

Case 4.1

A 15-year-old Thai woman from Pathumthani

Chief complaint: Indurated slow-growing subcutaneous plaque on left popliteal fossa for 2 months



Present illness: Two months ago, the patient developed small erythematous subcutaneous nodule on left popliteal fossa. The lesion gradually increased in size and formed painless indurated plaque without ulceration. There was no history of trauma or insect bite. She went to a private hospital which incision and drainage was performed. Tissue was also sent for histopathology. Intravenous antibiotics were prescribed for 4 days but the lesion did not improve.

Past history: Healthy

Physical examination:

VS: BT 36.7°C, RR 20/min, PR 78/min, BP 106/67mmHg

GA: Good consciousness, sthenic built

HEENT: Not pale, no jaundice

CVS&RS: WNL

Lymph node: Not palpable

Abdomen: No hepatosplenomegaly

Skin examination:

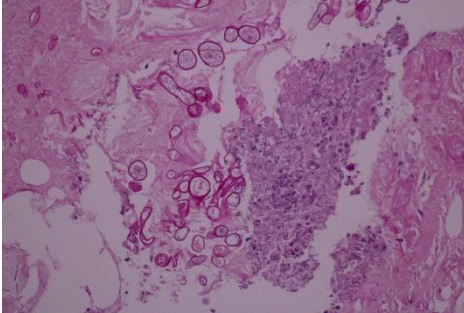
Solitary erythematous to brownish indurated plaque with central ulcer, sized 1x2 cm in diameter

Histopathology: (S15-000919, Left popliteal fossa)

-Nodular and diffuse inflammatory cell infiltrate of lymphocytes, histiocytes, admixed with some multinucleated giant cells, neutrophils, eosinophils in the deep dermis and subcutaneous tissue

-Extensive fat necrosis, some with basophilic amorphous material giving the feature of saponification in subcutaneous tissue

-Large thin wall broad hyphae with multinucleated histiocyte and necrotic foci



Special stains: GMS and PAS highlight thin wall broad hyphae within subcutaneous tissue

Investigations:

CBC: WBC 8,170/uL (PMN 61%, L29%, Mo 5%, Eo 5%),
Hb 11.6g/dL, Hct 37.1%, Platelet 475,000/uL

LFT/Cr: WNL

MRI Left knee: Infiltrative lesion on the posterior aspect of Lt knee involving skin, subcutaneous tissue, deep fascia and soft tissue deep to the fascia. No muscle or bone involvement

Tissue culture for fungus: Basidiobolus spp.

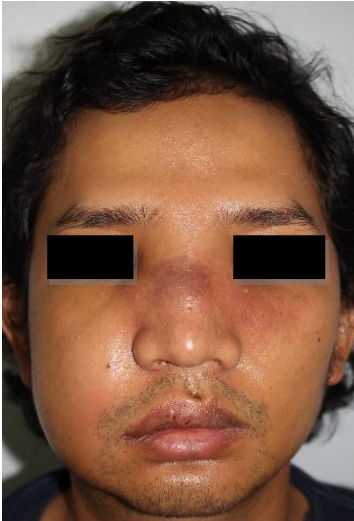
Diagnosis: Basidiobolomycosis

Treatment: Itraconazole solution 200 mg oral twice daily for 3 months

Case 4.2

A 32-year-old Thai man from Bangkok

Chief complaint: A painless enlargement of the nasal dorsum for 6 months



Present illness: The patient had developed a painless enlargement of the nasal dorsum for 6 months. His symptoms began as nasal congestion and progressive nasal blockage and were followed by gradual, painless enlargement of his nose. There was no history of trauma or injecting any substance into his nose. The initial evaluation by private hospital led to a diagnosis of nasal polyposis and he had undergone a polypectomy. After surgery, the symptom of nasal blockage had minimal improvement; however, his nose was still in the same size. He was referred to ear, nose and throat (ENT) specialist for examining a biopsy of his nose. The histopathology was interpreted as granulation tissue with chronic inflammation and an increase in fibrosis.

Gomori methenamine silver (GMS) stain failed to demonstrate organism. Then, he was referred to dermatologist for further management.

Past history: Healthy

Physical examination:

VS: BT 37.2°C, RR 20/min, PR 74/min, BP 110/70 mmHg

GA: Good consciousness, sthenic built

HEENT: Not pale, no jaundice, right nasal mucosa swelling

Lymph node: No palpable cervical node

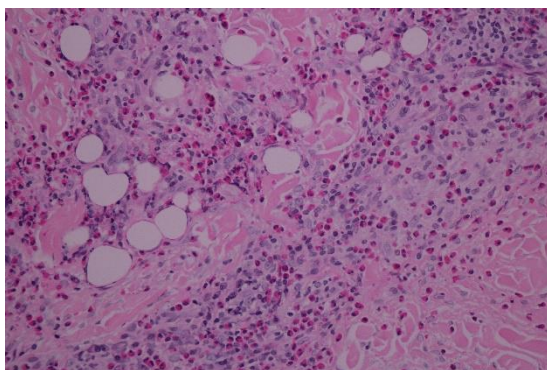
Abdomen: No hepatosplenomegaly

Skin examination:

Ill-defined erythematous to brownish subcutaneous plaque on nasal dorsum and both cheeks

Histopathology: (S15-024450, Right nasal dorsum)

Nodular and diffuse inflammatory cell infiltrate of lymphocytes, histiocytes, admixed with some multinucleated giant cells, neutrophils and numerous eosinophils in the deep dermis and subcutaneous tissue



Special stains: GMS and PAS fail to demonstrate organism

Investigations:

CBC: WBC 13,140/uL (PMN 76%, L 16%, Mo 5%, Eo 3%), Hb 14.6g/dL, Hct 43.7%, Platelet 245,000/uL

LFT/Cr: WNL, FBS: 93mg/dL, Anti-HIV: Negative

CT paranasal sinus: Diffuse non-enhancing infiltrative cutaneous and subcutaneous soft tissue swelling from mid forehead, nose, infraorbital region, philtrum and upper lip

Tissue culture for fungus: Conidiobolus spp.

Diagnosis: Conidiobolomycosis

Treatment: Intravenous amphotericin B 1 MKD for 4 days then itraconazole 200 mg oral twice daily plus terbinafine 250 mg oral once daily

Presenter: Saneerat Porntharukcharoen, MD

Consultant: Suthinee Rutnin, MD

Discussion:

Entomophthoramyces

(entomophthoromycosis) is a chronic subcutaneous infection caused by fungi from the order Entomophthorales. The two important genus in this group include Basidiobolus and Conidiobolus which are environmental saprophytes found worldwide and have been isolated from soil, vegetation while some also reside in the gut of frogs and reptiles^{1,2}. The prevalence of disease is high in tropical and subtropical regions,

particularly in equatorial Africa, Central America and India³. The infections are assumed to occur as a result of some form of minor traumatic implantation such as insect bite. While inhalation of spores may also play a role in disease transmission with *Conidiobolus*¹.

Unlike Mucormycosis, Entomophthoromycosis is localized disease, demonstrating no angioinvasion¹. The disease presents in two clinical distinct forms; Basidiobolomycosis caused by *Basidiobolus ranarum* and Conidiobolomycosis caused by *Conidiobolus coronatus* and *Conidiobolus incongruus*. These infections predominantly occur in immunocompetent host with male predominance⁴.

Basidiobolomycosis is mainly diagnosed in children (about 90% under the age of 20 year) and locates most commonly on the thigh and buttock^{4,5,6}. The presentation is a painless subcutaneous swelling with hard to woody induration of the soft tissue. Ulceration and sinus formation of underlying structures such as muscles, bones and joints are usually spared. Extracutaneous manifestations are reported in gastrointestinal, retroperitoneal and pulmonary systems^{7,8}.

In comparison, Conidiobolomycosis occurs predominantly in adult and often confines to the rhinofacial area¹. The infection begins in nasal mucosa and submucosa with the potential to spread to adjacent tissues, such as the paranasal sinus, nasal dorsum, upper lip and cheeks. As the infection spreads, subcutaneous nodules which usually firm and painless can be palpated through the skin and may progress to severe facial deformity. Patients may experience nasal stuffiness, draining and sinus pain⁹. Although

disseminated infection is rare, systemic conidiobolomycosis has been described in respiratory system and surrounding structures in the neck and mediastinum¹⁰.

The diagnosis of entomophthoromycosis requires a high index of suspicion by the clinician. However, histopathology and mycological cultures remain the gold standard for definite diagnosis^{1,4}. The typical histopathology is the presence of thin-walled, broad, often aseptate hyphae with granulomatous inflammation and large numbers of eosinophils. There is often found refractile eosinophilic material (Splendore-Hoeppli phenomenon), surrounding the fungal hyphae^{1,4,11}. On fungal culture, *Basidiobolus* colonies were identified by their waxy and yellowish-gray appearance with many radial folds. Thick-walled zygospores with beak-like appendages are the characteristic microscopic feature of *Basidiobolus ranarum*^{1,11}. While *Conidiobolus* colonies are white, becoming beige to brown, with a pale reverse. They are also waxy to powdery with folding and furrowing. On microscopic examination, there are round to pyriform conidiospore with prominent papillae. Some conidiospores are circled by many hair-like appendages called villae^{1,4,11}. In case of negative cultures, molecular identification and serologic testing may help to confirm diagnosis⁴. Clinical characteristic and comparison between *Basidiobolomycosis* and *Conidiobolomycosis* are summarized in table1

The treatment has not been well-defined because the disease is infrequently reported. Potassium iodide¹², cotrimoxazole¹³, amphotericin B¹⁴, itraconazole¹⁵, fluconazole¹, terbinafine¹⁶ and surgical debridement¹ have been used in various

combination^{1,13,16,17,18}. In vitro susceptibility testing may be helpful in guiding therapy^{1,4}.

Table1 Clinical characteristics and comparison between Basidiobolomycosis and Conidiobolomycosis

	Basidiobolomycosis	Conidiobolomycosis
Organisms	Basidiobolus ranarum	Conidiobolus cornatus Conidiobolus incongruus
Immune status	Immunocompetent	
Age	Children	Adult
Sex	Male > Female	
Location	Thigh, buttock, trunk	Face, nose
Clinical presentation	Painless subcutaneous swelling with hard to woody induration of the soft tissue	Nasal obstruction followed by progressive swelling mass over the nasal area, both cheeks and frontal region
Histopathology	Thin-walled, broad, often aseptate hyphae with mixed cell infiltration and numerous eosinophils Splendore-Hoeppli phenomenon	
Fungal colonies	Yellowish-grey, waxy, radially folded colonies with covered by a fine, powdery, white surface	White, beige or brown, waxy to powdery colonies with folding and furrowing
Microscopic examination	Conidiophore with either narrow or inflated apices Thick-walled zygospores with beak-like appendages	Round conidiospores with prominent papillae Some conidiospores may produce hair-like appendages called villae

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