Ulcerated yellow-brown nodules on the chest

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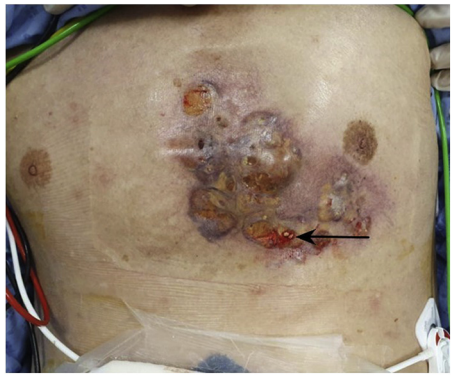

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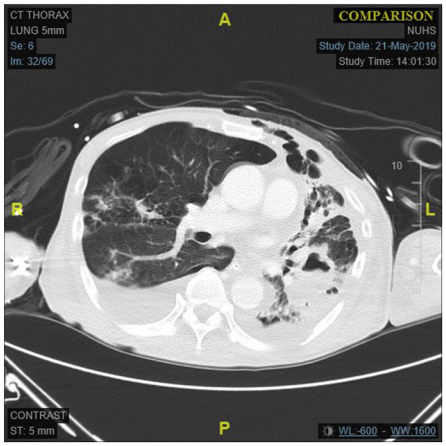

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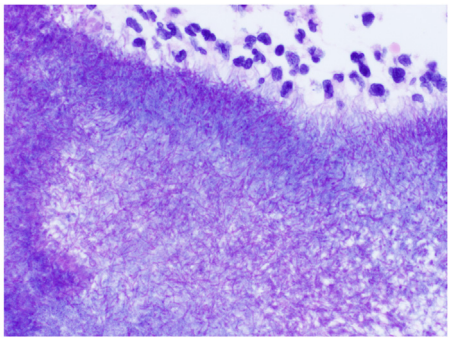

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A 67-year-old Chinese man was admitted to an intensive care unit in Singapore for the first presentation of diabetic ketoacidosis. There was no other significant past medical history. Examination of his chest revealed ulcerated yellow-brown firm nodules overlying telangiectatic patches with punctae containing clusters of yellow granules (*arrow*) (Fig 1). Further history revealed the progression of these skin lesions over 6 months. Computed tomography revealed abnormal soft tissue and gas pockets extending into the left anterior chest wall, with overlying skin defects with extensive consolidative changes (Fig 2). An incisional skin biopsy was performed (Fig 3).

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Question 1: What is the most likely diagnosis?

A. Tuberculosis

B. Mucormycosis

C. Actinomycosis

D. Nocardiosis

E. Botryomycosis

Answers:

A. Tuberculosis — Incorrect. Although tuberculosis is endemic in Southeast Asia, pulmonary infections typically involve the upper lobes and uncommonly invade through the chest wall. A histopathologic examination should instead show tuberculoid granulomas with the presence of acid-fast bacilli.

B. Mucormycosis — Incorrect. Mucormycosis is a fulminant invasive infection by filamentous fungi of the order Mucorales, which predominantly affects patients with poorly controlled diabetes (particularly in the setting of ketoacidosis) due to phagocyte dysfunction.[1] However, on microscopy, mucormycosis would exhibit classical "ribbon-like" angioinvasive hyphae.

C. Actinomycosis — Correct. *Actinomyces* infections are characterized by their chronicity, progression across tissue boundaries, and mass-like features with the formation of sinus tracts discharging "sulfur granules."[2] The presence of cavitary pulmonary disease with extension through the chest wall (empyema necessitans) is highly suggestive of actinomycosis, with the presence of slender filamentous organisms on histopathology clinching the diagnosis.

D. Nocardiosis — Incorrect. Although nocardial infection can also lead to chronic destructive disease with the formation of sinus tracts, the histopathologic findings are not consistent with that of nocardiosis, which is characterized by Gram positive, beaded, fine, right-angled branching filaments, which may fragment to form rods and cocci of varying sizes.

E. Botryomycosis — Incorrect. Botryomycosis is a chronic suppurative infection due to a granulomatous response to bacterial pathogens, most commonly *Staphylococcus aureus*. Although botryomycosis also tends to form granules, a microscopic examination would reveal the presence of cocci or nonbranching bacilli.[3]

Question 2: Which of the following risk factors is associated with this disease?

A. Exposure to soil, organic matter, or aquatic habitats

B. Advanced age

C. Iron overload

D. Tropical climate

E. Poor oral hygiene

Answers:

A. Exposure to soil, organic matter, or aquatic habitats — Incorrect. Environmental exposure via inhalation or direct inoculation is more typical of *Nocardia* infections, which are ubiquitous environmental saprophytes. In contrast, *Actinomyces* species are exclusively endogenous organisms that colonize human mucous membranes and have never been cultured from nature.[2]

B. Advanced age — Incorrect. The peak incidence of actinomycosis has been reported to be from 30 to 60 years old, with incidence declining above the age of 60 years.[2]

C. Iron overload — Incorrect. Iron overload is a risk factor for mucormycosis, particularly in the setting of iron chelation with deferoxamine.[1]

D. Tropical climate — Incorrect. Actinomycosis is an endogenous organism that colonizes human mucous membranes, and the incidence of the disease is not related to geography.

E. Poor oral hygiene — Correct. Poor oral hygiene facilitates the growth of *Actinomyces* species, colonizers of the human oral mucosa. Aspiration of oral secretions then predisposes to the development of pulmonary infection. Accordingly, cervicofacial actinomycosis is the most common manifestation of actinomycosis, accounting for 50% of all cases, whereas central nervous system, thoracic, abdominal, and pelvic actinomycosis occur less frequently.[4]

Question 3: What is the most effective medical treatment for this disease?

A. Initial high dose parenteral penicillin G, followed by high dose oral penicillin V

B. Metronidazole

C. Liposomal amphotericin B

D. Long-term oral fluoroquinolone therapy

E. Rifampicin, isoniazid, pyrazinamide, and ethambutol

Answers:

A. Initial high dose parenteral penicillin G, followed by high dose oral penicillin V — Correct. *Actinomyces* are non—spore-forming, anaerobic Gram positive bacteria. Long-term intensive antibiotic therapy is the mainstay of treatment for actinomycosis. *Actinomyces* species have traditionally shown exquisite sensitivity to penicillin; however, prolonged treatment is necessary due to poor antibiotic penetration of the thick-walled masses and sulfur granules. This typically entails 2 to 6 weeks of initial parenteral antibiotics followed by oral antibiotics for 6 to 12 months.[2] Severe disease may require surgical management.

B. Metronidazole — Incorrect. Metronidazole should not be used to treat actinomycotic infections without added antimicrobial agents as it is not active against pathogenic actinomycetes.[5]

C. Liposomal amphotericin B — Incorrect. Although it may sound like one, actinomycosis is not a fungal infection. Liposomal amphotericin B is the treatment of choice for mucormycosis.

D. Long-term oral fluoroquinolone therapy — Incorrect. In vitro data suggest that fluoroquinolones should be avoided in actinomycosis. Other antibiotics that should be avoided include oxacillin, dicloxacillin, cephalexin, metronidazole, and aminoglycosides.[5]

E. Rifampicin, isoniazid, pyrazinamide, and ethambutol — Incorrect. This combination of antibiotics is the treatment of choice for tuberculosis.

Conflicts of interest

None disclosed.

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