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Congenital Systemic Candidiasis in A Term Infant: A Case Report

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Abstract

Systemic candidiasis is a common complication in neonatal wards; however, congenital systemic candidiasis is an extremely rare disease, which is detected in both full-term and premature infants, with less than 50 cases reported to date. We report a case of a full-term newborn who presented with generalized skin eruptions at birth. Blood, urine, and skin scraping cultures, blood tests, and lumbar puncture were performed. Blood, urine, and skin scraping cultures were positive, the etiological agent was Candida albicans. After six weeks of anti-fungal treatment with fluconazole, the newborn was cured. Early diagnosis is crucial to prevent complications caused by Candida albicans in newborns.

Keywords*: congenital; systemic candidiasis; term infant; Candida albicans.*

Introduction

Unlike hospital-acquired systemic candidiasis, which is common in neonatal intensive care units all over the world [1], congenital systemic candidiasis is extremely rare in both full-term and premature infants, with less than 50 cases reported in the medical literature to date [2]. It presents with varied clinical manifestations ranging from localized skin disease to invasive disease; i.e. pneumonia, meningitis, sepsis, and death [3].

It is a rare event that Candida infection of the uterus to be encountered as well as for the candida infection to appear at birth affecting the new-borne baby. Premature infants are susceptible to candidal infection mainly because their immune system is immature, and congenital candidiasis is very rare in term infants. We describe a case of a full-term neonate with congenital systemic candidiasis. The infant developed candidemia due to Candida albicans and the same yeast was also isolated from urine, and skin scraping culture showed the presence of Candida albicans

Case Presentation

A female infant born at 40 weeks gestation, with a birth weight of 3280 g, was delivered by cesarean section due to scoliosis, right hydronephrosis, active stagnation, and suspected intrauterine infection in her mother. The infant's mother was a healthy 24-year-old with a history of two abortions, and this was her third pregnancy. Her prenatal screening tests (including gonorrhea, chlamydia, syphilis, rubella, group B streptococcus, and complete blood count) were unremarkable, and Candida albicans had not been detected in her vaginal secretion 6 months ago. Intravenous (IV) cefuroxime sodium therapy was initiated during labour for maternal fever. The Apgar score was 9/10 (colour, 1 point) at 1 minute, 8/10 (colour, muscle tone, 2 points) at 5 minutes, and 9/10 (muscle tone, 1 point) at 10 minutes, and her amniotic fluid was clear without meconium staining. She was admitted to the neonatal intensive care unit because of groaning and spitting.

At birth, the infant presented with a generalized erythematous, papular eruption over the face, trunk and extremities (Figure 1A). Three days later, pustules and desquamation were observed, and the palms and soles were also affected (Figures 1B, C, D, and E). The smear of her skin scrapings was negative. Neither oral thrush nor perianal lesions were observed. Her physical examination was normal, except for transient respiratory distress and low flow nasal catheter oxygen inhalation administered for 2 days, with a decreased transmittance chest X-ray.

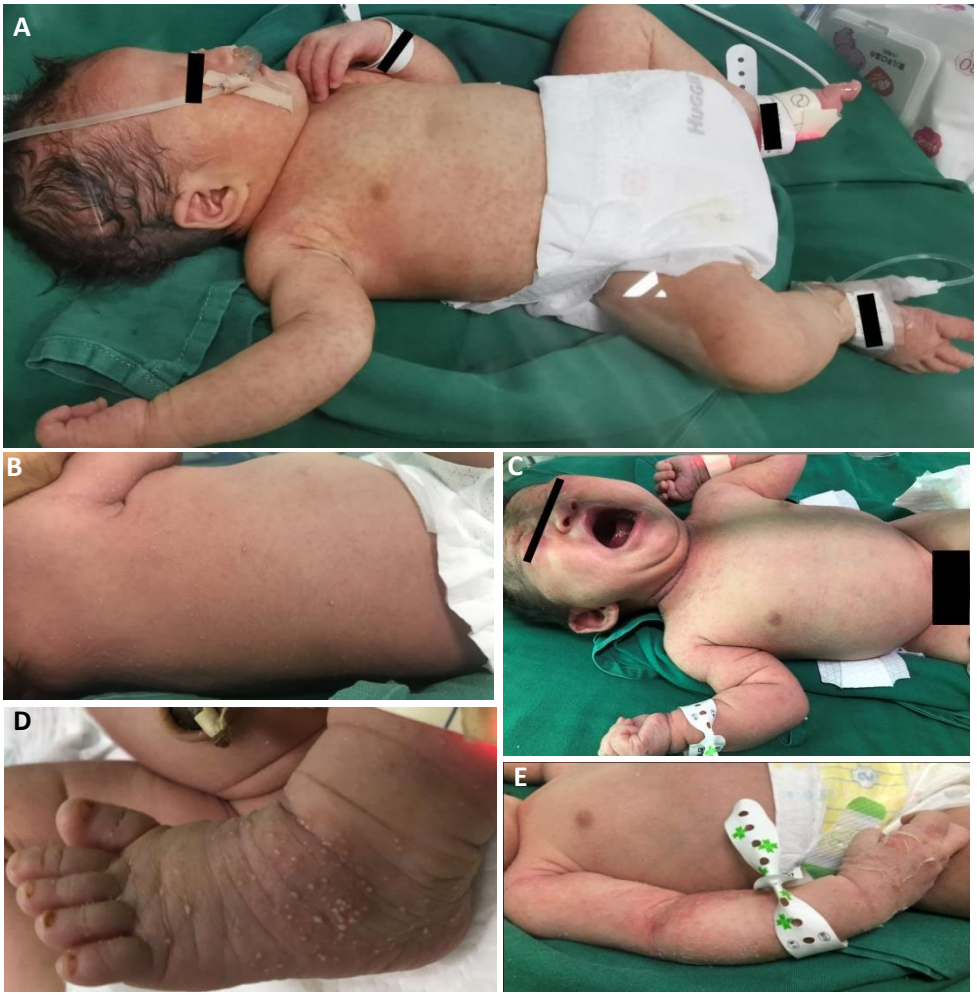

Figure 1. Full-term infant with congenital systemic candidiasis, presenting with generalized erythematous papules (A), pustules and desquamation, and involvement of the palms and soles (B, C, D, and E).

After 18 hours (hr,) her blood analyses showed an increase in a C-reactive protein (CRP) (68.17 mg/L) and leukocytosis with left shift; consequently, a lumbar puncture was performed. Cerebrospinal fluid (CSF) test can exclude central nervous system infection; hence, we injected cefoperazone-sulbactam and penicillin intravenously for 7 days.

On day 7 following her birth, the baby's previous skin rash had desquamated and excoriated lesions persisted. The baby performed well clinically, and her blood cell count (WBC) and CRP levels were in the normal range; then antibiotics were stopped. However, blood, urine, and skin scraping cultures obtained on admission were positive and identified Candida albicans, 1, 3-β-D-glucan assay was negative, the infant was continued on IV fluconazole (6 mg/kg.d) and topical skin antifungal therapy (Miconazole Nitrate). On day 13 (one week after IV fluconazole), fungi, bacteria, and viruses were not detected in blood by High-Throughput Sequencing (HTS), the retests of blood and urine culture were negative. On day 20 (two weeks after IV fluconazole), the infant's WBC count was 13.22×10^9/L with a differential of 55.4% neutrophils, 26.1% lymphocytes, CRP 122.63 mg/L, and procalcitonin (PCT) >49.83 ng/ml, but the infant appeared well clinically throughout this period, and Chest X-ray and temperature were normal. Blood culture, urine culture, and lumbar puncture for CSF analysis were performed again. Blood and CSF cultures remained negative, but urine culture showed growth of Enterococcus faecalis (accounting for 10%) and Escherichia coli (10^5 cfu/mL, accounting for 90%), urine routine showed bacteria (BACT) 38/μL and nitrite (NIT)+. It was suggested that the infant had bacterial urinary tract infection; then the third urine culture was performed and she was continued on IV ceftazidime for 8 days. At the same time, fluconazole was administered orally for 4 weeks, with a total duration of 6 weeks, including IV fluconazole. Cutaneous lesions disappeared on day 22. However, after that, the female infant had recurrent bacterial urinary tract infections and blood culture was negative. The third urine culture showed growth of Escherichia coli (10^5 cfu/mL). After 7 days of IV Piperacillin-tazobactam, Enterococcus faecalis (10^5 cfu/mL) was cultured from the 4th and the 5th urine samples. We replaced piperacillin-tazobactam with IV vancomycin for 10 days. Each episode of urinary tract infection was sensitive to antibiotic treatment, with no obvious clinical manifestations (or only slightly less milk intake, no crying during urination and urethral orifice redness and swelling).

Due to recurrent bacterial urinary tract infections, we suspected whether she had immune deficiency, and conducted blood immunity-related gene screening and immune function tests, including quantitative immunoglobulin and T cell number and function analysis, which showed normal immune function. She was also suspected of having vesicoureteral reflux; however, voiding cystourethrography was not performed because of difficulty in holding urine. At completion of a 10-day course of IV vancomycin, two repeat urine cultures were sterile, two urine routine examinations were normal, and audiometry was normal. An ophthalmologic examination, brain magnetic resonance imaging (MRI), chest CT (Figure 2A), liver, renal, and bladder ultrasonography and 99mTc-DMSA static renal imaging (Figure 2B) were normal. An echocardiogram revealed a small atrial septal defect and patent foramen ovale (0.19 cm, 0.13 cm) without endocarditis (Figure 2C). Two months later, the infant was discharged and showed good development.

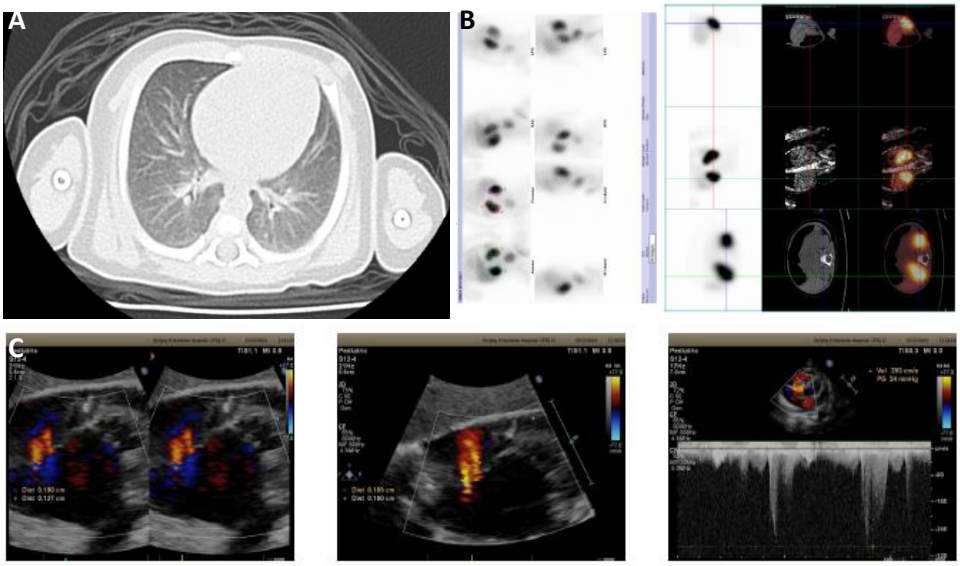

Figure 2. Chest CT indicating normal lungs, no candida lung infection (A). 99mTc-DMSA static renal imaging showing normal kidney without acute pyelonephritis or scar (B). Echocardiogram revealing a small atrial septal defect and patent foramen ovale (0.19 cm, 0.13 cm) without endocarditis (C).

Discussion

As mentioned earlier, congenital systemic candidiasis is an extremely rare disease caused by intrauterine or intrapartum infection with Candida. A number of PubMed surveys have been conducted using various combinations of the following terms: "congenital", "systemic", "candidiasis", "candidemia", "invasive" "disseminated" "intrauterine", and "candida". A total of 45 cases have been published in English journals over the past 55 years, which can be traced back to 1966 at the earliest [4]. Systemic infection is defined as the positive culture of blood, urine, or CSF for Candida, or the manifestation of Candida in histopathology (HP) or culture specimens obtained from autopsy. Candida albicans is a common micro-organism in female genitalia. Although it is an opportunistic fungus, if there is any rupture of fetal membranes and foreign bodies in the uterus or cervix, the risk of ascending infection will increase, which can lead to chorioamnionitis [5], and then cause Candida placental infection, and infant skin and/or system involvement [6].

Congenital candidiasis has a variety of clinical manifestations, from diffuse erythema rash with or without blisters and pustules to systemic diseases, involving invasive infections of blood, urine or lungs, and the skin may be affected or unaffected [7]. Most cases have skin lesions at birth or within 6 days after birth. Other clinical features may include onychomycosis, mucositis, and acute chorionic inflammation with yellow and white spots on the placenta and umbilical cord [8]. Typical pustules usually appear on the palms and soles of feet. The lesions vary in form, and different stages are often observed simultaneously [9]. In this case, the newborn developed diffuse red macula after birth, and then gradually developed pustules and desquamation, and the palms and soles were also affected. This infant was treated with intravenous fluconazole and topical skin antifungal therapy (miconazole nitrate applied to the affected skin), and skin lesions disappeared on day 22.

Candidemia and invasive candidiasis have attracted the most attention in clinical trials. Candidemia has been reported to be associated with an as high as 47% attributable mortality [10]; thus, early diagnosis and treatment are very critical. Especially for high-risk infants, such as those who are aged less than 25 weeks of gestation, those with thrombocytopenia during blood culture, and those with a history of exposure to third-generation cephalosporins or carbapenems within 7 days before blood culture, once candida infection is suspected, empirical antifungal treatment should be considered [11-12]. Invasive focal infection in newborn infants is usually caused by

hematogenous spread of Candida to a single organ system, involving blood, urinary tract, CNS, eyes, heart valves, bones, or joints [13]. Blood culture is considered the gold standard for detection of candidiasis, with high specificity but poor sensitivity [14]. Positive blood cultures for Candida should almost never be considered a contamination. Also, blood cultures are only 50 percent sensitive for detecting infection in adults [15], and the small amount of blood used in infantile cultures makes it more difficult to isolate the species of Candida (candidiasis) in blood. Candida urinary tract infection is rare in healthy newborns. In contrast, candidiuria is more common in neonatal and pediatric ICUs, especially in premature infants [16]. Due to the limitations of culture in diagnosing candida infection, other tests have been used. For example, 1, 3-β -d-glucan, a fungal cell wall component, has been used to diagnose a variety of fungal infections, including candida, but it has a sensitivity of only 60% [12], and our infant's test was negative. High-throughput sequencing techniques have also been used to detect DNA in candida blood and urine samples, which may be more sensitive than blood cultures to detect fungal diseases [17]. In this report, Candida albicans was isolated not only from skin scrapings, but also from blood and urine cultures at admission, which definitely established the diagnosis of congenital systemic candidiasis, with invasive Candida albicans infection and cutaneous candidiasis. In addition to candidiuria albicans, our infant was found to have repeated urinary tract infections with different types of bacteria, but her immune function was normal and kidney ultrasound and DSMA showed normal kidneys. Urinary tract infection was cured after sensitive antibiotic treatment. However, it is necessary to check urine routine and urine culture regularly. If there is repeated urinary tract infection, it is necessary to perform voiding cystourethrography to determine whether there is a vesicoureteral reflux. Eye and central nervous system tests, such as fundus examination and CSF tests, are also normal. There is no redness, swelling, deformation of joints, and no restriction of movement. Muscle strength and tension of limbs are normal, and bone and joint infection can be excluded.

Systemic antifungal agents that have been shown to be effective in the treatment of candidiasis include the following four major categories [18]: the polyenes (AMB-D, L-AMB, AmB lipid complex and AmB colloidal dispersions), the triazoles (fluconazole, itraconazole, voriconazole, and posaconazole), the echinocandins (caspofungin, anidulafungin, and micafungin), and flucytosine. According to Antifungal Susceptibility Testing, this infant was treated with fluconazole intravenously for 2 weeks and orally for 4 weeks, with a total treatment course of 6 weeks. The infant's blood metagenomic HTS for pathogen detection was negative after one week of antifungal treatment. Finally, neonatal congenital systemic candidiasis was cured.

Conclusions

Congenital systemic candidiasis in full-term infants is extremely rare, and the clinical manifestations differ from those reported in premature infants. Its clinical symptoms are relatively mild, which may be related to immune maturity. However, the skin rash is obvious. Clinicians should be highly vigilant against diffuse erythema and pustules at birth, especially involving the palms and soles.

Author Contributions

H.-H.Z. primarily wrote and edited the case report; H.-H.Z., Z.Z., L.L., Y.-Z.Z., and Y.-X. D performed patient evaluation and treatment; H.-H.Z., L.-J.Y., and Y.-X. D performed original draft preparation and revision; H.-H. Z performed manuscript submission; L.-J.Y. and Y.-X. D performed revision and supervision the paper. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement
All relevant data are within the manuscript.

Conflicts of Interest
The authors declare no conflicts of interest.

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