

Vascular Pythiosis Caused by *Pythium Aphanidermatum*: The First Case Report in Asia

Pannaporn Thongsuk

King Chulalongkorn Memorial Hospital <https://orcid.org/0000-0002-5502-2368>

Rongpong Plongla

King Chulalongkorn Memorial Hospital

Arsa Thammahong

King Chulalongkorn Memorial Hospital

Jaruwan Tiewsurin

Buddhachinaraj Phitsanulok Hospital

Navaporn Worasilchai

King Chulalongkorn Memorial Hospital

Ariya Chindamporn

King Chulalongkorn Memorial Hospital

Chusana Suankratay (✉ Csuankratay@gmail.com)

Department of Medicine, Faculty of Medicine, Chulalongkorn University

Case report

Keywords: pythiosis, *Pythium*, *Pythium insidiosum*, *Pythium aphanidermatum*, case report

Posted Date: May 6th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-495660/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at European Journal of Medical Research on November 14th, 2021. See the published version at <https://doi.org/10.1186/s40001-021-00603-w>.

Abstract

Background: *Pythium*, soil-borne plant pathogens, are in the class Oomycetes. They are not true fungi, but are related to diatom and algae. There are 2 human pathogens including *P. insidiosum* and *P. aphanidermatum*. To date, only 1 case of pythiosis caused by *P. aphanidermatum* has been reported. We present herein the first case of *P. aphanidermatum* vascular pythiosis in Asia.

Case presentation: A 47-year-old Thai woman, living in North Thailand, with β thalassemia/hemoglobin E presented with acute recurrent arterial insufficiency of both legs. Emergent embolectomy with clot removal was performed. The pathology of the clot exhibited noncaseous granulomatous inflammation with many fungal hyphal elements. PCR identified *P. aphanidermatum* with 100% identity. Finally diagnosis is vascular pythiosis. Unfortunately, inoperation due to extensive abdominal aorta involvement, the patient eventually expired after treatment with itraconazole, terbinafine, azithromycin, and doxycycline.

Conclusions : To date, only 1 case of pythiosis caused by *P. aphanidermatum* has been reported. We present herein the first case of *P. aphanidermatum* vascular pythiosis in Asia.

Introduction

Pythium are soil-borne plant pathogens in swampy areas in Thailand and many tropical and subtropical countries.¹ Based on the phylogeny, they are more related to diatom and algae than fungi. They belong to the family Pythiaceae, order Pythiales, class Oomycetes, phylum Oomycota, and kingdom Straminipila.¹ Pythiosis is an emerging, life-threatening infectious disease in humans.²⁻⁵ *Pythium* have 2 forms including perpendicular branching hyphae and biflagellate zoospore.⁶ The zoospore play a major role in the pathogenesis in humans; it swims to attach and invade the host tissue.^{6,7} To date, there has been the largest case series of pythiosis reported from Thailand⁵, however, the disease was reported from Australia, Asia, and America.³ Most of the patients are farmers with predisposing thalassemia and other hemoglobinopathies. There are 4 categories of clinical manifestations including 1) vascular (most of cases), 2) ocular, 3) skin and subcutaneous, and disseminated pythiosis.^{2,5}

There are 2 human pathogens including *P. insidiosum* and *P. aphanidermatum*. To date, only 1 case of pythiosis caused by *P. aphanidermatum* has been reported.⁸ We present herein the first case of vascular pythiosis caused by *P. aphanidermatum* in Asia.

Case Presentation

The case

A 47-year-old Thai woman, living at Maesot, Tak, North Thailand, with β thalassemia/hemoglobin E, was referred from a provincial hospital for further investigations regarding acute arterial insufficiency of both

legs. Two months prior to admission (PTA), she noted a self-limited blackish painful nodule at left labia minor. Few weeks later, she developed a low-grade fever with bilateral groin pain. One month PTA, she had severe pain at left foot, and a diagnosis of acute arterial insufficiency was made a doctor at provincial hospital. Emergent embolectomy with clot removal at left common iliac artery was performed. Few days after hospitalization, there was a recurrent limb ischemia, and embolectomy was performed again. One week after hospitalization, the pathology of the clot exhibited noncaseous granulomatous inflammation with many fungal hyphal elements (Figure A), and hence the patient was referred to King Chulalongkorn Memorial Hospital (KCMH), Bangkok, Thailand, for further investigations. Unfortunately, the operation could not be performed due to the computed tomogram angiogram showing circumferential soft plaques along distal aorta, bilateral common iliac arteries, and external iliac arteries as well as near total occlusion of bilateral internal iliac arteries (Figure B). Serum IgG titers against *P. insidiosum* was 1: 800 (in-house enzyme-linked immunosorbent assay, KCMH), and serum β -D-glucan was 523 pg/mL. The definite identification of the organism from the clot, by amplifying the internal transcribed spacer (ITS) of ribosomal DNA using the polymerase chain reaction (PCR) technique with sequencing of the amplicon and GenBankBLAST searching as previously described⁹, was *P. aphanidermatum* (100% identity). Unfortunately, the patient eventually expired 2 weeks after treatment with itraconazole, terbinafine, azithromycin, and doxycycline as well as an iron chelator, deferoxamine.

Discussion And Conclusions

The first case of pythiosis caused by *P. aphanidermatum* infection was described by Calvano and colleagues in the year 2011. The patient was a 21-year-old Hispanic male soldier who had extensive wound infection affecting both legs, right arm, and buttock in a explosive device blast injury in Afghanistan.⁸ The patient underwent multiple operations for tissue debridements of legs without improvement, finally needing bilateral hip disarticulation. He expired 16 weeks after his final operation despite antifungal treatment with liposomal amphotericin B and voriconazole. Pre- and post-disarticulation fungal cultures of the necrotic tissues from both legs recovered *Mucor circinelloides*, *Aspergillus flavus*, and *P. aphanidermatum*. From the authors' opinion, it was not clear whether the infection caused by *P. aphanidermatum* was a coinfection or not. Our case had vascular pythiosis without known history of trauma, similar to those caused by *P. insidiosum* in most studies.

To date, there have been 2 genera of the class Oomycetes causing human diseases including *Pythium* and *Lagenidium*.^{2,10} *Lagenidium giganteum* was reported to cause keratitis mimicking ocular pythiosis caused by *P. insidiosum*.¹⁰ Of the genus *Pythium*, there have been 2 species of human pathogens including *P. insidiosum* and *P. aphanidermatum*. *P. aphanidermatum* is also a plant pathogen.¹¹ The biologic behavior as well as the human diseases caused by this organism, a member of the class Oomycetes, are similar to those caused by *P. insidiosum*. In addition, the morphology from the pathology of clinical specimens could not be distinguished between the 2 species. Both of them are irregularly branching, pauciseptate hyphae present within the arterial walls.⁸ Hence, the differentiation between the 2 species requires the molecular technique using the PCR technique with primers specific for ITS region of

ribosomal DNA. In our case, we previously thought that her vascular pythiosis was unquestionably caused by *P. insidiosum*. Surprisingly, it turned out to be *P. aphanidermatum*. We believe that vascular pythiosis can be caused by either *P. insidiosum* or *P. aphanidermatum*, and the latter may be underestimated due to similar clinical manifestations, morphology, and false positive serum antibody using *P. insidiosum* enzyme-linked immunosorbent assay, as in our case.

Of the most reported cases of vascular pythiosis, the skin at the foot is the most entry site of infection.^{2,5} After the inoculation, the organism is angiotropic to the arterial wall, usually the dorsalis pedis or posterior tibial artery. The organism will slowly ascend via arterial wall to the distal aorta, and cause occlusion from a thrombus and/or fibrosis, resulting in arterial insufficiency of the leg. Our patient presented with a blackish painful nodule at genitalia which is likely the entry site of infection. And then the organism ascended bilaterally along the arterial wall to the internal iliac arteries, common iliac arteries, and finally the distal aorta. The postulation is confirmed by the findings from computed tomogram angiogram which demonstrating the near total occlusion of internal and common iliac arteries as well as distal aorta, with preserved arteries of both legs.

Due to no effective antimicrobials against *Pythium*, the surgery is the main choice of treatment of vascular pythiosis, usually amputation of the involved limb with organism-free surgical margin by microscopic demonstration.^{2,5} In our patient, the radical surgery could not be performed, and immunotherapy with vaccine was not available. Hence, itraconazole and terbinafine with adjunctive therapy with azithromycin and doxycycline were given to the patient. Susaengrat and colleagues recently published 2 vascular pythiosis cases for whom radical surgery could not be performed, who were successfully treated with adjunctive azithromycin and doxycycline.¹²

To date, only 1 case of pythiosis caused by *P. aphanidermatum* has been reported. We present herein the first case of *P. aphanidermatum* vascular pythiosis in Asia. There are no differences between pythiosis caused by *P. aphanidermatum* and *P. insidiosum* regarding the clinical manifestations, the predisposing conditions, and cross-reaction of serum antibody with our in-house enzyme-linked immunosorbent assay against *P. insidiosum*.

Declarations

Ethics approval and consent to participate:

ethics approval and consent

Consent for publication:

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

Availability of data and materials:

- Calvano TP et.al., Pythium aphanidermatum infection following combat trauma, Journal of Clinical Microbiology, 03 Aug 2011, 49(10):3710-3713

DOI: [10.1128/jcm.01209-11](https://doi.org/10.1128/jcm.01209-11)

- Frank N. Martin, Mycologia, Vol. 92, No. 4 (Jul. - Aug., 2000), <https://doi.org/10.2307/3761428>,
<https://www.jstor.org/stable/3761428>

- Permpalung N, Worasilchai N, Chindamporn A. Human pythiosis: emergence of fungal-like organism. 2019. doi: 10.1007/s11046-019-00412-0

Competing interests:

"The authors declare that they have no competing interests"

Funding:

No funding was obtained for this study.

Authors' contributions:

PT wrote the manuscript. NW and AC analyzed and interpreted the patient's PCR result. CS supervised the writing and edited the manuscript. All authors read and approved the final manuscript

Acknowledgements:

Not applicable.

Patient perspective:

N/A

Informed consent:

N/A

References

1. Martin FN. Phylogenetic relationships among some *Pythium* species inferred from sequence analysis of the mitochondrially encoded cytochrome oxidase II gene. Mycologia. 2000;92:711–27.
2. Permpalung N, Worasilchai N, Chindamporn A. Human pythiosis: emergence of fungal-like organism. 2019. doi: 10.1007/s11046-019-00412-0. Online ahead of print.
3. Franco DM, Aronson JF, Hawkins HK, Gallagher JJ, Mendoza L, McGinnis MR, et al. Systemic *Pythium insidiosum* in a pediatric burn patient. Burns 2010;36:e68-71.

4. Rivierre C, Laprie C, Guiard-Marigny O, Bergeaud P, Berthelemy M, Guillot J. Pythiosis in Africa. *Emerg Infect Dis* 2005;11:479-81.
5. Krajaejun T, Sathapatayavongs B, Prachartam R, Nitiyanant P, Leelachaikul P, Wanachiwanawin W, et al. Clinical and epidemiological analyses of human pythiosis in Thailand. *Clin Infect Dis* 2006;43:569-76.
6. De Cock AW, Mendoza L, Padhye AA, Ajello L, Kaufman L. *Pythium insidiosum* sp. nov., the etiologic agent of pythiosis. *J Clin Microbiol* 1987;25:344-9.
7. Mendoza L, Hernandez F, Ajello L. Life cycle of the human and animal oomycete pathogen *Pythium insidiosum*. *J Clin Microbiol* 1993;31:2967-73.
8. Calvano TP, Blatz PJ, Vento TJ, Wickes BL, Sutton DA, Thompson EH, et al. *Pythium aphanidermatum* Infection following combat trauma. *J Clin Microbiol* 2011;49:3710-3.
9. Kunavisarut S, Nimvorapan T, Methasiri S. *Pythium* corneal ulcer in Ramathibodi Hospital. *J Med Assoc Thai* 2003;86:338–42.
10. Reinprayoon U, Permpalung N, Kasetuwan N, Plongla R, Mendoza L, Chindamporn A. *Lagenidium* sp. ocular infection mimicking ocular pythiosis. *J Clin Microbiol* 2013;51:2778-80.
11. Heine G, Tikum G, Horst W. The effect of silicon on the infection by and spread of *Pythium aphanidermatum* in single roots of tomato and bitter melon. *J Exp Bot* 2007;58:569–77.
12. Sussaengrat N, Torvorapanit P, Plongla R, Chuleerarux N, Manothummetha K, Tuangsirisup J, Worasilchai N, Chindamporn A, Permpalung N. [Adjunctive antibacterial agents as a salvage therapy in relapsed vascular pythiosis patients.](#) *Int J Infect Dis* 2019;88:27-30.

Figures

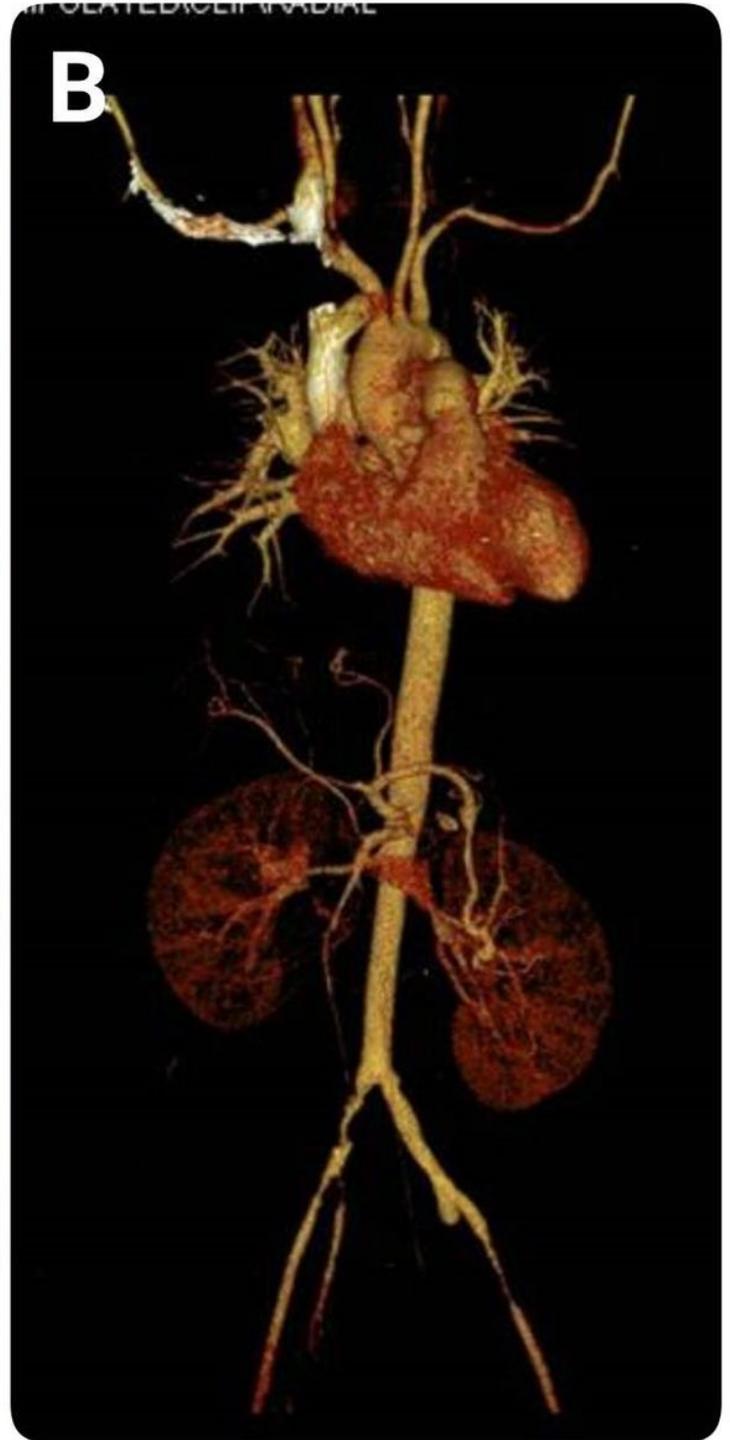
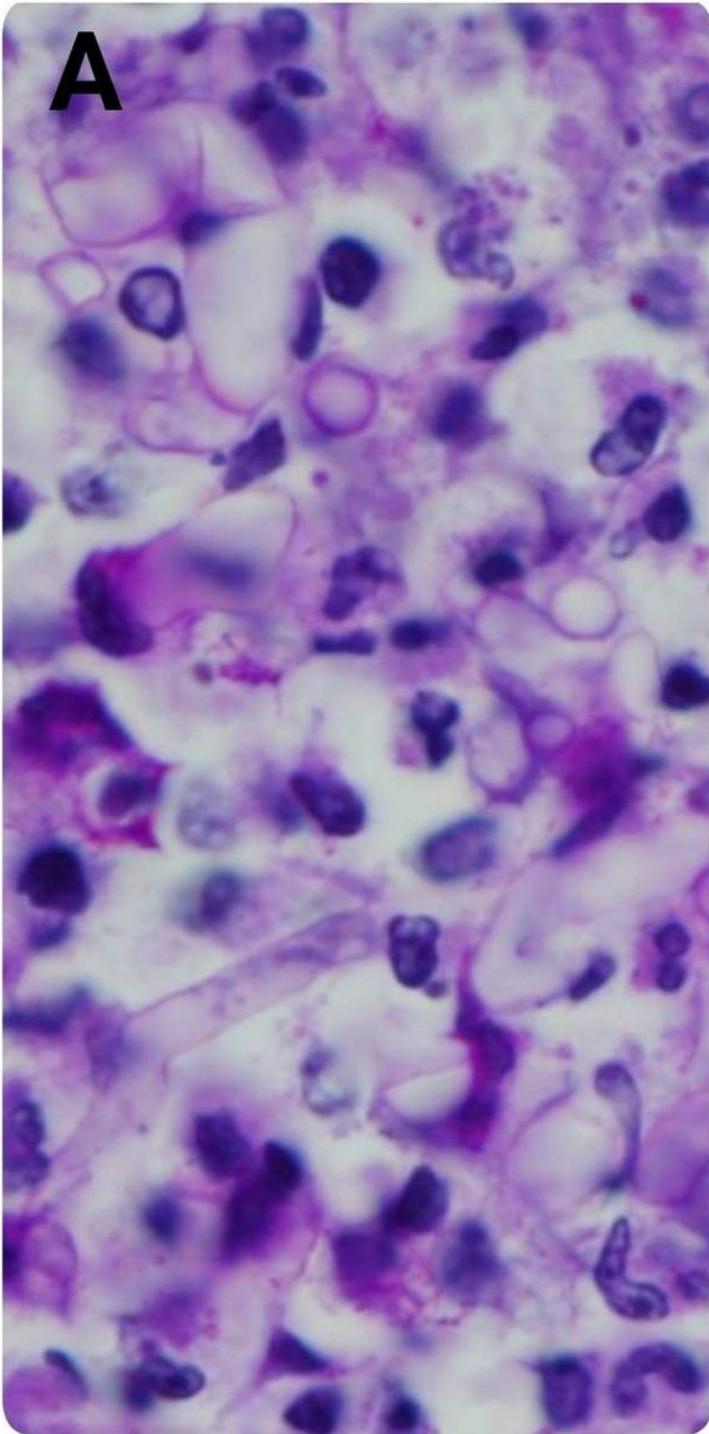


Figure 1

A: hematoxylin and eosin stain of the clot showing many fungal hyphae B: computed tomogram angiogram showing near total occlusion of bilateral internal iliac arteries and narrowing of distal aorta and bilateral common iliac arteries.