Subcutaneous Basidiobolomycosis: A Report of Young Thai Lady

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ABSTRACT:

Subcutaneous basidiobolomycosis is a rare chronic granulomatous infection caused by *Basidiobolus ranarum*. We present the case of a 22-year-old Thai woman who, without a history of trauma, presented with painless masses extending from the left flank to the left thigh over the course of one year. Notably, the condition failed to respond to a six-month course of anti-tuberculosis medication. Subsequent investigations, including skin biopsy, tissue culture, and polymerase chain reaction, conclusively confirmed the diagnosis of subcutaneous basidiobolomycosis. Remarkably, neither clinical assessments nor imaging revealed involvement of other organs except for left posterior gluteus maximus and left lateral tensor fascia latae muscle. The patient achieved complete resolution following a two-month administration of itraconazole at a dosage of 400mg per day.

Key words: Basidiobolomycosis, Subcutaneous Basidiobolomycosis, Painless Mass, Painless Subcutaneous Mass

Introduction

Subcutaneous basidiobolomycosis is a rare chronic granulomatous infection caused by *Basidiobolus ranarum*. Management approaches often derive from case reports and expert opinions, given the absence of established guidelines to date. Here, we report a Thai woman presenting with subcutaneous basidiobolomycosis, which was successfully treated with oral itraconazole.

Case Report

A 22-year-old previously healthy Thai female presented with painless masses extending from the left flank to the left thigh over a period of 1 year. She denied any history of trauma. She had been treated with anti-tuberculosis drugs for six months based on granulomatous inflammation observed on histopathology but failed to respond prior to referral. Examination revealed multiple painless, hard subcutaneous swellings with smooth, round edges and overlying hyperpigmentation. These were observed on the left flank, measuring 12x8 cm, on the left groin, measuring 5x2 cm, and on the left thigh, measuring 10x6 cm. (Figure 1). Routine laboratory investigations showed no abnormality and anti-HIV also showed negative results.

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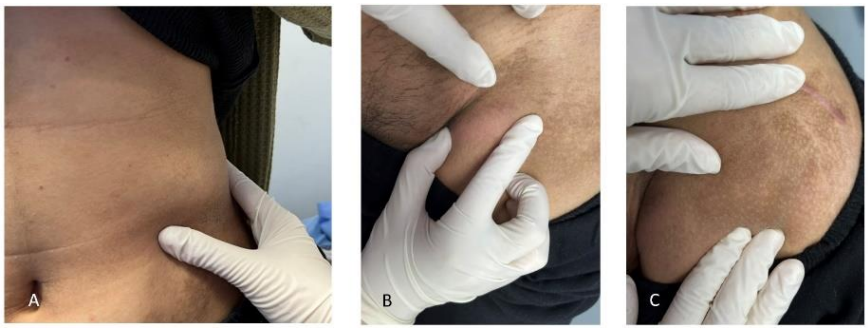

Figure 1 Painless, hard subcutaneous swellings with smooth, round edges and overlying hyperpigmentation were observed on (A) the left flank (12x8 cm), (B) the left groin (5x2 cm), and (C) the left thigh (10x6 cm).

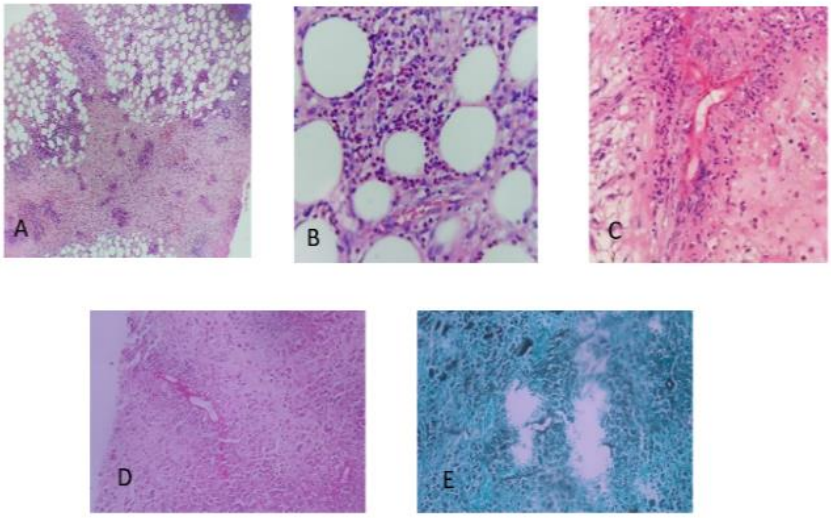

Figure 2 Histopathology showed (A, B) septal and lobular panniculitis with eosinophil predominance (40X and 400X, H&E). (C) Broad, thin-walled, ribbon-like, aseptate hyphae with wide-angle branching and Splendore-Hoeppli phenomenon (400X, H&E). (D) PAS stain (400 X), (E) GMS stain (400X).

Biopsy revealed septal and lobular panniculitis with eosinophil predominance, along with broad, thin-walled, ribbon-like, aseptate hyphae exhibiting wide-angle branching and featuring the Splendore-Hoeppli phenomenon. (Figure 2). The MRI revealed high signal intensity on T1 and T2 in the subcutaneous tissue around the left hip, lower back, and left buttock, involving the left posterior gluteus maximus and the left lateral tensor fascia latae muscle. (Figure 3). Tissue culture and polymerase chain reaction (PCR) test showed *Basidiobolus ranarum* (Figure 4). The patient was prescribed a daily dosage of 400 mg of itraconazole for a 12-month treatment duration, as recommended by the Infectious Disease team. Complete resolution was achieved after 2 months of treatment. At the time of writing, the patient had been undergoing treatment for 10 months with no signs of recurrence.

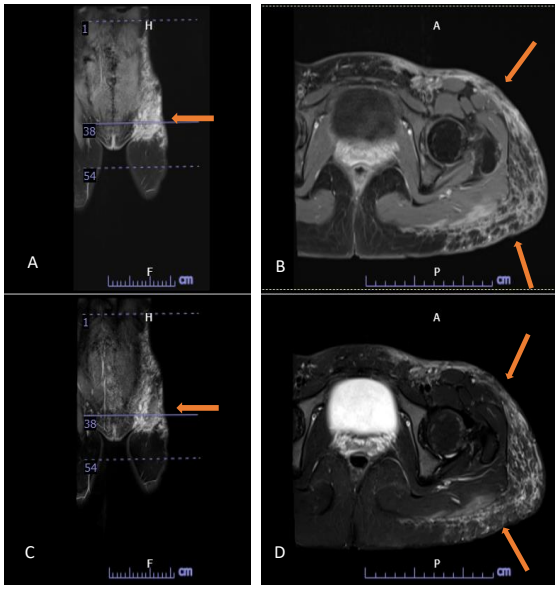

Figure 3 The MRI revealed high signal intensity enhancement and diffusion restriction along the fascia of the subcutaneous tissue around the left hip, lower back, and left buttock, involving the posterior aspect of the left gluteus maximus and the left lateral tensor fascia latae muscle.
(A, B) high signal intensity on T1
(C, D) high signal intensity on T2

Discussion

Subcutaneous basidiobolomycosis, formerly referred to as subcutaneous phycomycosis or subcutaneous zygomycosis, is a chronic granulomatous infection caused by *Basiodiobolus ranarum*. This filamentous fungus is commonly found in various habitats including amphibians, reptiles, horses, dogs, bats, woodlice, soil, and plant debris[1,2]. Basidiobolomycosis usually occurs in immunocompetent children and young adults who live in tropical and subtropical areas via traumatic implantation[1-4]. The clinical manifestation of subcutaneous basidiobolomycosis typically begins as a subcutaneous nodule, which then slowly progresses to a painless disc-shaped, hard-woody, large mobile mass. This mass can be raised by inserting the fingers underneath, and it usually presents with a normal or hyperpigmented surface, commonly observed on the trunk, buttocks, and thighs[2,4,5]. Histological findings typically comprise thin walled, broad, often aseptate hyphae or hyphal fragments with an eosinophilic sheath (Splendore-Hoeppli phenomenon). However, the gold standard for diagnosis is fungal culture, which is grown on standard mycology medium (e.g., Sabouraud dextrose agar, potato dextrose agar, or cornmeal agar). The fungus typically exhibits moderate growth at 30°C, while growth is slower at 37°C[1,3,4,6]. The colony of *Basidiobolus ranarum* showed characteristic of creamy white, dense, radially furrowed, and waxy with a heaped-up center and the microscopic examination with Lactophenol cotton blue mount revealed non-septate hyphae and thick-walled zygospores with beak-like structure[1-8]. The disease is slowly progressive, rarely disseminated, rarely life-threatening, and is usually initially misdiagnosed as a chronic abscess, tuberculosis (as in our case), or soft tissue malignancy[1,7]. Imaging by computed tomography or magnetic resonance allows for a more definitive assessment of the extent of infection and enables healthcare providers to monitor therapeutic response[1].

In Thailand, at least 19 cases of subcutaneous basidiobolomycosis have been reported since 1965, as shown in Table 1.

Table 1 Summary of published subcutaneous basidiobolomycosis case reports from Thailand

Author., year	Age/Sex	Infection site	Duration before treatment	Treatment	Outcome
Chantarakul N, et al., 1965[a 12]	17mo./M	Right scapula	5 months	Total excision	Completely resolved
Thasnakorn P., et al., 1969[13]	61 yr./M	Right calf	1 month	Total excision	N/A
Riganti M., 1987[a 14]	21yr./ M	Right thigh	1 year	Co - trimoxazole (no dose mentioned) 4 tablets per day for 30 days	Completely resolved
Singalavanija S., 1987[a 15]	12yr./ M	Right buttock Right groin	2 months	Co-trimoxazole 7-10 mg/kg/day for 2 months and then with saturated potassium iodide (KI) 30 mg/kg/day for 6 months	-Partially improvement to co-trimoxazole -Completely resolved after KI
Prakitrittranon W.,1992[16]	54 yr./ F	face, neck, trunk and both upper extremities	3 years	Co-trimoxazole 2tabs/d for 1 months Then Saturated Potassium Iodide 30mg/kg/d for 3months Then Co-trimoxazole 2tabs/d for 2years then ketoconazole 400mg/d for 2months	Completely resolved
Viravan S., 1997[17]	3 yr./ M	Right scapula, trunk, neck, upper extremities, left thigh	26 months	Co-trimoxazole 8mg/kg/day	-Improvement seen at 2weeks, - Completely resolved in 19 weeks
Mahaisavariya P., 1999[18]	38yr./ F	Arm	NA	Co-trimoxazole	Completely resolved
	15yr./ F	Abdomen, thigh	NA	Co-trimoxazole	Much improved
Chiewchanvit S, et al., 2002[19]	25yr./ F	Leg	N/A	Potassium iodide at 20-25 mg/kg/d	success
	15yr./ F	N/A	N/A	Potassium iodide at 20-25 mg/kg/d	success
	7yr./ F	Trunk, chin, extremities	5 years	Potassium iodide at 20-25 mg/kg/d	success
	77yr./ F	Right elbow	3 months	Potassium iodide at 20-25 mg/kg/d	success
	56yr./ F	Left axilla	1 year	Co-trimoxazole	success
Choonhakarn C, Inthraburan K., 2004[20]	55 yr./ F	Right thigh, Right leg Abdominal wall, Retrovesical region extending to the urinary bladder wall.	5 months	Co-trimoxazole (480/2400 mg) /day then potassium iodide (KI) (30 mg/kg/day) added at fouth week. Received medication for 3 months in total.	Subcutaneous improvement after 3 months of medical therapy improvement of the infiltrative lesions within the pelvic organs seen after 2 months of treatment

Table 1 Summary of published subcutaneous basidiobolomycosis case reports from Thailand

Author., year	Age/Sex	Infection site	Duration before treatment	Treatment	Outcome
Kraimak S, Jabjumratsang P., 2012[21]	14yr./ F	Right Thigh	6 months	potassium iodide 20 mg/kg/day	Improvement seen after 4 weeks of treatment
Mahamaytakit N., et al., 2014[4]	10mo./ F	Upper lip	6 weeks	Amphotericin B titrate up to 1mg/kg/day for 2weeks along with itraconazole 5mg/kg/day for 5months	Improvement seen 2 weeks after the treatment.
	2yr./ F	Left buttock	7 months	Itraconazole 5mg/kg/day for 3 mo.	Improvement seen 2 weeks after the treatment.
Rermluk N., et al., 2017[10]	27yr./ M	Left breast	4 months	itraconazole solution (200 mg twice a day) for 4 weeks	Improvement seen 2 weeks after the treatment.
Our case	22 yr./ F	Left thigh, left buttock, trunk	1 year	Itraconazole 400mg/day	Complete resolution was achieved after 2 months of treatment.

[a]: No fungal identification via culture or PCR N/A: Not available M=Male, F=Female

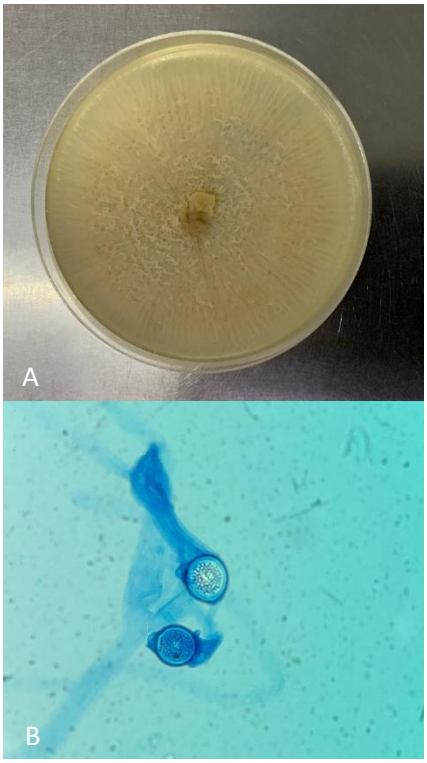

Figure 4 (A) Colony of *Basidiobolus ranarum* showed characteristic of creamy white, dense, radially furrowed, and waxy with a heaped-up center. (B) The microscopic morphology of *Basidiobolus ranarum* showed non-septate hyphae and thick-wall zygospores with beak-like structure.

Differential diagnoses of subcutaneous basidiobolomycosis are broad which included soft tissue tumor and other infections such as *Mycobacterium* spp., or mucomycosis. In contrast to basidiobolomycosis, mucormycosis, formerly classified as zygomycosis alongside basidiobolomycosis, manifests aggressive behavior, leading to rapid progression characterized by angioinvasion and necrosis. It commonly affects the face and extremities of immunocompromised hosts. The histopathology of mucormycosis revealed non-septate or sparsely septate hyphae with evidence of angioinvasion and the presence of necrotic areas. Differentiation is important because mucormycosis is highly aggressive, requiring urgent and aggressive management[9].

Currently, there is no gold standard for treatment of subcutaneous basidiobolomycosis, many successful treatments were reported in literature such as itraconazole and potassium iodide. Itraconazole, a member of the azole group, demonstrates a low minimum inhibitory concentration (MIC) against *Basidiobolus* spp and has shown efficacy in numerous

reports[3,4,8,10]. The dose and duration of itraconazole are varied, some recommended 100-400 mg/day for at least 6-12 months of treatment[2,6,8,10]. Complete resolution can be seen as early as 1 month after itraconazole initiation[6,7].

To achieve a favorable outcome, the bioavailability of itraconazole is one aspect that should be considered. According to a review by Karel De Beule and Jef Van Gestel, itraconazole oral solution has higher bioavailability than capsules, by up to 37%, but may cause gastrointestinal side effects due to its ingredients. When prescribing the oral solution, it should be taken on an empty stomach. As for capsules, they should be taken after a meal, and to enhance capsule bioavailability, coadministration with an acidic beverage is recommended[11].

Although subcutaneous basidiobolomycosis is an uncommon disease, maintaining a high index of suspicion is crucial for achieving an accurate diagnosis. The clinical presentation might not be specific and typically includes painless, slow-growing subcutaneous masses on the extremities, which should raise suspicion. Diagnosis requires tissue biopsy and fungal identification (via culture or PCR).

Here we present a case of subcutaneous basidiobolomycosis, which was previously misdiagnosed and treated as tuberculosis. Her imaging revealed the lesion extended to the muscle layer. The 12-month course of itraconazole 400mg per day was chosen based on the extension of the disease. The infection was clinically completely resolved within 2 months of treatment.

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