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Case Report

Generalized erythroderma in a neonate: Rare presentation of nosocomial candidemia with *Candida tropicalis*

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ABSTRACT

Candida species are currently one of the most common causes of nosocomial infection in neonatal intensive care units with *Candida tropicalis* emerging as a frequent offending agent. Colonization precedes systemic invasive fungal infections in neonates. It generally manifests with lethargy, increased apneic episodes, feeding intolerance, late-onset thrombocytopenia, hypoglycemia, unexplained hyperglycemia, poor perfusion, and need for increased ventilator requirement. We report a 10-day-old neonate, with late-onset sepsis by *C. tropicalis*, presenting as generalized erythroderma. We present this case to highlight that nosocomial candidemia with *C. tropicalis* can present as generalized erythroderma in neonates. Maintaining adequate oral or parenteral fluid intake with monitoring of serum electrolytes is mandatory.

Key words: *Generalized erythroderma, Candida tropicalis, Congenital candidiasis, Hypernatremia, Neonatal encephalopathy, Netherton syndrome*

Candida infections are frequent and major causes of septicemia in neonatal intensive care units (NICUs), and they are associated with high morbidity and mortality rates [1]. While *Candida albicans* has historically been the most frequently isolated species, *Candida tropicalis* has rarely been isolated in neonates [1,2]. Acquisition of *C. tropicalis* very likely occurs in the NICU by cross-colonization [3,4]. Infections range from superficial colonization to widely disseminated, life-threatening disease. Invasive fungal infections occur in previously colonized neonates more frequently than in non-colonized neonates [4]. Systemic candidiasis is a serious form of nosocomial late-onset infection in infants admitted to NICUs and particularly developing beyond the 7th day of life in the presence of risk factors such as the presence of central venous catheter, total parenteral nutrition, use of broad spectrum antibiotics, especially 3rd generation cephalosporins [2,4]. Its presentation varies from lethargy, increased apneic episodes, feed intolerance, late-onset thrombocytopenia, hypoglycemia, unexplained hyperglycemia, poor perfusion, and need for increased ventilator requirement [2,5]. We report a 10-day-old neonate, diagnosed with systemic candidiasis by *C. tropicalis*, who presented with generalized erythroderma. Nosocomial candidiasis presenting as generalized erythroderma is not reported in the literature.

CASE REPORT

A preterm male neonate with birth weight of 1.9 kg, born at 35.2 weeks gestation to a primigravida by vaginal route presented on 10 days of life to our center with generalized erythroderma and mild respiratory distress. He developed respiratory distress soon after birth for which he was treated with non-invasive respiratory support along with intravenous antibiotics at previous center. Sepsis screen was normal and blood culture was sterile, and he was discharged on 7th day. He remained asymptomatic for next 2 days and then came to us on day 10 of life with complaints of red rash over the body. Cutaneous examination revealed generalized erythroderma and few ruptured bullae with wet base (Figs. 1 and 2).

His laboratory investigations showed hemoglobin of 11.2 g/dL, total leukocyte count of 28,000/mm^3 with differential count of P:47; L:32; M:15; E:6, and platelet count of 60,000/mm^3. His liver function tests were within normal limits total serum bilirubin - 0.6 mg/L, serum glutamic-oxaloacetic transaminase - 46 U/L, serum glutamate pyruvate transaminase - 38 U/L, alkaline phosphatase - 136 U/L, total serum protein - 6.2 g/dL, and albumin - 2.8 g/dL. He also had hypernatremia (158 mEq/L), hyperglycemia (298 mg/dL), and metabolic acidosis. Mother's human immunodeficiency virus (HIV) and venereal disease research laboratory status were normal. Baby's immunological

profile was within normal limits and showed IgG - 134 mg/dL (41-268), IgA - 6.8 mg/dL (0.8-15.4), IgM - 21 mg/dL (7.1-37.2) [6]; CD19 B-lymphocyte 10% (507/mm^3), CD3 T-lymphocyte 77% (3903/mm^3), and NK cells 7% (355/mm^3). His nitroblue tetrazolium slide test was positive (98%, normal - 95-100%).

Tzanck smear of skin scrapings did not show multinucleated giant cells. KOH preparation was positive for budding yeast cells and pseudohyphae. Blood culture grew *C. tropicalis*. CSF and urine evaluation, USG KUB region, 2D echocardiography, and ophthalmological evaluation were normal. There was no evidence of oropharyngeal and perineal thrush. He was treated with intravenous amphotericin B (IV AMB) and topical ketoconazole along with fluid adjustment for hypernatremia. Over the next 3 days, his sodium level returned to normal. Healing of skin lesions followed over next 2 weeks (Fig. 3). IV AMB was continued for 3 weeks. Subsequently, he was discharged with advice of outpatient follow-up.

DISCUSSION

Generalized redness has an alarming appearance and infant's general state of well-being is directly related to the extent of the disease. Generalized erythroderma or red baby syndrome is defined as an inflammatory disorder affecting more than 90% of the body surface area [7]. A large number of conditions may manifest as life-threatening erythroderma in the newborn, namely, staphylococcal scalded skin syndrome (SSSS), non-bullous ichthyosiform erythroderma, congenital candidiasis (CC), Omenn syndrome, graft-versus-host disease, Netherton syndrome, atopic dermatitis, seborrheic dermatitis, and diffuse cutaneous mastocytosis and some inborn-errors such as holocarboxylase deficiency [7]. Infectious causes of erythroderma should always be considered first.

Laboratory evaluation should include complete blood cell count, KOH preparation (or calcofluor white immunofluorescence technique), Tzanck smear, Syphilis serologic studies and HIV assay, quantitative immunoglobulin assays, tests of cell-mediated immunity, skeletal survey, hair examination, and skin biopsy. Serum electrolyte and albumin concentrations should be measured because children with erythroderma are at risk of hypernatremic dehydration and loss of albumin from enteral and transcutaneous protein losses. A full blood count should be supplemented by more detailed immunological studies if Omen syndrome or graft versus host reaction is suspected.

Although congenital and neonatal SSSS have been described, it usually manifests in infants and children up to the age of 5 years. Moreover, mucus membrane is not involved in SSSS because the target of staphylococcal exfoliative toxin is not present in mucous membranes while the present case had involvement of oral cavity [7]. Skin biopsy reveals a split in the superficial epidermis and culture of blister contents is negative [7]. CC is characterized by widely scattered macules, papules, and pustules or confluent exfoliative erythroderma, and it presents at birth or within 6 days of life [8]. Nail involvement, in the form of paronychia and dystrophy, is seen in CC. Furthermore, mucosal and napkin area are spared in CC [8]. Our case presented on day 10 of life and had involvement of oral mucosa and napkin area but no nail involvement.

Figure 1: Generalised erythroderma

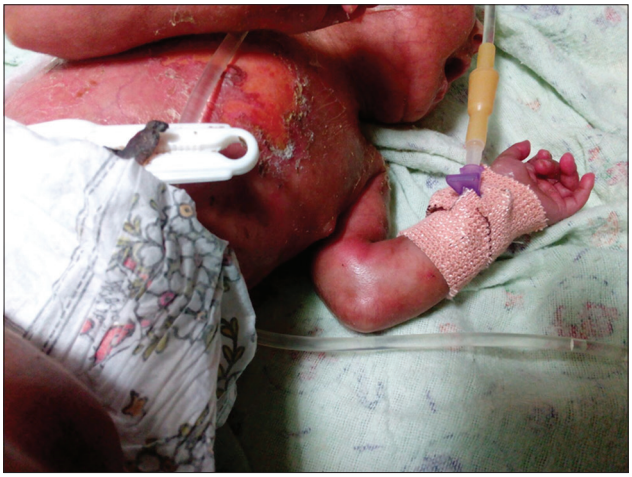

Figure 2: Ruptured bullae with wet base in the background of erythroderma

Figure 3: Healing of skin lesions

Immunological disorders associated with erythroderma are mainly, primary immunodeficiencies, e.g., severe combined immunodeficiency, Wiskott-Aldrich syndrome, hyperimmunoglobulin E syndrome, Omenn syndrome, secondary immunodeficiencies (AIDS, graft-versus-host disease), Langerhans cell histiocytosis, neonatal lupus, and diffuse

cutaneous mastocytosis [7]. Because of the protective effect of maternal immunity, congenital immunodeficiency syndromes are rarely symptomatic at birth. Skin biopsy helps to distinguish among the ichthyosis associated abnormalities: Lamellar ichthyosis, congenital non-bullous ichthyosiform erythroderma, epidermolytic hyperkeratosis, X-linked ichthyosis, multiple sulfatase deficiency, neutral lipid storage disease, Sjögren-Larsson syndrome, trichothiodystrophy, Netherton syndrome, and X-linked dominant chondrodysplasia punctata [9].

Netherton syndrome is characterized by a triad of generalized exfoliative dermatitis, sparse hair with trichorrhexis invaginata, ("bamboo hair") and atopic features. It usually presents at birth as erythroderma. Because of the early paucity of hair, it can take some time before the diagnosis of Netherton syndrome is confirmed; although, examination of eyebrows or eyelashes is often rewarding [10]. Apart from raised total IgE and multiple positive specific IgE reactions, there are no consistent immunological abnormalities in Netherton syndrome. We have not done hair biopsy in this case, but immunoglobulins levels were normal.

Holocarboxylase synthetase deficiency presents with neonatal erythroderma and alopecia, whereas biotinidase deficiency presents later (mean age of onset 3 months) with hypotonia, lethargy, and seizures; the skin lesions resemble acrodermatitis enteropathica [11] and the alopecia is usually patchy. Essential fatty acid deficiency is known to cause an ichthyosiform erythroderma. Erythroderma has been described in neonates with ceftriaxone and vancomycin [12]. Vancomycin causes a generalized erythema and hypotension owing to histamine release. Seborrheic dermatitis and atopic dermatitis may rarely present with generalized erythroderma in neonates. Psoriasis at birth or in the neonatal age is very rare. Diffuse cutaneous mastocytosis can present at birth or in the neonatal period as diffuse erythroderma [13].

Candida species are currently one of the most common causes of nosocomial infection in NICUs [1]. Studies evaluating gastrointestinal tract colonization document approximately 5% of neonates are colonized with *Candida* on admission to the NICU; up to 50% are colonized by the end of the first week and almost three-fourths by the end of the first month of life [3]. The pathogenesis of invasive candidiasis involves a common sequence of events in all at-risk hosts: Colonization, resulting from adhesion of the yeast to the skin or mucosal epithelium (particularly the gastrointestinal tract); penetration of the epithelial barriers; locally invasive or widely disseminated disease. Dissemination to deep visceral organs results from hematogenous spread.

An outbreak of candidemia due to *C. tropicalis* involving 16 neonates (gestational age 28-36 weeks) is reported [14]. All infants had received parenteral nutrition and at least one course of antibiotics. The most common clinical manifestations included episodes of acute respiratory distress and lack of response to antibacterial, antibiotic therapy. *C. tropicalis* was recovered from blood in all the 16 infants, and urine cultures were positive in 14 infants. Environmental sampling done from mattresses and blankets used for neonates also yielded the same organism [14]. In our case, the baby probably acquired infection from a stay in the previous center.

CONCLUSION

Irrespective of its cause, neonatal erythroderma is a potentially life-threatening condition. Erythrodermic neonates and infants are at risk of hypernatremic dehydration and acidosis. Maintaining adequate oral or parenteral fluid intake with monitoring of serum electrolytes is mandatory.

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