We present the case of a preterm neonate who was born with respiratory distress and a papulo-vesicular rash that was diagnosed as congenital candidiasis (CC). The mother was asymptomatic. The cutaneous eruption and respiratory distress improved following treatment with systemic antifungals. Congenital candidiasis ranges in presentation from isolated cutaneous involvement to severe multisystem disease. Given its rarity among neonatal skin eruptions, heightened suspicion is required for prompt diagnosis and treatment.

Congenital Candidiasis: An Uncommon Skin Eruption Presenting at Birth

Rick Siriratsivawong, MD; Michelle Pavlis, MD; Saul R. Hymes, MD; Jonathan P. Mintzer, MD

Practice Points
• A high index of suspicion is required for the diagnosis of congenital candidiasis in the context of neonatal skin eruptions.
• Congenital candidiasis can present at birth in the absence of maternal symptoms of candidal infection.
• Early diagnosis and treatment of congenital candidiasis is crucial for the prevention of severe systemic infection.

Congenital candidiasis (CC) is a rare infection that typically presents within the first 6 days of life and ranges from a diffuse skin eruption to severe systemic disease, with or without cutaneous involvement, fetal demise, or early neonatal death. The majority of cases (82%) present as cutaneous eruptions that are typically detected within 24 hours of birth. Given the broad differential diagnosis for rashes in newborns that appear similar to more common eruptions, the diagnosis of CC may be delayed, causing an increased risk for adverse sequelae. Therefore, a heightened index of suspicion is required in promptly making the diagnosis and instituting appropriate treatment.

Case Report
A male neonate was born via spontaneous vaginal delivery at 37 weeks’ gestation with an Apgar score of 6/7 at 1 and 5 minutes. The mother reported treatment with nitrofurantoin during the week prior to delivery for a suspected urinary tract infection. All standard maternal prenatal laboratory tests were normal, except for positive group B streptococci colonization for which she received intrapartum ampicillin prophylaxis. The mother presented to our institution in preterm labor. Spontaneous rupture of the amniotic membrane occurred 12 hours prior to delivery with clear fluid. No prenatal fever, vaginal bleeding, or vaginal discharge was noted.

At birth, the patient demonstrated poor respiratory effort and a depressed heart rate (<100 beats per minute), which were rapidly corrected using positive pressure ventilation. Physical examination in the delivery room revealed numerous 1- to 2-mm erythematous papules and vesicles on the scalp, face, anterior aspect of the chest, abdomen, and extremities (Figure 1), with sparing of the posterior aspect of the trunk, palms, and soles. The patient was
subsequently transferred to the hospital’s neonatal intensive care unit.

In the neonatal intensive care unit a portable chest radiograph demonstrated a diffuse, coarse, interstitial pattern (Figure 2), and an infectious disease process was suspected to rule out fungal pneumonia. A sepsis evaluation also was performed. Empiric treatment with ampicillin, gentamicin, and acyclovir was initiated for possible bacterial or disseminated herpes simplex virus (HSV) infection.

The skin eruption persisted overnight and the dermatology department was consulted the following morning. A sample vesicle was unroofed for evaluation. A potassium hydroxide (KOH) preparation demonstrated yeast, and a Wright stain showed numerous neutrophils with visible yeast (Figure 3). Based on the clinical findings and chest radiograph, liposomal amphotericin B was started for presumptive disseminated CC. Placental examination revealed microabscesses of the placenta and umbilical cord (not shown), with yeast noted on Grocott-Gomori methenamine-silver stain (Figure 4). Further workup did not reveal involvement of other organ systems.

Antibacterial and antiviral coverage was discontinued 2 days following delivery with negative systemic bacterial cultures, including HSV polymerase chain reaction. The papulovesicular eruption resolved over several days without progressing to pustules. With clinical improvement and absence of evidence of a more severe fungal infection, liposomal amphotericin B was switched after 3 days to oral fluconazole for 10 days, followed by discharge from the hospital 10 days after delivery.

Comment

This case demonstrates an unusual presentation of CC. Although CC typically occurs in the setting of maternal vaginal discharge as well as in cases with a greater degree of prematurity, our case occurred in a nearly full-term neonate with systemic signs of respiratory distress and a diffuse skin eruption present at birth in the absence of maternal symptoms. Moreover, placental and umbilical cord pathology was notable for an infectious disease process. The lack of maternal symptoms in our case resulted in a low index of suspicion for this potentially severe infection.

Congenital candidiasis was first described in 1958, with approximately 100 reported cases in the literature by 2000. The most common presentation of CC is a generalized eruption of small macules, papules, and/or pustules on a 5- to 10-mm erythematous base involving the trunk, extensor surfaces, skin folds, and occasionally the palms and soles, but sparing the diaper area. In some cases, nail dystrophy can occur and nail plate involvement may be the sole manifestation of candidiasis. Premature neonates are at higher risk for systemic involvement and may present with more severe burnlike plaques at birth.

Congenital candidiasis is caused by in utero exposure to Candida species. Predisposing factors include cervical foreign bodies (eg, intrauterine...
device, cerclage), candidal vulvovaginitis, chorioamnionitis, and maternal exposure to antibiotics prior to the immediate antepartum period. One of the risk factors in our patient was maternal antibiotic exposure. The pathogenesis of CC likely involves vertical ascension of a maternal candidal infection, resulting in amniotic fluid infection and chorioamnionitis or funisitis, as observed in our patient. Grossly yellow plaques arranged in a necklacelike pattern and focal white microabscesses typically are seen. The skin eruption results from direct exposure to infected amniotic fluid, whereas systemic infection occurs following placental and/or umbilical cord involvement. Preterm neonates with decreased skin barrier function and overall impaired immunity may be at increased risk from topical exposure to infected amniotic fluid alone.

Diagnosis of CC is best achieved in consultation with a dermatologist by performing skin scrapings for KOH preparation, which generally demonstrates budding yeast and pseudohyphae. In addition to the yeast seen on KOH preparation in our case, a Wright stain demonstrated mostly neutrophils with rare eosinophils, which made a diagnosis of erythema toxicum less likely; the presence of yeast made pustular melanosis equally unlikely. In vesicular presentations, a Tzanck test should be performed to assess for HSV and varicella infections.

Although Candida albicans is a common vaginal pathogen in up to 35% of women, less than 1% of placentas demonstrate yeast on microscopy. In CC, however, the placenta and umbilical cord can demonstrate both gross and microscopic evidence of fungal infection, as seen in our patient. Grossly yellow plaques arranged in a necklacelike pattern and focal white microabscesses typically are seen. Microscopy may demonstrate yeast and pseudohyphae with a dense inflammatory reaction composed of polymorphonuclear leukocytes and mononuclear cells.

In full-term neonates with isolated skin disease, typical management is topical antifungals; however, in patients with systemic disease, a workup for infection of other organ systems should be initiated and systemic antifungal therapy should be initiated. Because preterm and low-birth-weight neonates are at a greater risk for systemic involvement and death, systemic antifungal therapy is recommended in these patients. Additionally, systemic treatment should be started for neonates with clinical or laboratory evidence of sepsis or if positive blood, urine, and/or cerebrospinal fluid cultures are reported. In less acutely ill neonates and at centers where C albicans predominates over azole-resistant or azole-tolerant Candida species such as Candida krusei or Candida glabrata, fluconazole may be appropriate for empiric therapy; otherwise, amphotericin B is appropriate. All systemic treatment should be guided by culture and sensitivities results.

The severity of illness at birth in our preterm neonate with multifocal pneumonia and yeast funisitis suggests that this infection was more than a simple case of CC. The clinical presentation of CC in our patient was rare because of the lack of maternal symptoms. Aldana-Valenzuela et al reported an additional case of systemic disease in a full-term neonate presenting with severe pneumonia and a skin rash with similarly rapid improvement following appropriate systemic treatment. Because of the potential risk for undertreating, we elected for an...
extended period (ie, 10 days) of antifungal coverage. Our case demonstrates some of the difficulties inherent in diagnosing and managing this uncommon pediatric disease entity.

REFERENCES