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

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Consultant: Suthinee Rutnin, MD

Discussion: Entomophthoramycosis
(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. The prevalence of disease is high in tropical and subtropical regions,
particularly in equatorial Africa, Central America and India\textsuperscript{3}. 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\textsuperscript{1}.

Unlike Mucormycosis, Entomophthoramycosis is localized disease, demonstrating no angioinvasion\textsuperscript{1}. 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 predominance\textsuperscript{4}.

Basidiobolomycosis is mainly diagnosed in children (about 90\% under the age of 20 year) and locates most commonly on the thigh and buttock\textsuperscript{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\textsuperscript{7,8}.

In comparison, Conidiobolomycosis occurs predominantly in adult and often confines to the rhinofacial area\textsuperscript{1}. 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 pain\textsuperscript{9}. Although
disseminated infection is rare, systemic conidiobolomycosis has been described in respiratory system and surrounding structures in the neck and mediastinum\textsuperscript{10}.

The diagnosis of entomophthoramycosis requires a high index of suspicion by the clinician. However, histopathology and mycological cultures remain the gold standard for definite diagnosis\textsuperscript{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-Hoepli phenomenon), surrounding the fungal hyphae\textsuperscript{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\textsuperscript{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\textsuperscript{1,4,11}. In case of negative cultures, molecular identification and serologic testing may help to confirm diagnosis\textsuperscript{4}. 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 iodide\textsuperscript{12}, cotrimoxazole\textsuperscript{13}, amphotericin B\textsuperscript{14}, itraconazole\textsuperscript{15}, fluconazole\textsuperscript{1}, terbinafine\textsuperscript{16} and surgical debridement\textsuperscript{1} have been used in various
combination\textsuperscript{1,13,16,17,18}. In vitro susceptibility testing may be helpful in guiding therapy\textsuperscript{1,4}.

**Table 1 Clinical characteristics and comparison between Basidiobolomycosis and Conidiobolomycosis**

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