Case report

Fungal infection in an immunocompetent host presenting a perioral mass

Ornrumpha Tanago[1], Darintr Sosothikul[1], Supanun Lauhasurayotin[1], Kanhatai Chiengthong[1], Hansamon Poparn[1], Suvaporn Anugulruengkitt[2] and Piti Techavichit[1]

[1]Integrative and Innovative Hematology/Oncology Research Unit; [2]Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University

Abstract

Fungal infection is less common among children, but usually constitutes an opportunistic infection among immunocompromised hosts. However, some rare fungal infections can also occur among immunocompetent hosts. Entomophthoromycosis caused by fungus in the phylum Zygomycota, is a rare disease among immunocompetent hosts. Herein, we described 1 case of a 1-year-old girl presenting a perioral mass for three months. The mass was not tender and did not improve after treatment with empiric antibiotics. Initial laboratory investigations were within normal limits. MRI of paranasal sinus revealed a mass of 1.8 x 5.4 x 3.8 cm. In addition, a tissue biopsy was performed, in which the tissue histopathology revealed mixed inflammatory cells with nonseptate hyphae surrounded by eosinophils. This finding was consistent with the Splendore-Hoeppli reaction. Although tissue culture for fungus was negative, the patient was treated with itraconazole and complete response was observed within 7 months. This case report described a diagnosis of Entomophthoromycosis from tissue histopathology and a good response observed after treating with antifungal agents.

Keywords : ● *Entomophthoromycosis* ● *Deep fungal infection* ● *Discoid subcutaneous mass* ● *Zygomycota*

J Hematol Transfus Med. 2023;33:67-72.

Received 22 February 2023 Corrected 24 February 2023 Accepted 6 March 2023

Correspondence should be addressed to Ornrumpha Tanago, MD., Integrative and Innovative Hematology/Oncology Research Unit, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok Thailand

รายงานผู้ป่วย

การติดเชื้อราในเด็กภูมิคุ้มกันปกติที่มีอาการมาด้วยก้อนรอบริมฝีปาก

อรรัมภา ตานะโก[1] ดารินทร์ ซอโสตถิกุล[1] สุภานัน เลาหสุรโยธิน[1] กาญจน์หทัย เชียงทอง[1] หรรษมน โพธิ์ผ่าน[1]
สุวพร อนุกูลเรืองกิตติ์[2] และ ปิติ เตชะวิจิตร์[1]
[1]สาขาวิชาโลหิตวิทยาและมะเร็งในเด็ก [2]สาขาวิชาโรคติดเชื้อ ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

บทคัดย่อ

การติดเชื้อราในเด็กพบได้ไม่บ่อย ส่วนมากมักพบเป็นเชื้อฉวยโอกาสในเด็กที่มีภูมิคุ้มกันต่ำ อย่างไรก็ตามการติดเชื้อราก็สามารถพบได้ในผู้ป่วยเด็กที่มีภูมิคุ้มกันปกติ โรค Entomophthoromycosis เกิดจากการติดเชื้อราในกลุ่มไฟลัม Zygomycota โดยพบได้น้อยและมักพบในผู้ป่วยที่มีภูมิคุ้มกันปกติ ผู้ป่วยเด็กหญิง อายุ 1 ปีพบก้อนที่บริเวณริมฝีปากเป็นระยะเวลา 3 เดือน ลักษณะก้อนกดไม่เจ็บ อาการไม่ดีขึ้นหลังได้รับการรักษาด้วยยาปฏิชีวนะ ผลการตรวจเพิ่มเติมทางห้องปฏิบัติการแรกรับอยู่ในเกณฑ์ปกติ ตรวจ MRI บริเวณ paranasal sinus พบก้อนขนาด 1.8 x 5.4 x 3.8 เซนติเมตร หลังจากนั้นผู้ป่วยได้รับการตัดชิ้นเนื้อเพื่อยืนยันการวินิจฉัย ผลทางพยาธิวิทยาพบลักษณะเซลล์อักเสบชนิดต่างๆ และพบ non-septate hyphae ที่ถูกล้อมรอบด้วยเม็ดเลือดขาว Eosinophils จากลักษณะทางพยาธิวิทยาดังกล่าวเข้าได้กับ Splendore-Hoeppli reaction นอกจากนี้ไม่พบเชื้อราจากผลเพาะเชื้อจากชิ้นเนื้อ อย่างไรก็ตามผู้ป่วยได้รับการรักษาด้วย itraconazole และขนาดก้อนยุบลงทั้งหมดภายในระยะเวลา 7 เดือน รายงานผู้ป่วยฉบับนี้กล่าวถึงการวินิจฉัยโรค Entomophthoromycosis จากผลทางพยาธิวิทยาเป็นสำคัญและพบว่าผู้ป่วยมีการตอบสนองที่ดีต่อการรักษาด้วยยาต้านเชื้อรา

คำสำคัญ : ● *โรค Entomophthoromycosis* ● *การติดเชื้อราในชั้นลึก* ● *ก้อนในชั้นใต้ผิวหนัง* ● *ไฟลัม Zygomycota*
วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2566;33:67-72

Introduction

Fungal infection is less common among children. Usually, fungal infection is opportunistic in an immunocompromised host. However, a rare fungal infection can occur among immunocompetent hosts and may delay diagnosis due to unawareness. Entomophthoromycosis is one of the rare fungal infections among immunocompetent hosts and typically presents with a deep subcutaneous mass. This subcutaneous mass can mimic malignancy causes. Therefore, cases should be properly investigated to confirm a definite diagnosis. This case report described a one-year-old Thai girl presenting a perioral mass.

Case presentation

The one-year-old Thai girl presented a perioral mass for three months before admission. Her mother noticed that her left cheek was swelling and erythematous. The perioral mass was not tender, and she presented no fever. She was admitted to the local hospital for intravenous antibiotics for four days and then switched to an oral antibiotic. Unfortunately, no optimal response was observed. One month later, the perioral mass gradually progressed. She exhibited no underlying disease and received a vaccination according to the EPI.

Her physical examination revealed an ill-defined border subcutaneous mass 3 x 3 cm at the upper lip extending to the left cheek with purpuric overlying skin and hard consistency. Her weight and height were at the 50th percentile. She had no lymphadenopathy and no hepatosplenomegaly. Her complete blood count showed Hb 10.4 g/dL with normal WBC (10,610/uL), platelet count (140,000/uL), and her coagulogram was within normal limits.

An ultrasound of the mass located at her lip and cheek was performed. The results showed an ill-defined infiltrative heterogenous echoic lesion occupying the subcutaneous tissue at the left side of the upper lip and lower medial aspect of the left cheek with moderate internal vascularity. (Figure 1) The MRI paranasal sinus showed a 1.8 x 5.4 x 3.8 cm mass at the upper lip and philtrum with extension intense homogenous enhancement with internal flow voids, multiple subcentimeter bilateral cervical nodes and bilateral retropharyngeal nodes (Figure 2)

In addition, a core needle biopsy from her left buccal mass was performed. The tissue biopsy gram stain and culture for bacteria were negative, but the GMS stain was positive for nonseptate hyphae. Her tissue pathology showed that the granuloma was composed of epithelioid cells and a few multinucleated giant cells. Also, a mixed inflammatory cell infiltrate was composed of lymphohistiocytes, neutrophils and many eosinophils. A few large nonseptate hyphae were observed in the granuloma. They were surrounded by eosinophilic amorphous material which was called the Splendore-Hoeppli reaction (Figure 3). This pathognomonic tissue pathology is compatible with entomopthoromycosis even though her tissue biopsy culture for fungus was negative.

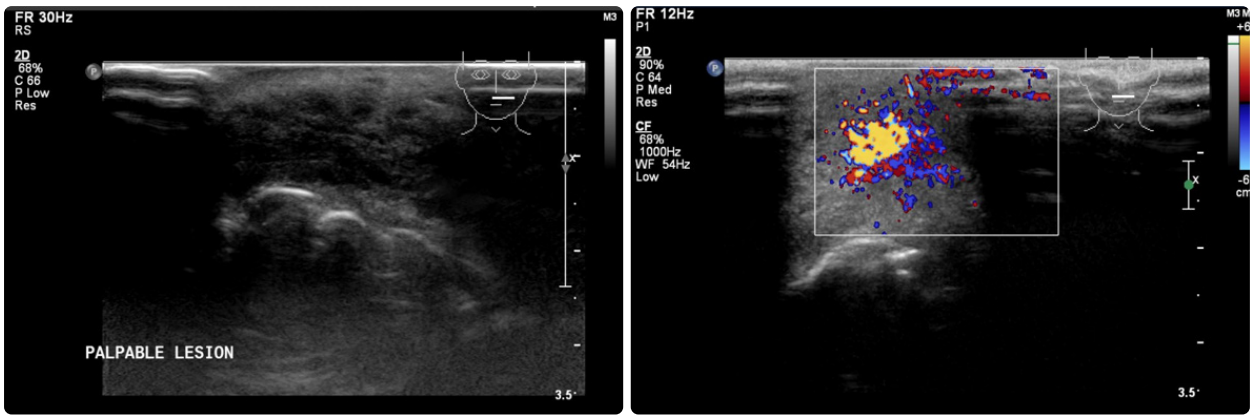

Figure 1 Ultrasound of upper lip and left cheek revealed an ill-defined infiltrative lesion in subcutaneous tissue with moderate internal vascularity.

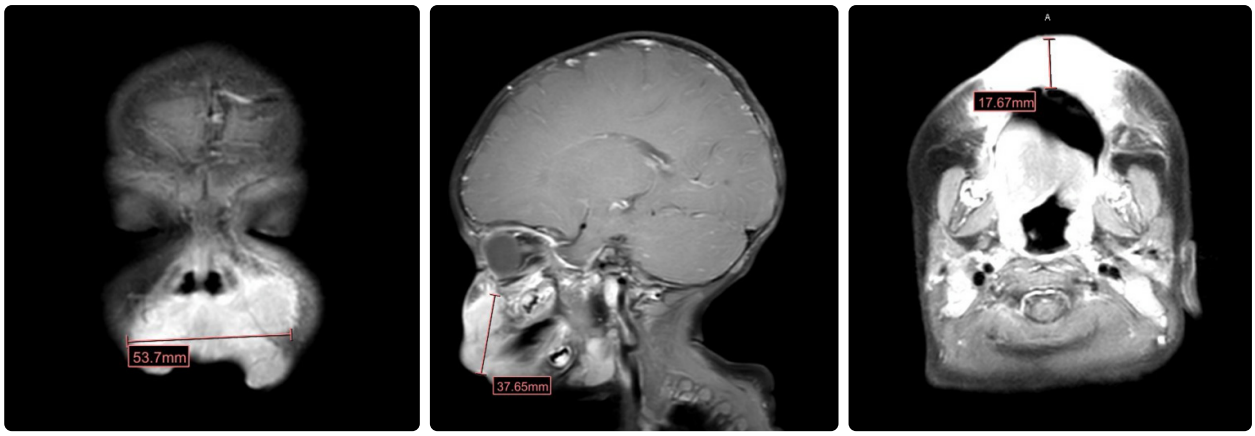

Figure 2 MRI of the paranasal sinus revealed a 1.8 x 5.4 x 3.8 cm mass at the upper lip and philtrum.

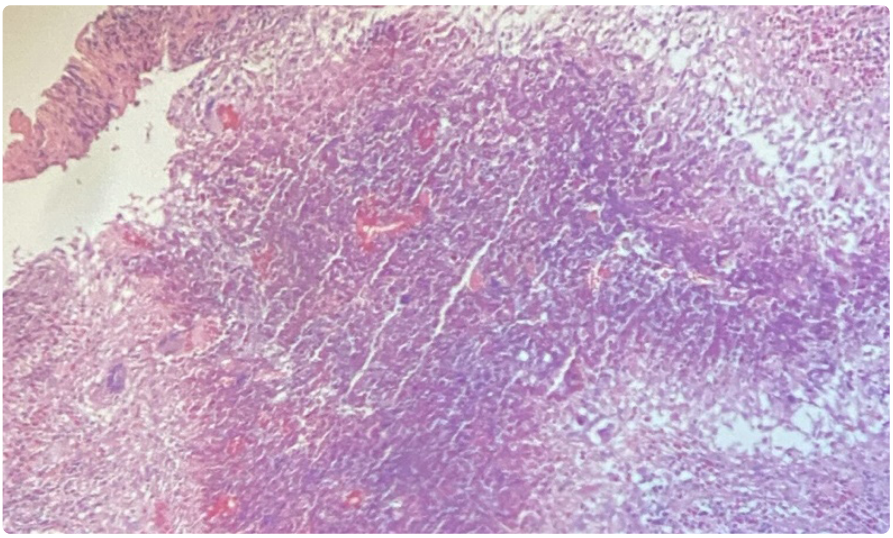

Figure 3 Core needle biopsy from the left perioral mass showed a few large non-septate hyphae surrounded by eosinophilic material.

Figure 4 Patient before and after antifungal treatment

Subsequently, the patient received a diagnosis of entomophthoromycosis from her tissue pathology. She received itraconazole 5 mg/kg/dose orally twice daily and her itraconazole level was monitored regularly. Her symptoms significantly improved after five days of treatment, and she had a complete response within seven months.

Discussion

Entomophthoromycosis is a rare fungal infection of the skin and subcutaneous tissue. One related study showed entomophthoromycosis was a predominant disease among children and young adults.[1] Most patients' age was under 10 years. Moreover, entomophthoromycosis mainly affects immunocompetent hosts. These cases have been reported from both tropical and subtropical regions.

Basidiobolus ranarum, Conidiobolus coronatus and Conidiobolus incongruous, in the order Entomophthoromycota, are common human pathogens caused by Entomophthoromycosis. Both are in the Zygomycota phylum.[2] This pathogen is commonly found in soil, leaf litter, water and decaying organic wastes. However, patients were accidentally inoculated by inconspicuous injuries such as thorn pricks, scratches, insect bites and contaminated injection needles. Patients may not recognize a history of minor injury leading to suspicion of fungal infection.

After the fungal infection, the patient will develop a discoid subcutaneous mass, usually painless. This mass could be found in the craniofacial, trunk, limb, buttocks, lungs and gastrointestinal tract. Typically, the mass should progress slowly with a mean duration of six months.[3] The disseminated form or visceral organ involvement is rarely reported. Due to the gradual clinical onset of the subcutaneous mass, the patient may receive a wrong diagnosis. The differential diagnosis of entomophthoromycosis includes soft tissue sarcoma, lymphoma, vascular malformation, infantile fibromatosis and other infections. The range of delayed diagnosis is between one and eight months.[4] Blood tests may not be specific for diagnosis, so a definite diagnosis should include combined tissue histopathology and culture.

The characteristic histopathologic features include eosinophilic material around multiple septate hyphae and granuloma formation. This characteristic is described as the Splendore-Hoeppli phenomenon which is not specific to individual organisms. This phenomenon could be seen in other infections or noninfectious causes such as hypereosinophilic syndrome.[5] From this characteristic and the absence of vascular invasion, entomophthoromycosis should be considered. Although tissue culture should be performed to confirm a definite diagnosis, some patients may delay diagnosis because of nonspecific results of histopathologic features.

Using systemic antifungal therapy is the most effective treatment for entomophthoromycosis. Imidazoles such as itraconazole are favored over other antifungal drugs. Amphotericin B is not recommended due high minimal inhibitory concentrations (MICs) for most isolates and rapidly developing resistance. Cotrimoxazole has been used with varying outcomes. The treatment duration varies from two to eight months or after the complete resolution of lesion for one month. Our patient was treated with itraconazole for seven months. In addition, using potassium iodide and hyperbaric oxygen is another treatment of choice,[6] and compliance is one of the crucial factors for successful treatment. No role exists for surgery, except biopsy to establish the diagnosis.

Conclusion

Entomophthoromycosis is a rare, deep fungal infection in an immunocompetent host presenting a slow-growing subcutaneous mass. A high index of suspicion is needed to avoid delayed diagnosis. The presence of characteristic tissue histopathology and culture can confirm a definite diagnosis. The most effective treatment is using antifungal drugs with good compliance.

References

1. *Sackey A, Ghartey N, Gyasi R. Subcutaneous basidiobolomycosis: a case report. Ghana Med J. 2017;51:43-6.*
2. *Shaikh N, Hussain KA, Petraitiene R, Schuetz AN, Walsh TJ. Entomophthoramycosis: a neglected tropical mycosis. Clin Microbiol Infect. 2016;22:688-94.*
3. *Takia L, Jat KR, Singh A, Priya MP, Seth R, Meena JP, et al. Entomophthoromycosis in a child: delayed diagnosis and extensive involvement. Indian J Pathol Microbiol. 2020;63:648-50.*
4. *Raveethiran V, Mangayarkarasi V, Kousalya M, Viswanathan P, Dhanalakshmi M, Anandi V, et al. Subcutaneous entomophthoromycosis mimicking soft-tissue sarcoma in children. J Pediatr Surg. 2015;50:1150-5.*
5. *Hussein MR. Mucocutaneous Splendore-Hoeppli phenomenon. J Cutan Pathol. 2008;35:979-88.*
6. *Raja R, Nair S, Katchabeswaran R, Venkatakarthikeyan C. Entomophthoromycosis presenting as a nasal mass. Indian J Otolaryngol Head Neck Surg. 2021;74:1207-9.*