Rapid response to infliximab in a patient with recalcitrant pyoderma gangrenosum and rheumatoid arthritis

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Abstract

Pyoderma gangrenosum (PG) is a rare, chronic, recurrent cutaneous ulcerative disease. The pathogenesis of PG remains unknown but the association of this condition with inflammatory bowel disease and rheumatoid arthritis makes it likely that TNF-α plays an integral role in the development of the disease, with TNF-α inhibitors having been reported as therapy in resistant cases. Here-in we report a case of resistant pyoderma gangrenosum in a patient with rheumatoid arthritis which showed rapid response to infliximab.

Introduction

Pyoderma gangrenosum is a rare, chronic, recurrent cutaneous ulcerative disease. It is an immune mediated inflammatory condition and commonly occur on the lower extremities (pretibial area), but can occur anywhere including mucous membranes. Pyoderma gangrenosum is idiopathic in 25%-50% of patients but is also associated with several systemic diseases such as inflammatory bowel disease (20-30%) and rheumatoid arthritis (20%).

PG commonly affects females between 20 and 50 years of age.

Classic presentation of pyoderma gangrenosum is an ulcer with irregular undermined edges and gunmetal colour border which heals with atrophic cribriform pigmented scars. There are several clinical variants of pyoderma gangrenosum, namely vesiculo-bullous, pustular, superficial granulomatous, pyostomatitis vegetans.

Defects in cellular immunity, monocyte and neutrophil function and humoral immunity have been reported in pathogenesis of pyoderma gangrenosum. TNF-α, IL8 and IL17 are the main pathogenic cytokines.

Conventional management of PG includes topical therapy, often in combination with systemic agents. Local treatment includes gentle wound cleaning and dressing, topical corticosteroids, topical tacrolimus and intralesional injection of corticosteroids. The mainstay of systemic treatment is immunosuppression. Oral corticosteroids are most often used initially, but a number of other immunomodulators have been used in the management of PG. Infliximab is a monoclonal antibody against TNF-α and has been approved for the use in resistant Pyoderma gangrenosum associated with inflammatory bowel disease and rheumatoid arthritis.

Case report

A 24 year old female presented with a chronic ulcer over left leg of two years duration. She had large joint inflammatory arthritis involving bilateral knee joints, ankle joints and shoulder joints for one-year duration. She did not have systemic symptoms such as loss of appetite, weight loss, nocturnal fever or gastrointestinal symptoms such as abdominal pain and chronic diarrhea.

Examination revealed a shallow ulcer with granulation tissue in the base, undermined edges and gunmetal colour border. Rest of the clinical examination including joints was normal.

Incisional biopsy at the ulcer edge revealed perivascular infiltration of lymphocytes and infiltration extending into subcutaneous fat.

Serological examinations showed positive result for rheumatoid factor (RF) (176 IU/ml), negative results of anticyclic citrullinated peptide antibody (ACPA) and antinuclear antibodies (ANA). Her upper GI endoscopy and lower GI endoscopy were normal.

The patient was initially treated with oral prednisolone 1mg/kg dose, oral methotrexate 15mg weekly and methyl prednisolone pulse therapy. As the response to systemic immunosuppression was poor even after one year of treatment, the patient was

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commenced on intra venous infliximab 5mg / kg dose 0, 2, and 6 weeks, and every 8 weeks thereafter, in combination with oral prednisolone and methotrexate which were subsequently discontinued. Signs of improvement were observed after the second course of infliximab, and the size of the ulcer started reducing with simultaneous improvement of joint symptoms. Ulcer completely healed after third dose of infliximab.

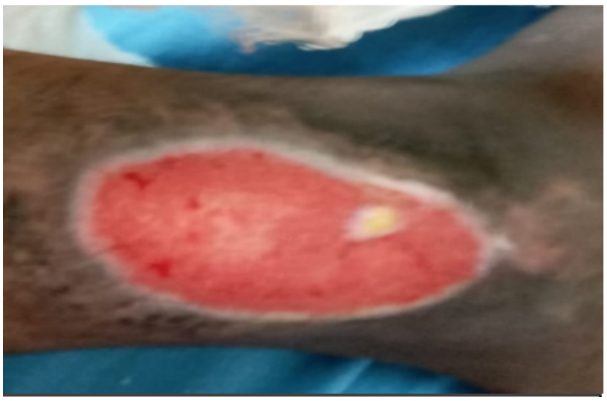

Figure 1. *At inital presentation.*

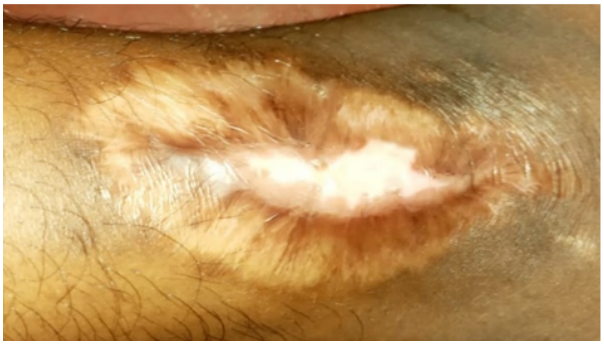

Figure 2. *After third dose of infliximab.*

Discussion

This case demonstrates the benefits of infliximab in healing of rheumatoid arthritis associated resistant PG ulcers.

The mainstays of systemic treatment include corticosteroids and immunosuppressive agents. Immunosuppressive drugs that are used in treatment of pyoderma gangrenosum are MTX, cyclosporine, azathioprine, cyclophosphamide, MMF, tacrolimus and dapsone. These drugs are known to be associated with serious side effects, including myelosuppression, nephrotoxicity, and hepatotoxicity. Antimicrobial treatments such as minocycline have also been used with some success.

Infliximab is a chimeric monoclonal antibody for TNF-a that is administered intravenously. In the literature a few recent case reports have demonstrated good response to treatment of pyoderma gangrenosum with infliximab.

Our patient who is a young female of the child bearing age has had a recalcitrant PG in despite aggressive systemic therapy which affected her functional and psychological status. Infliximab showed rapid clinical improvement after second course of injection with complete healing after third course.

When introducing biologics for recalcitrant dermatological conditions one should consider cost efficacy, in the setting of a developing country like Sri Lanka. Infliximab has relatively low cost when comparing with the other biologics available in Sri Lanka specially due to availability of biosimilars. It has convenient dosing regimen as well. Improvement in functional status of the patient and reduction in health care resource utilization as a result of biologic use have largely offset the increased drug costs.

Hence infliximab should be considered in the setting of a recalcitrant pyoderma gangrenosum with rheumatoid arthritis when the conventional therapies have failed, as both conditions will benefit from this valuable therapeutic option.

References

1. Jean L, Bolognia, Joseph L. Jorizzo, Julie. V Schaffer. Dermatology, 4th edition.
2. Christopher EM. Griffiths, Jonathan Barker, Tanya Bleiker, Robert Chalmers, Daniel Creamer. Rook's Textbook of Dermatology, Ninth Edition.
3. Masahiro T, Takeshi N, *et al*. Use of infliximab in a patient with pyoderma gangrenosum and rheumatoid arthritis. *Modern Rheumatology* 2010; **20**: 598-601.
4. Swale VJ, Saha M, *et al*. Pyoderma gangrenosum outside the context of inflammatory bowel disease treated successfully with infliximab. *Clinical and experimental Dermatology* 2005; **30**: 134-6.