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Subcutaneous entomophthoromycosis mimicking soft-tissue sarcoma in children ☆

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ABSTRACT

Aim: Subcutaneous entomophthoromycosis (EM) is an uncommon fungal infection of childhood. This article is intended to draw the attention of pediatric surgeons to the fact that EM can mimic soft-tissue tumor.
Methods: It is a retrospective review of 16 children treated for subcutaneous EM between 2000 and 2013.
Results: The median age of patients was 3.5 years. The typical lesion was a discoid subcutaneous mass that can be easily lifted from deeper tissues (the doughnut lifting sign). Lesions were mostly distributed in the lower half of body. All the patients were immunocompetent. Correct clinical diagnosis was made only in 4 cases while others were mistaken for a tumor. All the 8 children who underwent wide excision of the pseudotumor had local recurrence. Supersaturated solution of potassium iodide was curative in 11 cases while addition of itraconazole was needed in one case. One child died of muti-drug resistant infection. The mean treatment duration was 4.7 months months (range 2–8 months).
Conclusion: Subcutaneous EM can mimic soft-tissue tumor. High index of suspicion is essential to avoid misdiagnosis and inappropriate treatment. A newly described "doughnut-lifting sign' may be helpful in clinical diagnosis. Emergence of multi-drug resistant infection is a source of concern.

Entomophthoromycosis (EM) is an uncommon fungal infection caused by entomophthoromycota [1,2]. The phylum is named so because the fungi are often used as bio-insecticides (entomo = insect; phthoro = destroyer). *Basidiobolus ranarum* and *Conidiobolus coronatus* are the two common opportunistic pathogens of this group. Both of them are saprophytes commonly found in soil and decaying organic wastes. Accidental inoculation by inconspicuous injuries such as thorn pricks, scratches, insect bites and contaminated injection-needles may cause human infections [3]. It was first described from Indonesia in 1956 by Lie Kian Joe who reported 2 children with *Basidiobolus* infection [4]. Subsequently, Burkitt published a large series of 31 cases from Uganda [2]. EM is common in tropical areas such as sub-Saharan Africa [2], South East Asia [5], and Brazil [6]. However, probably due to international travels, it is increasingly been reported from non-endemic areas such as USA [7], Australia [8], Germany [9], Arabian peninsula [10], Portugal [11] and Netherlands [12].

EM is predominantly a disease of pediatric age group [2,5]. In Burkitt's series 63% of patients were under the age of 9 and 30% were adolescents while only 7% were adults [2]. The infection is mostly confined to subcutaneous tissue, although, disseminated forms [12–14] and visceral involvement [10,15] are rarely reported. Even in endemic areas, subcutaneous EM is frequently mistaken for soft tissue sarcoma or lymphoma [6,16,17]. Consequently, inappropriate investigations and delay in treatment are not uncommon. In this paper we narrate our clinical experience with 16 cases of subcutaneous EM and intend to draw the attention of pediatric surgeons to the deceptive clinical presentation of this uncommon but emerging entity.

1. Methods and materials

Between 2000 and 2013 the principal author (VR) was involved in the management of 17 children suffering from EM at 4 different institutions namely Rajah Muthiah Medical College (Chidambaram), Dhanvantri Medical Center (Chidambaram), Sri Ramasamy Memorial Medical College (Chennai) and Hindu Mission Hospital (Chennai). Clinical details of the patients were retrospectively reviewed. One case was excluded as the case record could not be retrieved. One case, that has already been reported elsewhere [18], is included in the study.

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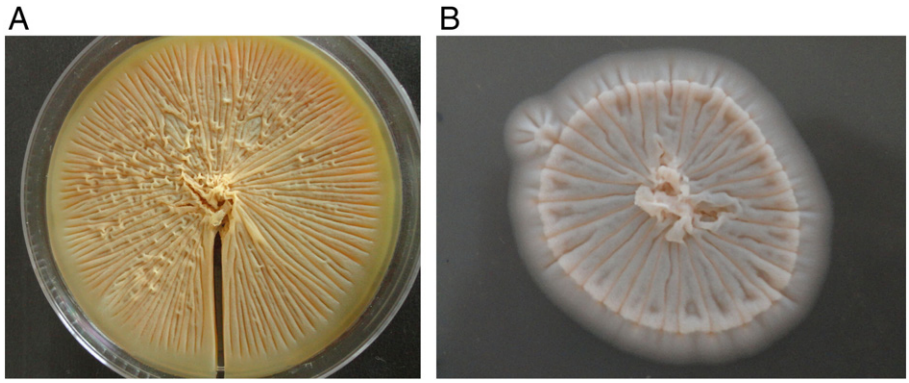

Fig. 1. Difference in the colony morphology of *Basidiobolus* (A) and *Conidiobolus* (B). Flat, furrowed, waxy, yellow colonies are typical of *Basidiobolus*. In contrast, *Conidiobolus* colonies are white, buff and powdery with short aerial mycelium.

Diagnosis of EM was accepted if the fungus is demonstrated in either histology or culture. In addition to the routine Hematoxylin-eosin (HAE) stained histological preparation, special fungal stains such as periodic acid-Schiff (PAS), Gomori's methenamine silver (GMS) were used selectively. Presence of Splendore-Hoeppli phenomenon (encasement of fungal hyphae by eosinophilic debris and eosinophilic leukocytes), presence of characteristic (broad, aseptate, empty-looking, twisted-ribbon like) fungal hyphae and absence of vascular invasion were considered diagnostic of EM [19]. Minced tissue specimens were cultured in Sabouraud's dextrose agar medium. Fungal culture became routine only after 2008 before which it was done sparingly when histological diagnosis was difficult. Lactophenol cotton blue mount was used to study the fungal morphology. *Basidiobolus* and *Conidiobolus* were distinguished by their characteristic colony morphology (Fig. 1) and zygospores (Fig. 2). Serodiagnosis was not practiced. Routine in-vitro antifungal susceptibility testing was established in 2011 when a multi-drug resistant case was encountered [20]. All the patients were screened for immunodeficiency. Periodic thyroid function tests, estimation of serum electrolytes and electrocardiogram (ECG) were done in patients receiving potassium iodide treatment.

Orally administered supersaturated solution of potassium iodide (SSKI) was the treatment of our choice. The solution (not commercially available) was prepared by hospital pharmacy by dissolving pure crystals of potassium iodide in warm distilled water and the solution was dispensed in light-proof glass bottles. The dosage of SSKI was 30 to 50 mg/kg/day [2,21]. SSKI contains approximately 47 mg of potassium iodide in each drop [21] Therefore the rule of thumb for dosage was one drop of SSKI/kg/day. Treatment was started with half the estimated dose (20 mg/kg/day) and it was gradually increased over the next 4 to 6 days gauging the child's tolerance. Patients who received oral SSKI were hospitalized for the initial 72 hours to monitor serum potassium levels and cardiac arrhythmia. Thereafter, home administration of the drug was continued until the lesion was cured. Therapeutic endpoint was arbitrarily set at 8 weeks beyond complete resolution of all palpable indurations. Drug resistance was suspected when the lesion did not show any resolution even after 3 weeks of treatment.

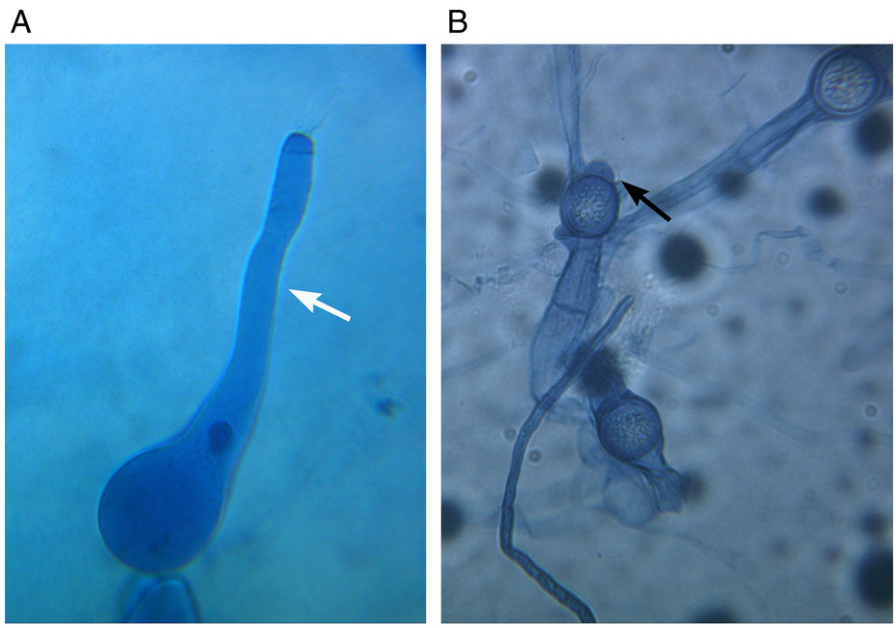

Fig. 2. Morphological difference in the zygospore of *Basidiobolus* (A) and *Conidiobolus* (B). Beak-shaped remnants of copulation tubes (arrow) are typical of *Basidiobolus*. Papilla protruding from conidia (arrow) is characteristic of Conidiobolus. Lactophenol cotton blue preparation 400×.