First-line Therapy Response in Patients with Pyoderma Gangrenosum: A Retrospective Study

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Introduction

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis, with 50-70% of patients presenting with concomitant **PG-related conditions** including inflammatory bowel disease, inflammatory arthritis, hematological disorders, and malignancies.[1]

Challenges with PG treatment paradigm today:

- No standardized or FDA-approved therapies
- Extrapolated from uncontrolled studies and experience
- Traditional first-line therapies prednisone or cyclosporine (CsA) have serious toxicities
- Response to therapies is unpredictable[2]

Goal of study:

- Help guide initial treatment choice by identifying patient or clinical characteristics associated with response to prednisone/CsA alone

Methods

Retrospective review identified 26 PG subjects treated with first-line prednisone or CsA between 2008-2023 at an academic institution. PG was defined as treating physician's diagnosis and application of 3 established diagnostic frameworks.[3, 4, 5] Each subject met a median of 2 criteria, and the PARACELSUS framework captured the highest number of subjects (n=19).

Response to treatment was categorized as:

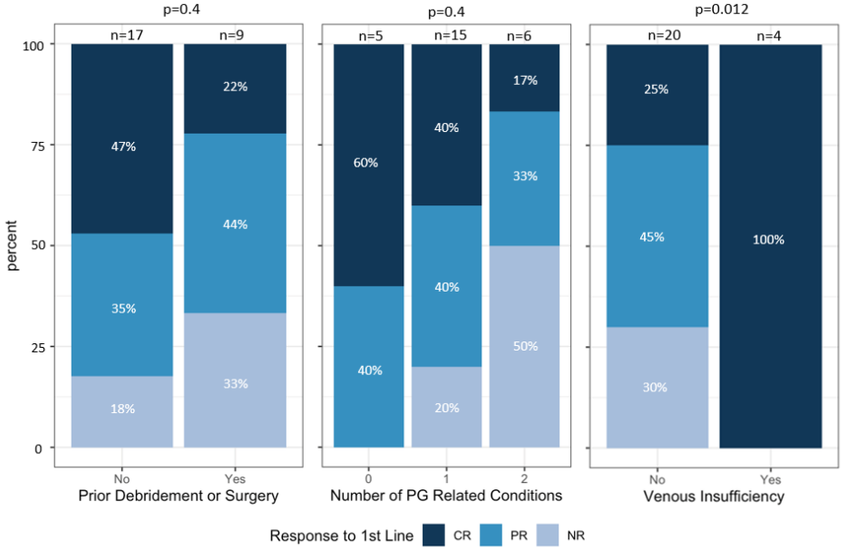
- Complete response (CR), full resolution of inflammatory lesion and ability to taper off prednisone and CsA
- Partial response (PR), reduction in ulcer size
- No response (NR), no reduction in inflammation or ulcer size

To test the association between selected variables and response (CR vs PR/NR), Fisher's exact test was used for categorical variables and Wilcoxon Rank-sum test for continuous variables, and significance defined as $p<0.05$.

Results

- 10 out of 26 subjects (38%) had CR; 16 out of 26 subjects (62%) had PR/NR
- All 4 subjects with documented **venous insufficiency** had CR (p=0.012)
- Inverse relationship with CR and **PG-related conditions** (p=0.4):
  - 0 PG-related conditions: 3 out of 5 subjects (60%) had CR
  - 1 PG-related condition: 6 out of 15 subjects (40%) had CR
  - 2 PG-related conditions: 1 out of 6 subjects (17%) had CR
- All 3 subjects with **inflammatory arthritis** had PR/NR (p=0.3)
- History of **debridement or surgery** preceding PG onset may adversely impact outcome (p=0.4):
  - Without prior hx: 8 out of 17 subjects (47%) had CR
  - With prior hx: 2 out of 9 subjects (22%) had CR

Fig 1. Proportion of Treatment Response Type Across Various Clinical Characteristics



Discussion

This study suggests that PG patients with:

- **Venous insufficiency** are better candidates for standard first-line therapy
- **Comorbid PG-related conditions** or **recent debridement or surgery** may benefit from concurrent initiation of additional therapeutic agents to achieve faster disease control and decrease morbidity from prolonged exposure to first-line agents

The association of venous insufficiency with CR is surprising, given impaired wound healing with venous stasis. However, chart review confirmed no medications altering the wound healing process, though increased adherence to compression dressings could be a confounding factor.

Shared pathophysiologic processes driving PG and PG-related conditions may account for greater success in targeting a common pathologic pathway over broad immunosuppression alone, perhaps particularly so for inflammatory arthritis. Our data also suggests that standard first-line treatment is not sufficient to control PG actively demonstrating pathergy.

Limitations include:

- Single-institution retrospective study design
- Small sample size
- Reliance on clinical characteristics in setting of variable response to therapies – tools such as single cell RNA sequencing may be more appropriate to identify individualized treatment[6]

References

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