Case Report: Subcutaneous Basidiobolomycosis in Pregnancy

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ABSTRACT:
Subcutaneous basidiobolomycosis is an unusual fungal infection caused by *Basidiobolus ranarum.* The infection is typically painless, firm, and slowly enlargement nodules on extremities, buttock, and trunk. Diagnosis is based on clinical features, histopathology, and fungal culture. The disease is more common in children and males are more affected than females. However, there is limited information available on whether subcutaneous basidiobolomycosis occurs in pregnancy. We report a case of basidiobolomycosis in 32-year-old, 3rd trimester pregnant female from Myanmar. Diagnosed is based on clinical features and histopathology. After delivery, she received intravenous amphotericin B for one month followed by oral itraconazole. Her left leg decreased in size and returned to normal after 5 months.
Key words: Basidiobolomycosis, Pregnancy, Entomophthoromycosis

Introduction

Entomophthoromycosis is a rare fungal infection caused by members of the order Entomophthorales. Entomophthorales comprised of *Basidiobolus* and *Conidiobolus* genera which have two clinically distinct forms in subcutaneous entomophthoromycosis and rhinofacial entomophthoromycosis respectively[1-3].

Subcutaneous basidiobolomycosis is caused by *Basidiobolus* spp., which commonly found in soil, insects, decaying organic matter and in the faces of amphibians and reptiles. *Basidiobolus ranarum* was first isolated in 1886 from frogs by Eidam and more prevalent in tropical and subtropical regions particularly India, Pakistan, Uganda, Kenya, Ivory Coast, Myanmar, Ghana and South America[2].

Here we report a case of subcutaneous basidiobolomycosis in a 32-year-old Myanmar female with 25 weeks of gestation presented with unilateral indurated plaque on left leg and flank who diagnosed basidiobolomycosis based on clinical feature and histopathology. To the best of our knowledge, this is the first case of basidiobolomycosis in pregnancy in Thailand.

Case report

The 32-year-old female from Myanmar presented with a 5-years history of progressive swelling of her left leg and buttock. She said it first presented with erythematous nodule on her left leg and without any treatment the lesion was progressive enlargement. On her arrival, she was pregnant with 25-week of gestation. She never had any underlying disease or history of drug and food allergy. She denied smoking, alcohol drinking or herbal drug use. There is no family member experienced the same condition as the patient and no history of malignancy in family. She used to work as farmer at Myanmar. The fetus was healthy with regularly antenatal care by obstetrician. On physical examination, vital signs are stable without fever or

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hypertension. She has unilateral, painless, ill-defined purplish indurated plaque on her left upper leg, buttock, flank, and labia majora. Her whole left leg was marked swelling without pitting edema. (Figure 1A-B) There is no lymphadenopathy and no other gastrointestinal symptom. The incisional biopsy was performed on her left flank.

Figure 1A Unilateral ill-defined purplish indurated plaque with marked left leg swelling
Figure 1B Ill-defined purplish indurated plaque extend on her left buttock and left flank

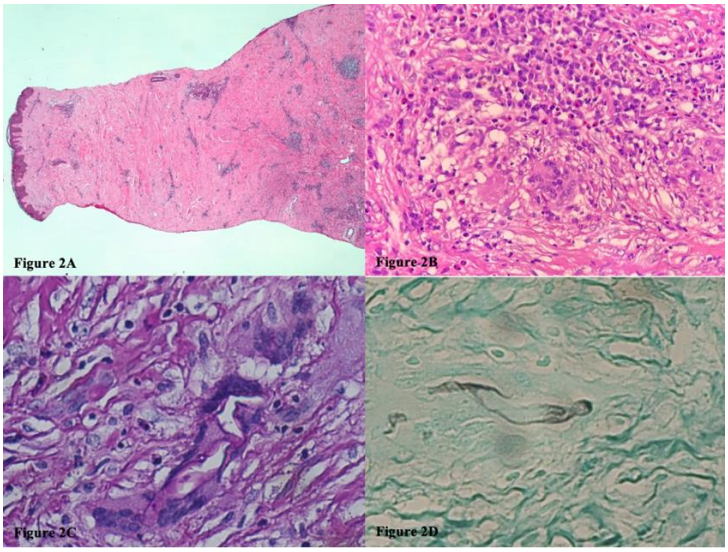

Figure 2A Nodular and diffuse inflammatory cell infiltration at dermis. (H&E, X25)
Figure 2B Focal granuloma with lymphocytes, neutrophils, eosinophils, and multinucleated giant cell. (H&E, X200)
Figure 2C Aseptate broad thin-wall hyphae surround by inflammatory cell on Periodic acid-Schiff (PAS) stain (PAS, X600)
Figure 2D Aseptate broad thin-wall hyphae on Gomori methenamine silver (GMS) stain (GMS, X600)

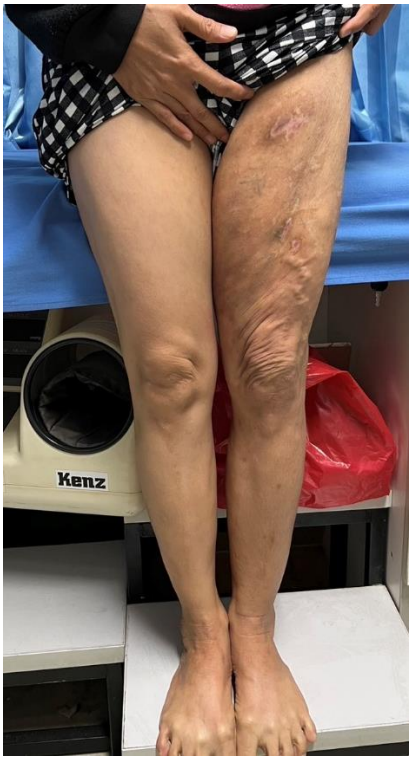

Figure 3 After 5 months of treatment, her left leg is return to normal size

Tissue biopsy showed nodular and diffuse inflammatory cell infiltration with lymphocytes, neutrophils, eosinophils, histiocytes and multinucleated giant cells, some of those engulfing broad thin-wall collapse hyphae in association with diffuse fibrosis in the deep dermis. (Figure 2A-B) Periodic acid-Schiff and Gomori methenamine silver stain are highlight the thin wall fungal. (Figure 2C-D) The result of the following laboratory test such as complete blood count, renal and liver function test are within normal limit. Anti-HIV was negative, and microfilaria was not found. Tissue culture for bacterial, tuberculosis and fungus are negative all. Serum D-dimer was 0.62 mg/dL. Doppler ultrasound was done without any evidence of deep vein thrombosis. The overall studies suggest basidiobolomycosis. After discussion with dermatologist, infectious disease specialist and obstetrician, we design to start treatment after her delivery.

She underwent cesarean section at 37^{+3} weeks of gestation due to placenta previa low lying and pre-eclampsia without severe feature. A midline incision was made for the cesarean section, and there were no obstructions during the procedure. Her female baby was well-being with normal birthweight and APGAR 9,9,10. CT whole abdomen include chest with both legs with contrast was done with the result of enlarged all muscle of the left thigh and leg possible effect of lymphatic or venous occlusion, there is soft tissue density at skin and subcutaneous tissue of the left anterior, lateral, and posterior abdominal wall, which extend to left gluteal region and entire left leg. Few enlarged paraaortic lymph nodes up to 0.7 cm. that could be reactive lymph node at peritoneum and retroperitoneum. Chest, liver, biliary system, pancreas, adrenal gland, and kidney are unremarkable, and no obvious evidence of deep vein thrombosis or arterial occlusion. She was started treatment with intravenous amphotericin B 1 mg/kg/day for 1 month because of extensive lesion then switched to oral itraconazole 400 mg/day. After treatment, her left leg has been decreasing in sized and result normal at 5 months. (Figure 3) Infectious disease specialist plan to continued treatment at least 1 year and confirm reimaging study with MRI before stop medication.

Discussion

Subcutaneous basidiobolomycosis is a rare fungal infection caused by *Basidiobolus ranarum*[1]. Initially the phylum Zygomycota include order Mucorales and Entomophthorales. Mucorales include the genera of *Rhizopus*, *Mucor* and *Lichtheimia*, the Entomopthorales comprise of Basidiobolus and Conidiobolus genera. Not only the confusing of term zygomycosis that has been incorrectly used interchangeably with mucormycosis but

also difference of key phylogenetic between Mucorales and Entomophthorales, a reclassification was introduced. A new subphylum, Entomophthoromycota has been created comprises three classes: Basidiobolomycetes (*Basidiobolus* spp.), Neozygitomycetes (*Neozygitis* spp.), and Entomophthoramycetes (*Conidiobolus* spp., and others)[1, 2, 4].

Basidiobolus ranarum was first described by Eidam in 1886 from frog excrement[5]. The first four human cases were reported in 1956 from Indonesia[6]. It is a saprotrophic fungus commonly found in soil, decaying organic matter, the intestinal tract, and excreta of amphibians and reptiles. The infection is endemic in tropical and subtropical region and more frequently in children. Males are more common than females with the ratio of 8:1 from all cases of the world.[4] The mode of infection is exactly not known but it is assumed that transmission may occur via minor trauma such as insect bites, thorn prick, use of 'toilet leaves' to clean after defecation or inhalation of spore[5,7].

Basidiobolus ranarum mainly affects subcutaneous tissue and intestinal tract in immunocompetent host[4]. Typical subcutaneous infection manifest as slow progressive painless firm indurated subcutaneous nodule on lower extremities and buttock, which if untreated may enlarges peripherally. The affected limb may become swollen two or three-fold and with no pitting on pressure. The overlying skin may be normal, purplish or hyperpigmentation and rarely found ulceration. General conditions were considered good without fever and lymph nodes were usually not involved[4, 5, 7].

Histopathologically, Entomophthoromycota is differentiated from other fungi by their characteristic hyphal morphology which are broad, thin wall, ribbon-like, and mostly aseptate with right or wide-angle branching. The inflammatory reaction consists of granulomatous reaction composed of lymphocytes, plasma cells, epithelioid, multinucleated giant cell, and eosinophils. The Splendore-Hoeppli phenomenon characterized as an eosinophilic hyaline material around hyphae in hematoxylin eosin-stain can be finding. But this finding is not pathognomonic of entomophthoromycosis as this can also seen in other infection such as sporotrichosis, blastomycosis, and schistosomiasis[3].

Diagnosis of basidiobolus infection is typically histopathological feature and mycological culture. The valuable specimen is tissue biopsy and not pus as this has better chance of showing fungal element. Cultures can be negative on many occasions as hyphae in specimens may be damaged during tissue processing. In culture-negative cases, molecular identification can be considered to confirm the diagnosis using freshly frozen or paraffin-embedded tissue. Imaging with CT or MRI should be performed for further evaluation the extent of infection, therapeutic response, and help surgeons plan invasive procedures[3, 4, 8].

Treatment consists of medical management with prolong antifungal therapy, surgery and considered hyperbaric oxygen. Effective treatment includes potassium iodide (KI), imidazole, amphotericin B and co-trimoxazole. A suggested dose of KI 30 mg/kg/day has been used. Itraconazole 100-200 mg daily has been tried with complete resolution. Due to relative resistance to antifungals, prolonged treatment approximately 6-12 months and combination of treatment is recommended[3, 4, 7, 8].

Based on current research, there have been no reported cases of basidiobolomycosis during pregnancy. However, previous knowledge suggests that this condition is typically confined to the skin and intestinal tract and dose not systemically involved.[2,3] In this case, she does not show any signs of gastrointestinal involvement and her pregnancy is progressing well. Amphotericin B is classified as a pregnancy category B drug[9] and there is no indication for preterm delivery. We believe that

waiting until delivery before starting antifungal treatment would be the safest course of action, to avoid any potential risk.

In conclusion, subcutaneous basidiobolomycosis is a rare fungal infection that commonly affected lower extremities, buttock, and trunk. The disease is more prevalence in children and male are more effect than female. However, there is limited incidence and management information about subcutaneous basidiobolomycosis in pregnancy. This case report highlights the suspicion required to diagnose the condition in pregnancy, management, maternofetal outcome, and successful treatment with intravenous amphotericin B followed by oral itraconazole.

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