



Rash in an Extremely Low Birth Weight Infant

Stephen M Akers¹, Panitan Yossuck¹, Autumn S Kiefer¹, Michelle L Mitchell² and Kathryn S Moffett^{3*}

¹Department of Pediatrics, West Virginia University, USA

²Department of Infectious Diseases, Children's Hospital of Wisconsin-Milwaukee Campus, USA

³Department of Pediatrics, West Virginia University, USA

Abstract

Primary cutaneous aspergillosis (PCA) is one of several invasive fungal infections that have increased in incidence in the last four decades. We present a case of an extremely low birth weight infant born at 24 weeks gestation diagnosed with cutaneous aspergillosis, highlighting the risk factors and clinical findings associated with neonatal PCA. Additionally we discuss use of serum galactomannan testing as well as combination amphotericin B and voriconazole therapy. Early recognition of lesions characteristic of PCA is required to ensure prompt diagnosis and treatment, potentially preventing dissemination with favorable outcomes.

Keywords: Primary cutaneous aspergillosis; Extremely low birth weight; Prematurity; Serum galactomannan, amphotericin; Voriconazole

Introduction

Primary cutaneous aspergillosis (PCA) is a rare but serious cause of invasive fungal infections in an extremely low birth weight infant. This case report highlights the importance of rapid recognition, diagnosis and treatment, as well as risk factors and clinical findings associated with neonatal PCA. Additionally we discuss our utility of serum galactomannan testing and options for treatment in a VLBW infant, both of which we report as novel.

Case Presentation

A 24-week gestation male, birth weight 620 gram, was born to a 27-year-old mother by vaginal delivery secondary to placental abruption and preterm labor. Following initial resuscitation, his first week of life was complicated by mechanical ventilation, placement of a central venous catheter, hypotension, leukopenia, and concern for sepsis. Treatment included ampicillin, gentamicin, changed to vancomycin and meropenem, as well as dopamine and hydrocortisone. Despite negative cultures, he was treated for 7 days for clinical sepsis.

On day of life 9, physical examination revealed a violaceous bullous lesion on the infant's back with surrounding erythematous papules. Blood cultures as well as surface swabs for herpes simplex virus (HSV) polymerase chain reaction (PCR) testing were obtained. Antimicrobial therapy with vancomycin, gentamicin, fluconazole, and acyclovir was initiated. The lesion quickly flattened, forming a necrotic plaque measuring 4 cm x 2 cm (Figure 1). Wound and tissue cultures revealed *Aspergillus fumigatus*; mold blood cultures were no growth. Herpes simplex virus PCR testing was negative and bacterial cultures were sterile. A punch biopsy was performed on the lesion; presence of *Aspergillus* was confirmed by histopathology which revealed invasive septate fungal elements and leukocytoclastic debris (see Figure 2) and polarizable material (see Figure 3). This confirmed the diagnosis of primary cutaneous aspergillosis (PCA).

Treatment was changed to amphotericin B, with addition of voriconazole when serum galactomannan antigen was detected (3.664 index with reference range: <0.5 index). Transthoracic echocardiogram, renal ultrasound, and eye exam did not reveal evidence of *A. fumigatus* dissemination; due to risk of fungal inoculation from the rash location during a lumbar puncture, no cerebrospinal fluid was obtained. Following 6 weeks of antifungal treatment and frequent excisional wound debridement, the lesion healed, leaving pink tissue with minimal scarring. At the end of treatment, serum galactomannan antigen was not detected.

Primary cutaneous aspergillosis (PCA) is an invasive fungal infection with increasing incidence in the last four decades. Extremely low birth weight (ELBW) infants, due to their immature skin/ lack

OPEN ACCESS

*Correspondence:

Kathryn S Moffett, Department of Pediatrics, West Virginia University, HSC-9214, Morgantown, USA, Fax 304-293-1216;

E-mail: kmoffett@hsc.wvu.edu

Received Date: 06 Nov 2018

Accepted Date: 21 Nov 2018

Published Date: 28 Nov 2018

Citation:

Akers SM, Yossuck P, Kiefer AS, Mitchell ML, Moffett KS. Rash in an Extremely Low Birth Weight Infant. *Ann Infect Dis Epidemiol.* 2018; 3(2): 1034.

ISSN: 2475-5664

Copyright © 2018 Kathryn S

Moffett. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

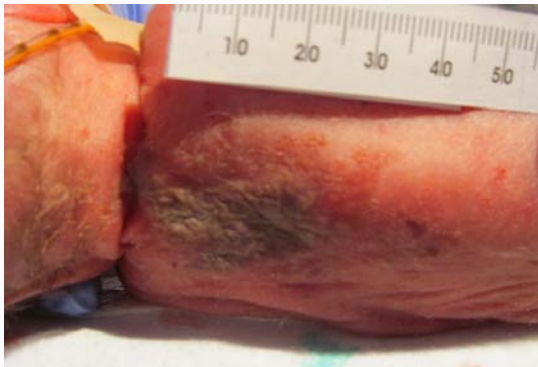


Figure 1: Appearance of the 4 cm x 2 cm necrotic lesion on the neonate's back two days after it first appeared.

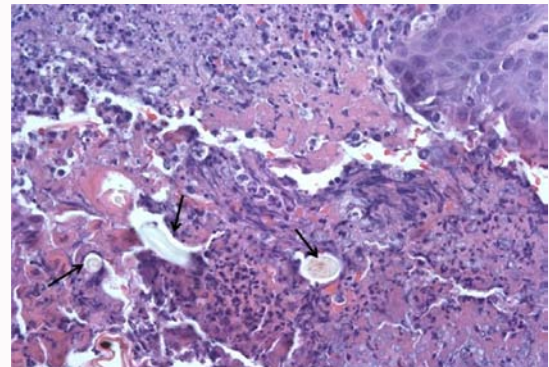


Figure 3: Biopsy with area of overlying scab containing polarizable material (arrows). (H&E stain) Original magnification x 400.

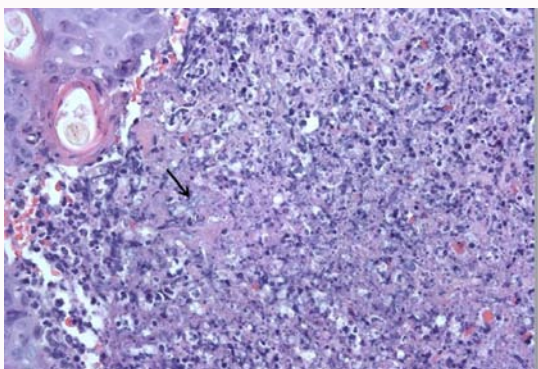


Figure 2: Biopsy with area of dermal infiltrate containing neutrophils, leukocytoclastic debris and fungal elements- (arrow) (H&E Stain) Original magnification x 400.

of barrier, receipt of broad-spectrum antibiotics, and poor immune function, are at risk for invasive aspergillosis of the respiratory tract, sinuses, or skin [1-11]. Pathogenesis occurs when *Aspergillus* conidia are deposited on mechanically disrupted skin after which subsequent invasion by fungal hyphae leads to infection [12,13]. Skin lesions are classically described as erythematous patches and/or plaques with necrotic ulcers.

A review of neonatal PCA highlights the risk factors and clinical presentation: 1) premature delivery, especially ELBW, 2) use of support devices, such as mechanical ventilation and central venous catheter, 3) exposure to corticosteroids, 4) receipt of broad-spectrum antibiotics, and 5) environmental exposure to *Aspergillus* [1-11]. Hospital renovation, as well as exposure to *Aspergillus*-contaminated latex gloves, has been linked to PCA outbreaks in neonatal intensive care units (NICUs) [12]. Renovations were being conducted at remote sites in our institution, but not directly in our NICU; environmental testing of the infant's NICU pod unit as well as ventilation duct work did not demonstrate environmental *Aspergillus* contamination. No other cases of PCA occurred in the 24 months following this case.

The use of serum galactomannan, a cell-wall product of *Aspergillus*, is a potential diagnostic marker of invasive aspergillosis, in addition to its usefulness to monitor treatment response [13,14]. Pediatric studies have demonstrated high sensitivity and specificity of galactomannan, 89% and 85% respectively, for aide in diagnosing invasive aspergillosis [13]. A limitation to the use of galactomannan in neonates includes a lack of studies performed as well as the inability to calculate the positive- and negative-predicted values of

galactomannan, given the unknown incidence of infection in the neonatal population. A neonatal factor which may influence false positive galactomannan testing includes gastrointestinal colonization with *Bifidobacterium* in these small patients [15]. It has been suggested, however, that in the clinical setting of PCA, a positive galactomannan test is diagnostic of disseminated disease [13]. Disseminated *Aspergillus* infection carries mortality approaching 77%; therefore the usefulness of galactomannan may be timely and lead to prompt diagnosis and treatment of PCA.

Successful treatment of PCA is accomplished by combined medical and surgical approaches [15]. Based largely on adult studies of pulmonary aspergillosis, guidelines recommend voriconazole as a first line agent for invasive aspergillosis, while most of the reported cases of PCA in the literature have been treated with amphotericin B [8]. Our patient was initially treated with amphotericin B, however when galactomannan levels were found to be elevated, combination therapy with voriconazole was successfully added. This case illustrates that studies are needed to delineate the role of serum galactomannan in suspected neonatal aspergillosis, as well as to provide definitive treatment guidelines of *Aspergillus* infection in neonates.

References

1. Woodruff CA, Hebert AA. Neonatal primary cutaneous aspergillosis: case report and review of the literature. *Pediatr Dermatol.* 2002;19(5):439-44.
2. Herron MD, Vanderhooft SL, Byington C, King JD. Aspergillosis in a 24-week newborn: a case report. *J Perinatol.* 2003;23(3):256-9.
3. Andresen J, Nygaard EA, Stordal K. Primary cutaneous aspergillosis (PCA)--a case report. *Acta Paediatr.* 2005;94(6):761-2.
4. Frankenbusch K, Eifinger F, Kribs A, Rengelshauseu J, Roth B. Severe primary cutaneous aspergillosis refractory to amphotericin B and the successful treatment with systemic voriconazole in two premature infants with extremely low birth weight. *J perinatol.* 2006;26(8):511-4.
5. Santos RP, Sanchez PJ, Mejias A, Benjamin DK, Walsh TJ, Patel S, et al. Successful medical treatment of cutaneous aspergillosis in a premature infant using liposomal amphotericin B, voriconazole and micafungin. *Pediatr Infect Dis J.* 2007;26(4): 364-66.
6. Etienne KA, Subudhi CP, Chadwick PR, Settle P, Moise J, Magill SS, et al. Investigation of a cluster of cutaneous aspergillosis in a neonatal intensive care unit. *J Hosp Infect.* 2011;79(4):344-8.
7. Rogdo B, Kahlert C, Diener PA, Micallef J. Primary cutaneous aspergillosis in a preterm neonate. *BMJ Case Rep.* 2014;2014.
8. Frick MA, Boix H, Camba Longueira F, Martin-Gomez MT, Rodrigo-Pendás JÁ, Soler-Palacin P. Primary Cutaneous Aspergillosis in a Preterm

- Infant. *Pediatr Infect Dis J*. 2016;35(6):704-6.
9. Gallais F, Denis J, Koobar O, Illenseger L, Astruc D, Herbrecht R, et al. Simultaneous primary invasive cutaneous aspergillosis in two preterm twins: case report and review of the literature. *BMC Infect Dis*. 2017;17(1):535.
 10. Kimura H, Mitsuto I, Taguchi R, Anzawa K, Mochizuki T. Primary cutaneous aspergillosis caused by *Aspergillus tamarii* in a premature infant with extremely low birth weight: A case report with short review. *J Dermatol*. 2018;45(5):622-5.
 11. Kusari H, Mitsuto I, Taguchi R, Anzawa K, Mochizuki T. A Primary cutaneous aspergillosis at the site of cyanoacrylate skin adhesive in a neonate. *Pediatr Dermatol*. 2018;35(4):494-7.
 12. Stock C, Veyrier M, Raberin H, Fascia P, Rayet I, Lavocat MP, et al. Severe cutaneous aspergillosis in a premature neonate linked to nonsterile disposable glove contamination? *Am J Infect Control*. 2012;40(5):465-7.
 13. Choi SH, Kang ES, Eo H, Yoo SY, Kim JH, Yoo KH, et al. *Aspergillus galactomannan* antigen assay and invasive aspergillosis in pediatric cancer patients and hematopoietic stem cell transplant recipients. *Pediatr Blood Cancer*. 2013;60(2): 316-22.
 14. Patterson TF, Thompson GR, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Executive summary: practice guidelines for the treatment and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):433-42.
 15. Arendrup MC, Fisher BT, Zaoutis TE. Invasive fungal infections in the paediatric and neonatal population: diagnostics and management issues. *J Clin Microbiol*. 2009;15(7): 613-24.