [9]. Other reports of *Curvularia* spp. subcutaneous infections have described relatively different skin lesions compared with this case including eumycetoma in a young adult, sternal wound infection in a neonate, and generalized subcutaneous nodules with pulmonary nodules in a previously healthy man [10–13]. Cerebral phaeohyphomycosis caused by *Curvularia* spp. has also been reported in previously healthy men presenting chronic headaches and cerebral masses with hemorrhage [5]. Unlike these cases, neurologic symptoms in this patient developed abruptly during excessive exertion, and both brain imaging and CSF examination were unremarkable. Therefore, heat stroke was diagnosed, and cerebral phaeohyphomycosis was considered unlikely. Diagnosis of this infection requires observation of the fungi invading tissue or recovery of the fungi in culture from an otherwise sterile site. Typical pathology is necessary to diagnose phaeohyphomycosis and gross and microscopic examination of cultured strains, showing dark colonies with usually darkly pigmented septate hyphae with widely variable conidia and conidiophores, respectively. Pleomorphism seen in dematiaceous organisms from histopathology is the most specific finding in microscopy. The Fontana-Masson stain helps to make melanin visible in dematiaceous molds and currently, no serological test can be recommended [6,8]. In this case, a skin tissue biopsy demonstrated a septate hyphae organism in vascular lumens and ulcers. Tissue culture subsequently revealed a fungus with brown conidia, cylindrical and septated with an enlarged central part, observed in microscopy, consistent with *Curvularia* spp. Additionally, 18 s rRNA from the fungal colony also identified *Curvularia lunata*. These findings definitively diagnosed cutaneous phaeohyphomycosis caused by *Curvularia lunata* [6,10]. Surgical debridement is essential to cure most of the infections caused by the dark-walled fungi. The use of either itraconazole, voriconazole or lipid formulations of AmB has successfully treated phaeohyphomycosis. Isavuconazole, and posaconazole are recommended medications with moderate efficacy to salvage treatment of phaeohyphomycosis. Standard treatment duration has yet to be established. The guideline group supports treatment until all signs and symptoms of infection have been resolved regardless of the type of antifungal agents administered [6,8]. In this case, we used only antifungal therapy and did not perform surgical debridement due to the small, multiple-site distribution. The patient was cured after a two-month course of antifungal treatment.

To the best of our knowledge, this case demonstrated the very first case report of cutaneous phaeohyphomycosis caused by *Curvularia lunata* in an immunocompetent individual presenting ecthyma-like skin lesions. However, we did not perform intensive work up of other acquired or inherited immunodeficiency syndromes other than HIV, although he was previously healthy, denied either history of recurrent infections or clinical signs compatible with those syndromes.

Conclusion

Ecthyma gangrenosum and ecthyma-like skin lesions typically manifest among immunocompromised patients, commonly associated with infections caused by *Pseudomonas aeruginosa* or other gram-negative bacteria. In cases where initial findings did not indicate a bacterial origin, particularly among immunocompetent individuals, investigating cutaneous phaeohyphomycosis should be consider as it represents an exceedingly rare cause of ecthyma-like lesions.

Authorship statement

All authors meet the ICMJE authorship criteria. All authors participated in the diagnosis, management and/or care of the patient. S.J, W.S., C.S. and W.N. wrote the draft and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

CRediT authorship contribution statement

Sitthipong Jinawong: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chutika Srisuttiyakorn:** Writing – review & editing, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Weranat Sookboon:** Writing – review & editing, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Worapong Nasomsong:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Patient declaration of consent statement

The patient has provided written informed consent for the publication of this report and the accompanying images.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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