Disseminated *Candida tropicalis* Infection Presented with Skin Rashes and Chorioretinitis in a Subcutaneous Panniculitis-like T-Cell Lymphoma Pediatric Patient

Pirakorn Sukonthaman MD, Chutika Srisuttiyakorn MD.
Division of Dermatology, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand.

ABSTRACT:
Candida tropicalis is one of the most common pathogens responsible for disseminated candidiasis, especially in immunocompromised patients. The dermatological lesion usually presents as erythematous papular eruptions. Ocular manifestation is one of the serious major complications, which presents as chorioretinitis and endophthalmitis, and may increase the mortality rate. We report a case of disseminated *C.tropicalis* infection presented with skin rashes and chorioretinitis in a subcutaneous panniculitis-like T-cell lymphoma pediatric patient.
Key words: *Candida tropicalis*, disseminated candidiasis, chorioretinitis, Subcutaneous Panniculitis-like T-Cell Lymphoma (SPTCL)

Introduction

Candida tropicalis is one of the most common pathogens responsible for disseminated candidiasis with skin infection. The risk factors include hematological malignancy, neutropenia, intensive cytotoxic chemotherapy, etc. The characteristic skin lesions are a maculopapular rash surrounded by an erythematous halo with a pale center. The ocular candidiasis is a major complication and increases the mortality rate. We report the disseminated *Candida tropicalis* infection with chorioretinitis in subcutaneous panniculitis-like T-cell lymphoma (SPTCL) patients as an indication of severity of the disease.

Case report

A 10-year-old boy with SPTCL presented to the pediatric department with submandibular mass, prolonged fever, and significant weight loss. He received chemotherapy sessions for high-risk anaplastic large cell lymphoma (HR-ALCL) protocol. However, after the second cycle of chemotherapy for 14 days, he developed febrile neutropenia and septic shock, and empirical antibiotics with meropenem and vancomycin were initiated. Nevertheless, he developed new rashes on his scalp, face, trunk, and extremities 6 days after the initiation of antibiotics.

Physical examination revealed vital signs as follows; body temperature 39.9c, blood pressure 115/65 mmHg, pulse rate 130 beats per minute, and respiratory rate 30 times per minute. He had an oral thrush on his tongue and there were multiple, ill-defined border, erythematous papules and some pustules on his scalp, face, trunk, and extremities. His fundoscopic examination was done by an ophthalmologist and revealed a well circumscribed whitish lesion size 1.5 disc diameter deep to his inner right retina. The lesion was suggestive of chorioretinitis. Other physical examination results were unremarkable.

Corresponding Author: Chutika Srisuttiyakorn MD, email: schuti101@gmail.com

Received: 29 June 2022 Revised: 6 December 2022 Accepted: 8 December 2022

Laboratory investigations showed complete blood count as follows; hemoglobin 9.4 g/dL, hematocrit 26.7%, white blood cells count 100/mm^3, and platelet of 17,000/mm^3. Other basic laboratory tests including renal function test, electrolyte and liver function test were unremarkable.

When a skin biopsy was performed on his left leg, the section showed nodular infiltration in the upper dermis with lymphohistiocytes and numerous round to oval yeast-like organisms. The GMS and PAS stains highlighted numerous budding yeasts with pseudohyphae in the upper dermis. but the tissue culture for fungus showed no growth. Nevertheless, the patient's blood cultures were positive for *Candida tropicalis.*

Amphotericin B (1mg/kg/dose) 50 mg intravenously every 24 hours was started since our hospital does not have echinocandins available. After 14 days of treatment, the cutaneous papules and pustules improved, and his chorioretinitis had also improved.

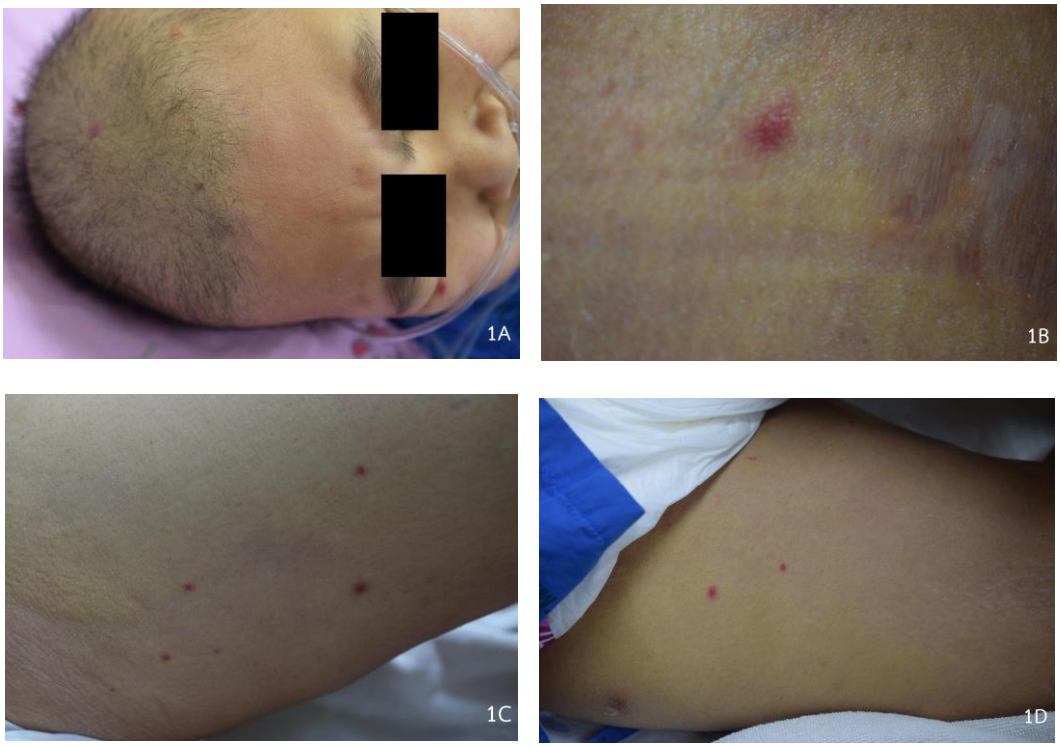

Figure 1 A-D Clinical manifestation of maculopapular rash on head, trunk and extremities

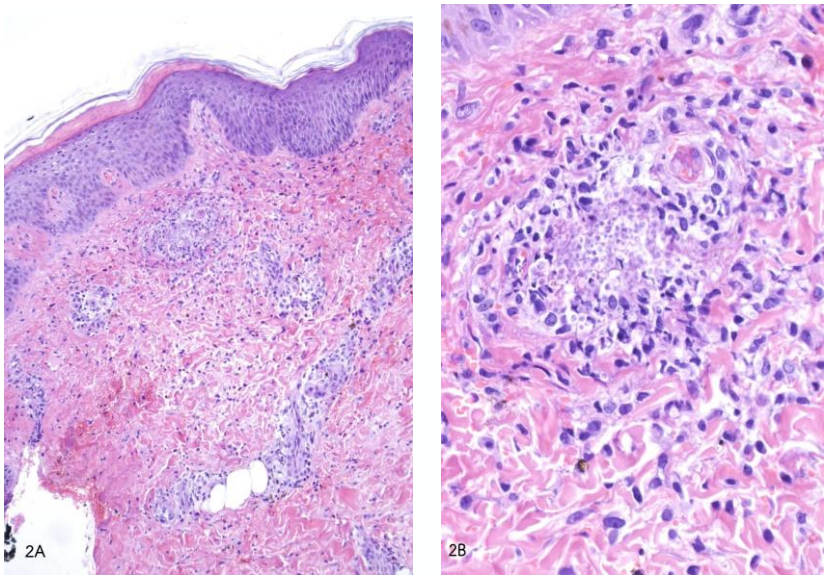

Figure 2 Nodular infiltration in the upper dermis with lymphohistiocytes and numerous round to oval yeast-like organisms (Figure 2A; H&E, X100, Figure 2B; H&E, X400)

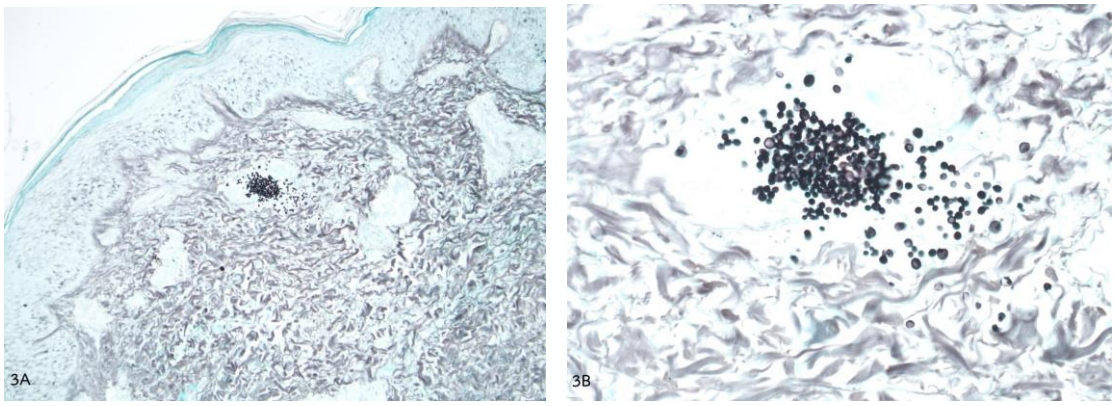

Figure 3 GMS stain shows numerous budding yeasts in the upper dermis with pseudohyphae (Figure 3A; GMS, X100, Figure 3B; GMS, X400)

Discussion

Candida tropicalis belong to genus Candida of the fungi kingdom[1]. Risk factors of systemic *C.tropicalis* infection include patients with immunocompromised status such as hematological malignancy, neutropenia, intensive cytotoxic chemotherapy, post ablative radiation therapy, corticosteroid and immunosuppressive drug use and also in patients who received prolonged antibiotics and were on central venous catheters[2].

Most common pathogens for disseminated candidiasis are *C.tropicalis*, followed by *C.krusei*, and *C.albicans*. However, in the patients who received fluconazole prophylaxis, *C.krusei* is the most frequent finding[3]. The classic clinical triad of candidemia are fever, rash and myalgia[4].

The cutaneous manifestations in disseminated candidiasis is around 10-30%[4]. Maculopapular rash surrounded by erythematous halo with characteristic pale center or necrosis is the most common cutaneous manifestation. Also, pustules, erythematous subcutaneous nodules, plaques and cutaneous abscesses can be found. The distribution usually involves the trunk and proximal extremities, but sometimes the head and face may be involved. If the patient has thrombocytopenia, purpura and hemorrhagic bullae may be observed[4,5,6]. There are also reports of *C.tropicalis* infection presented as ecthyma-like lesions[7].

C.tropicalis is also the most common agent for skin lesions in disseminated candidiasis, followed by *C.krusei,* and *C.albicans.* Other species such as *C.guilliermondii, C.glabrata* and *C.ciferrii* rarely cause cutaneous lesions[4,5,6]. Blood cultures are negative in up to 50% of cases which makes the diagnosis more difficult[8].

Histologic examination reveals one or several aggregates of hyphae and spores focally within the dermis, often at sites of vascular damage and generally visible only in sections stained with the PAS reaction or GMS. Some of the spores, which are 3 to 6 μm in diameter, show budding. They may present in an area of leukocytoclastic vasculitis, within a micro-abscess, or in an area of only mild inflammation. Due to the small size of *Candida spp*., step-sections through the biopsy specimen may be necessary to find them. The epidermis is usually unaffected[9].

Extracutaneous manifestations include endocarditis, esophagitis, meningitis, arthritis, hepatosplenic abscess and ocular manifestations such as chorioretinitis and endophthalmitis.

Ocular candidiasis is a major complication in disseminated candidiasis with an incidence around 16% of patients. The most common ocular manifestation is chorioretinitis and endophthalmitis. Other findings such as retinal hemorrhages, Roth spots, and cotton wool spots are also reported. The clinical outcome of candida chorioretinitis results in a better outcome and does not progress to endophthalmitis. The duration of candidemia was found to be significantly longer in patients with ocular candidiasis[10].

Disseminated candidiasis has a high mortality rate and the majority of clinical outcomes depend on the patient's immune status. In addition, in many places without echinocandins, which are first line therapy as empirical antifungal, the prognosis worsens. The Center of Disease Control treatment guidelines recommend using echinocandins such as caspofungin, micafungin, and anidulafungin as initial therapy in the treatment of disseminated candidiasis in neutropenic patients. If such medications are not available, lipid formulation amphotericin B, fluconazole and voriconazole can be used as alternative therapies with favorable outcome as the treatment given in our patient[11].

The recommended treatment for endogenous ocular candidiasis has not been established, but treatment with fluconazole and voriconazole has been reported with favorable results, due to the pharmacokinetics of penetrating the vitreous humor, when compared to treatment with echinocandins. There were also reports of successful treatments with voriconazole and amphotericin B followed by fluconazole for ocular candidiasis[10].

Conclusion

Disseminated *C.tropicalis* infection with chorioretinitis as a major complication may lead to an increased mortality rate. Early initiation of empirical antifungal therapy is required. Our case report emphasizes the importance of ocular examination in neutropenic patients as it may relate to the prognosis of severe diseases and complications.

References

1. Chai L YA, Denning DW, Warn P. Candida tropicalis in human disease. Crit Rev Microbiol 2010;36:282–98.
2. Kontoyiannis DP, Vaziri I, Hanna HA, Boktour M, Thornby J, Hachem R, et al. Risk Factors for Candida tropicalis fungemia in patients with cancer. Clin Infect Dis 2001;33:1676–81.
3. Guarana M, Nucci M. Acute disseminated candidiasis with skin lesions: a systematic review. Clin Microbiol Infect 2018;24:246–50.
4. Ahronowitz I, Leslie K. Yeast infections. In: Kang S, editor. Fitzpatrick's dermatology, 9th ed, 2-volume set. McGraw-Hill Education/Medical 2018:2952-64.
5. Bae GY, Lee HW, Chang SE, Moon KC, Lee MW, Choi JH, et al. Clinicopathologic review of 19 patients with systemic candidiasis with skin lesions. Int J Dermatol 2005;44:550–55.
6. Pedraz J, Delgado-Jiménez Y, Pérez-Gala S, Nam-Cha S, Fernández-Herrera J, García-Diez A. Cutaneous expression of systemic candidiasis. Clin Exp Dermatol 2009;34:106–10.
7. Beasley K, Panach K, Dominguez AR. Disseminated Candida tropicalis presenting with Ecthyma-Gangrenosum-like Lesions. Dermatol Online J 2016;22.
8. Clancy CJ, Nguyen MH. Finding the "missing 50%" of invasive candidiasis: How nonculture diagnostics will improve understanding of disease spectrum and transform patient care. Clin Infect Dis 2013;56:1284–92.
9. Hinshaw M, Longley JB. Fungal Diseases. In: Elder D, editor. Lever's Histopathology of Skin, 11th edition. Philadelphia: Lippincott Williams & Wilkins 2014:733-36
10. Oude Lashof AML, Rothova A, Sobel JD, Ruhnke M, Pappas PG, Viscoli C, et al. Ocular manifestations of candidemia. Clin Infect Dis 2011;53:262–8.
11. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. Clin Infect Dis 2016;62:e1-50.