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Authors

Scollan, Margaret

Levin, Laura

Lucky, Anne

et al.

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Characterization of Wound Microbes in Epidermolysis Bullosa: A Focus on Pseudomonas Aeruginosa

Margaret E Scollan, MSc[1], **Laura E. Levin, MD**[2], **Anne W. Lucky, MD**[3], **Kristen P. Hook, MD**[4], **Kathleen Peoples**[5], **Anna L Bruckner, MD**[6], **James A. Feinstein, MD MPH/MSPH**[7], **Elena Pope, MD**[8], **Catherine C. McCuaig, MD**[9], **Julie Powell, MD**[10], **Lawrence F. Eichenfield, MD**[11], **Moise L. Levy, MD**[12], **Lucia Diaz, MD**[13], **Sharon A. Glick, MD**[14], **Amy S. Paller, MD**[15], **John C. Browning, MD MBA**[16], **Kimberly D. Morel, MD**[17]

[1.]Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, USA

[2.]Department of Dermatology, Columbia University Irving Medical Center, New York, NY, USA

[3.]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[4.]Department of Dermatology, University of Minnesota Medical School, Minneapolis, MN, USA

[5.]Children's Hospital Colorado, Aurora, Colorado

[6.]Departments of Dermatology and Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA

[7.]Departments of Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA

[8.]Section of Dermatology, Division of Paediatric Medicine, Hospital for Sick Children, Toronto, ON, Canada

[9.]Departments of Pediatrics and Dermatology, CHU Sainte-Justine, University of Montreal, Montreal, QC, Canada

[10.]Department of Dermatology, CHU Sainte- Justine, University of Montreal, Montreal, QC, Canada

[11.]Departments of Pediatrics and Dermatology, University of California San Diego, San Diego, CA, USA

Corresponding Author: Margaret Scollan, Research Fellow, Department of Dermatology, Division of Pediatric Dermatology, Columbia University, 161 Fort Washington Avenue, 12th Floor, New York, NY 10032, margaret.e.scollan@gmail.com, Work: 212-305-0726, Fax: 212-342-3124.

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Dr. Glick: Investigator for Lenus Pharmaceuticals
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Dr. Morel: Investigator for Phoenix Tissue Repair

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[12.]Departments of Pediatrics and Dermatology, Dell Children's Medical Center, Austin, TX, USA

[13.]Department of Dermatology, Dell Children's Medical Center, Austin, TX, USA

[14.]Department of Dermatology, State University of New York Downstate Medical Center, Brooklyn, NY, USA

[15.]Departments of Pediatrics and Dermatology, Northwestern University, Chicago, IL, USA

[16.]Department of Dermatology, The Children's Hospital of San Antonio, San Antonio, TX, USA

[17.]Departments of Pediatrics and Dermatology, Columbia University Irving Medical Center, New York, NY, USA

Abstract

The most common bacteria isolated from wound cultures in patients recorded in the Epidermolysis Bullosa Clinical Characterization and Outcomes Database (EBCCOD) are *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Given the prevalence of *Pseudomonas Aeruginosa* in this patient population and prior research implicating *Pseudomonas Aeruginosa's* potential role in carcinogenesis, we sought to further analyze patient's with recorded wound cultures positive for *Pseudomonas aeruginosa* in the EBCCOD. The below research in brief, provides a descriptive analysis of this subset of patients and highlights potential avenues for future longitudinal studies that may have significant implications in our wound care management for patients with epidermolysis bullosa.

Introduction

Patients with epidermolysis bullosa (EB) require care of wounds that are often colonized or infected. The Epidermolysis Bullosa Clinical Characterization and Outcomes Database (EBCCOD) is a repository of information from patients with EB from centers in North America. The most common bacteria isolated from wound cultures in this patient population were *Staphylococcus aureus* (SA) and *Pseudomonas aeruginosa* (PA).[1] PA may colonize wounds, inhibit wound healing or lead to serious bacterial infections. *In vitro* studies have also implicated flagellated bacteria, like PA, as potential contributors to wound-induced tumor formation.[2] Given these findings, we sought to further characterize this subset of patients with recorded wound cultures positive for PA.

Methods

We conducted a retrospective analysis of patients in the EBCCOD, a Research Electronic Data Capture (REDCap) database maintained at the University of Colorado Denver through July 2021. Characteristics of patients with wound cultures positive for PA were analyzed including demographics, EB type, wound characteristics, and development of squamous cell carcinoma (SCC). Statistical analyses were performed using R version 4.0.5.

Results

Of 976 total patients, 203 patients had at least one positive wound culture for a pathogenic microbe. 17 patients had at least 1 wound culture performed, but with no growth or skin flora only. Of the 203 patients with at least 1 positive wound culture, 173 (85%) had at least one culture positive for SA (93 positive for methicillin-sensitive SA, 58 positive for methicillin-resistant SA, and 24 unknown susceptibilities) and 80 (39%) positive for PA (49 patients had cultures positive for both SA and PA).

Demographics

Of the 80 patients with a wound culture positive for PA, 38 patients were male and 42 were female. 2 had dominant dystrophic EB (DDEB), 59 had recessive dystrophic EB (RDEB), 15 had junctional EB, and 4 had EB simplex [Table 1]. The mean age of patients at the time of their first recorded culture positive for PA was 12.1 years (standard deviation (SD) 12, age range 0 to 67 years). The mean age of the patients at their first recorded culture positive for *Staphylococcus aureus* was 10.1 years (SD 10, age range 0 to 66.7 years).

Wound Characteristics and SCC

Of 203 patients with at least one positive culture, 132 patients had over 1 culture (average 7.4 cultures per patient). For patients with at least 1 wound culture positive for PA (80 total patients) there were 139 unique culture sites/locations on the body (average 1.7 unique sites per patient). PA was found in wounds on the head and neck (26%), lower extremities (38%), trunk (36%) and upper extremities (26%). Chronic wounds were reported as a feature of their skin findings in 42 (76%) patients, acute wounds in 13 (24%) (no information for 25 patients). 34 (60%) had wounds noted to have signs of infection and 23 did not (40%) (no information for 23 patients). However, wound chronicity and signs of infection were not correlated with the site or timing of the wound culture.

Squamous Cell Carcinoma

34 patients had a diagnosis of SCC recorded in the registry overall (patients with and without information regarding wound cultures) at the time of data collection. Of these 34 patients, 16 patients had a positive culture for a pathogenic bacterium and 18 had no recorded wound culture. Of the 16 patients with SCC and a recorded wound culture, 8 had a wound culture positive for PA and 13 had a wound culture positive for SA (7 with overlap). No patients with a diagnosis of SCC and a recorded culture, had a culture with no growth (or normal skin flora).

Average age of onset (using the date of SCC diagnosis recorded in registry) of patients with SCC with at least one recorded positive culture for PA, (total 8 patients, 7 with recorded age) was 23.97 years (age range 15.46–39.37 years, SD 7.4 years). Average age of onset of patients with a diagnosis of SCC, with a recorded positive culture to any other pathogenic bacteria (total 18 patients, 12 with recorded age) was 24.56 years (age range 14.41–34.75 years, SD 5.80).

Discussion

PA is commonly found in wounds of patients with EB. PA may colonize wounds, impede wound healing, or lead to serious bacterial infections. In our cohort, cultures positive for PA were found equally in males and females and more commonly in severe EB subtypes such as RDEB and JEB. PA was found on patient's wounds as early as infancy and on multiple locations of the body and more so in patients with chronic wounds. The mean age of patients at the time of their first recorded positive culture for PA was 12.1 years and the mean age of the patients at their first recorded positive culture of *Staphylococcus aureus* was 10.1 suggesting SA colonization precedes PA, however a variety of other factors, such as disease severity, wound care and timing of the culture impact the age of presentation of these microbes.

Of note, wound culture practices among physicians vary. Cultures may be taken in the absence of concern for infection for routine surveillance or for objective data of response to a treatment. The presence or absence of signs of wound infection was noted in the clinical information of the patient although interventions or effectiveness of interventions are not recorded in the registry. Additionally, patients are entered into the registry at various ages precluding culture information prior their participation.

Overall, patients with a diagnosis of SCC who were had a recorded culture, were more likely to have PA positive wounds than patients without SCC. The limited numbers of patients with both PA and SCC, preclude drawing conclusions of statistical significance.

Clinicians should have a heightened suspicion for PA, particularly in those patients with severe subtypes and/or chronic wounds. Future longitudinal studies are needed to better characterize wound characteristics, prognosis, and squamous cell carcinoma risk in patients with EB who are colonized or infected with PA.

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Table 1.

Demographic and EB type of patients with cultures positive for Pseudomonas Aeruginosa in the EBCCOD.

Sex	**Number of patients with culture positive for PA (n=80)**	**Percent (%)**
Male	38	47.5%
Female	42	52.5%
EB Type		
Dystrophic EB	61	76.3%
DDEB	2	2.5%
RDEB	59	73.8%
Junctional EB	15	18.8%
EB Simplex	4	5.0%