Severe Pyoderma Gangrenosum Associated with Etanercept Use

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Learning Objectives

1. To review the diagnostic criteria for pyoderma gangrenosum
2. To understand the potential utility of TNFα inhibitors and JAK inhibitors in the treatment of pyoderma gangrenosum
3. To understand the concept of paradoxical adverse events, particularly in the setting of treatment with biologic medications

Background

Pyoderma gangrenosum (PG) is a chronic relapsing neutrophilic dermatosis characterized by autoinflammation and cutaneous ulceration.1 TNFα inhibitors, including etanercept, have been reported in the literature to successfully control PG.2 Diagnosis of PG can be made when patients present with the two major criteria and at least two minor criteria of PG.1

Major criteria include:

- “Rapid progression of a painful, necrolytic, cutaneous ulcer with an irregular, violaceous, and undermined border”
- “Exclusion of other causes of cutaneous ulceration”

Minor criteria include:

- “History suggestive of pathergy”
- “Clinical finding of cribriform scarring”
- “Systemic diseases associated with PG”
- “Histopathologic findings”
- “Treatment response”

Case Description

A 75-year-old man with a 23-year history of rheumatoid arthritis (RA) was started on etanercept as an outpatient due to poor disease control.

Five months before the current presentation, he developed a painful ulcer with violaceous borders on his right leg after mild, incidental trauma.

Due to progressive worsening of this ulcer, a biopsy was performed three months prior to presentation, which showed ulceration with marked acute and chronic inflammation involving the dermis and subcutis, compatible with PG.

This patient therefore met both major criteria for PG, as well as minor criteria pertaining to pathergy, systemic disease, and histopathology.

The patient was treated with 20 mg prednisone daily, as well as minocycline and topical betamethasone.

Hospital Presentation

At the time of presentation, physical exam was notable for significant worsening of the PG (Figure 1).

- The largest lesion on the right lower shin was 9.0 cm by 5.5 cm with exposed tendon and suppurative malodorous drainage. This was surrounded by smaller ulcers with granulating bases.
- Multiple shallow ulcers were present on the left shin as well.
- Labs were significant for:
  - White blood count of 19,500 cells/mm3
  - Erythrocyte sedimentation rate of 55 mm/hr
  - C-reactive protein of 262.38 mg/L
  - Negative blood cultures

Hospital Course

- Etanercept was immediately discontinued in the setting of continued ulcer growth.
- The patient was started on prednisone, niacinamide, and hydromorphone for pain control.
- The patient underwent an MRI which showed an abscess under the largest ulcer. Drainage was pursued due to concern that an infectious abscess could exacerbate PG.
- Bacterial, acid fast bacilli, and mycology cultures resulted negative.
- Aggressive treatment of PG was pursued. The patient was started on tofacitinib for treatment of RA and PG.
- Several weeks later, the patient was noted to have slow healing and granulation of his wounds (Figure 2).

Conclusions

- The phenomenon of PG as a paradoxical adverse event in the setting of TNFα inhibitor use has been previously established, despite TNFα inhibitors being recognized as an efficacious treatment for PG. However, to our knowledge, this is the most severe case of PG possibly resulting from treatment with a TNFα inhibitor reported in the literature.
- Due to persistent disease despite discontinuation of etanercept, treatment with tofacitinib, a JAK inhibitor, was pursued. This led to improvement of bilateral ulcers, while simultaneously treating the patient’s RA to good effect.
- Further study of the role of TNFα inhibitors and JAK inhibitors in both the development and treatment of PG will be necessary in the future.

References


Figure 1: Images of the left and right lower extremity at the time of presentation to the Emergency Department.

Figure 2: Images of bilateral lower extremities following initiation of tofacitinib.