



#Thinkfungus case-based discussions: A patient with extensive cellulitis

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An 83-year-old male, retiree, living in Sa-Kaeo

- Well-controlled diabetes, HT, DLP 4 years
 - Glipizide, amlodipine, atenolol, doxazocin, simvastatin
- **Left thigh swelling for 5 days**
- 7 days prior
 - Scratched at his left thigh from a protruding nail from his DIY chair
 - No bleeding, no pain, nor obvious external wound
- 5 days prior
 - Swelling and redness at the area of injury with throbbing pain
 - No fever, able to walk
 - Applied herbal oil on the swollen area



Map of Thailand highlighting Sa Kaeo province



An 83-year-old male with left thigh swelling for 5 days

- 1 day prior
 - Went to a community hospital
 - More swelling, redness, and throbbing pain at left thigh
 - Unable to walk without support due to pain
 - No fever, no crepitus



An 83-year-old male with left thigh swelling for 5 days

What is the most likely diagnosis?

- a) Abscess/pyomyositis
- b) Infected wound
- c) Gas gangrene
- d) Hematoma



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An 83-year-old male with left thigh swelling for 5 days. What is the most likely diagnosis?

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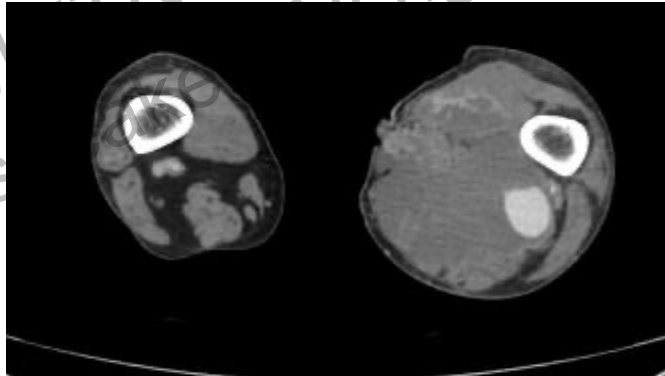
An 83-year-old male with left thigh swelling for 5 days

- Incision and drainage
 - Active bleeding
 - Referred to provincial hospital
 - BT 36.5°C, BP 126/57 mmHg, HR 90 bpm
 - Active arterial bleeding
 - Capillary refill < 2sec
 - Intact dorsalis pedis pulse 2+ bilaterally
 - CT angiography was performed



CT angiography of lower extremities

- Pseudoaneurysm (3.8x2.7x3.3 cm) from distal left superficial femoral artery
- Surrounding hematoma at medial aspect at distal thigh (11 cm in diameter)
- Good contrast opacity at other vessels – no severe stenosis



Refer for vascular surgery

An 83-year-old male with pseudoaneurysm at left SFA

What is the most likely etiology?

- a) Iatrogenic/ direct injury
- b) Bacterial infection *ie. S. aureus, B. pseudomallei, Salmonella, Clostridium*
- c) Invasive mould infection *ie. Aspergillosis, Mucormycosis*
- d) *Pythium insidiosum*

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An 83-year-old male with pseudoaneurysm at left SFA. What is the most likely etiology?

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Laboratory investigations

- CBC: Hb 9.3 g/dL, Hct 28.8%, MCV 79.6 fL, RDW 15.0%, Wbc 8850 cells/mm³ N66.6% L21.2%, Plt 333000/mm³
- PT 14.2 sec INR 1.26 aPTT 32.9 sec
- BUN 17 Cr 1.05 mg/dL Na 140, K 3.9, Cl 112, HCO₃ 19 mEq/L
- HbA1C 5.8%
- Anti-HIV: negative

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OR for open repair pseudoaneurysm of left superficial femoral artery with end-to-end anastomosis

- Operative findings
 - Left distal SFA pseudoaneurysm with contained hematoma 10x15 cm
 - The SFA defect about 1 cm. in length which involved about 50% in circumferential
 - An area of necrotic sartorius, vastus medialis and gracilis muscle around the injured point
- Amoxicillin/clavulanate IV
- Tdap and tetanus anti-toxoid

Post-operation hospital course



Post-operative D3



Post-operative D4



Post-operative D8

Rapidly progression of multiple necrotic tissue and muscles

Afebrile throughout the hospital admission

Aerobic culture of tissue: no growth

IV amoxicillin-clavulanate

An 83-year-old male with pseudoaneurysm at left SFA and progressive muscle necrosis

What is the most likely etiology?

- a) Iatrogenic/ direct injury
- b) Bacterial infection *ie. S. aureus, B. pseudomallei, Salmonella, Clostridium*
- c) Invasive mould infection *ie. Aspergillosis, Mucormycosis*
- d) *Pythium insidiosum*

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An 83-year-old male with pseudoaneurysm at left SFA and progressive muscle necrosis. What is the most likely etiology?

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An 83-year-old male with pseudoaneurysm at left SFA and progressive muscle necrosis

What investigation(s) would you perform?

- a) *Pythium insidiosum* antibody
- b) Fungal culture
- c) Serum *Aspergillus* galactomannan antigen
- d) Serum 1,3 beta-D-glucan

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An 83-year-old male with pseudoaneurysm at left SFA and progressive muscle necrosis. What investigation(s) would you perform?

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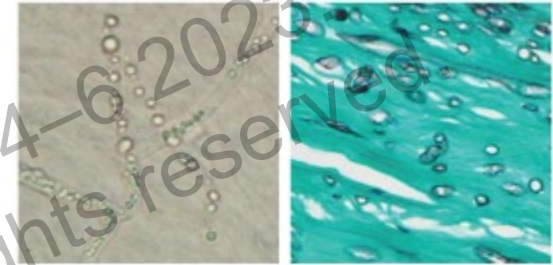
Vascular pythiosis

- *Pythium insidiosum*, *P. aphanidermatum*
(Thongsuk P, et al. Eur J Med Res 2021;26:132)
- Underrecognized and underestimated
 - Thalassemia and hemoglobinopathy
 - Agricultural exposure
- High morbidity and mortality (10–40%; <3 mo. without adequate surgery)
 - Antimicrobial agents *ie.* macrolides, tetracyclines can improve outcomes
 - Early recognition and early surgery are essential
- Duration of symptoms: median 3 months (7–365 days)
- Arterial insufficiency syndrome of the lower extremities
 - Intermittent claudication
 - Gangrenous ulceration
- Chronic non-healing skin lesions
- Vesicle/bulla, skin ulcers, cellulitis, necrotizing fasciitis
- Leg swelling
- Absence of arterial pulse
- Groin mass, abdominal mass (aneurysm-pulsatile mass)
- Fever, paresthesia
- Septic embolism

Vascular pythiosis: Laboratory diagnosis

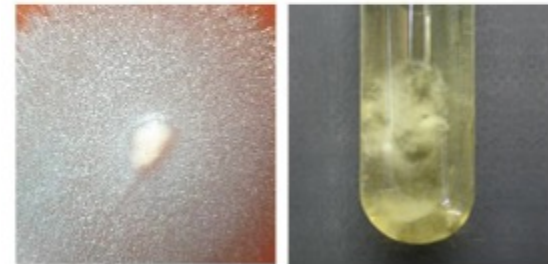
- *P. insidiosum* specific antibody (ID/ ELISA/ WB /Lateral flow)
- *P. insidiosum* isolation & zoospore production
- Molecular based: Identification/diagnosis
- Histopathology
- Biomarkers: 1,3 beta-D-glucan

Rare septate hyphae with 3-5 um diameter



KOH

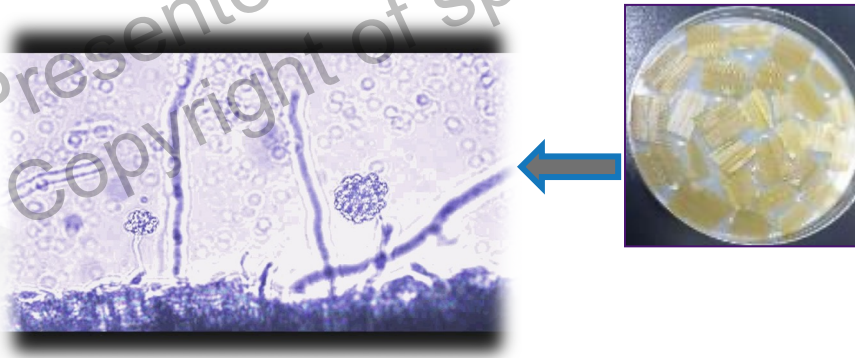
GMS



Blood agar

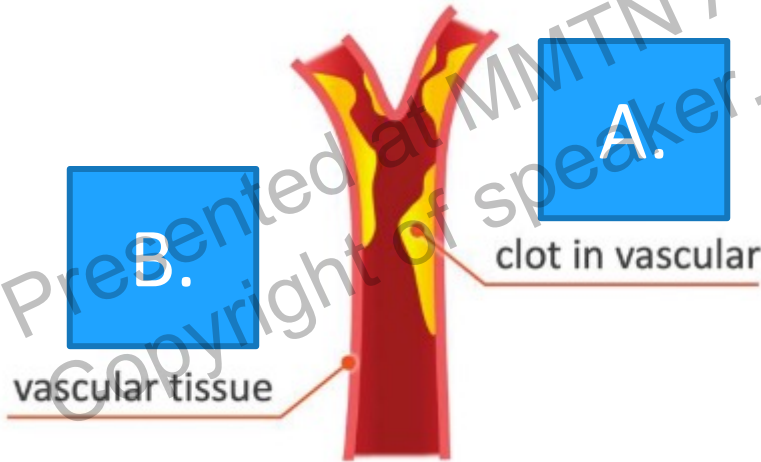
Sabouraud
Dextrose broth

25-35°C, beware of dry media
Rapid growth



Specimen collection and transportation for cultivation of *P. insidiosum*

- Transportation: room temperature, avoid on ice, in sterile distilled water/NSS



What is the proper specimen for cultivation of *P. insidiosum*?

Laboratory investigations

- *P. insidiosum* antibody: Negative
- Serum *Aspergillus* galactomannan: Negative 0.2



Tissue Wright stain



Tissue KOH smear

What is the most likely pathogen?

- A. Dematiaceus fungi
- B. Hyaline mold with frequently septate hyphae with dichotomous branching, compatible with *Aspergillus*
- C. Broad pauci-septate hyphae with right-angle branching, compatible with *Mucormycosis*
- D. Compatible with *P. insidiosum*

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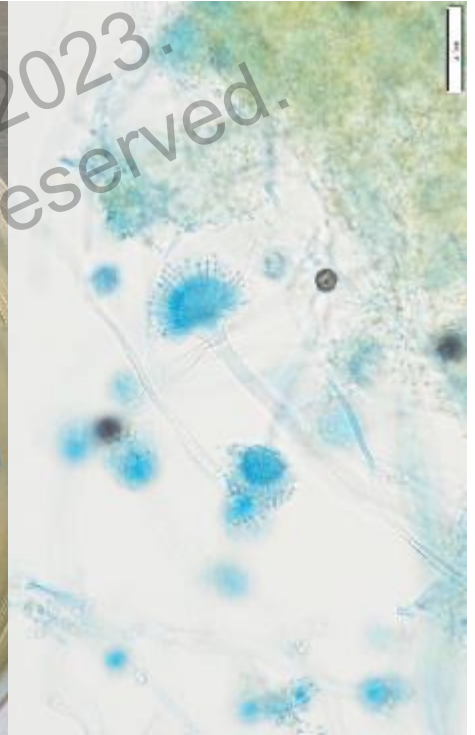


What is the most likely pathogen?

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Tissue culture for fungus



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Treatment

- Debridement
- Voriconazole



Pre-treatment



Post-treatment

Infected aneurysm

- Mechanisms
 - Hematogenous spread of infectious microemboli into the vasa vasorum of a normal caliber artery or a pre-existing aneurysm
 - Infection of a pre-existing intimal defect by circulating infectious agent
 - Contiguous involvement of the vessel from an adjacent source of sepsis
 - Direct infectious inoculation of the vessel wall at the time of vascular trauma
- The etiology has been changing, from endocarditis being the most common cause before the antibiotic era, to arterial trauma in the post-antibiotic era
 - **Shifting of the infectious agents**
 - *Enterococcus* and *Streptococcus* spp. secondary to endocarditis → *S. aureus*, *Salmonella* spp., other atypical bacteria, and *Aspergillus* spp.
 - This is believed to be due to increased IVDU and catheter for intravascular procedures.
 - Paucity of evidence for the diagnostic performance of GM, especially in non-neutropenic patients with endovascular infection
 - In most case reports of IA with endovascular infection showed negative results of GM
 - *A. alliaceus*, *A. carneus* may have negative or low-level GM

#Thinkfungus (and *Pythium*)

- A 83-year-old male presented with swollen left leg and pseudoaneurysm
 - Lack of systemic signs and symptoms *ie.* fever, chill
 - Early vascular involvement
 - Trauma/Injury Environmental exposure
 - Progression despite adequate surgery and appropriate antibacterial therapy; negative bacterial culture

Acknowledgement

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Thank you

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