Ustekinumab for Infliximab Resistant Peristomal Pyoderma Gangrenosum: Case Report

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ABSTRACT

Peristomal Pyoderma Gangrenosum is a subtype of Pyoderma Gangrenosum, characterized by a sterile inflammatory neutrophilic dermatosis that occurs near abdominal stomas. Most of these lesions are associated with an underlying disease, most commonly IBD. It can also occur in patients who have had an ileostomy or colostomy for other diseases such as malignancy or diverticular disease [1]. Peristomal pyoderma gangrenosum has been reported with an incidence of 0.6% among all patients with abdominal stomas [2]. Treatment of Peristomal PG often requires a combination of local wound care and systemic medications. Long term immunosuppression and TNF inhibitors are the drugs that have shown efficacy in treating PG. In this case report, we present an evidence of a potential additional line of treatment for peristomal pyoderma gangrenosum. Ustekinumab “Stelara”, a recently FDA approved drug for the treatment of IBD, has shown to be effective in treating our 58-year-old female who has been struggling with a refractory infliximab-resistant Peristomal PG for two years. Ustekinumab is a human IgG1k monoclonal antibody that blocks both IL-12 and IL-23 cytokines disrupting the chronic inflammation that is a hallmark of IBD.

Keywords: Ustekinumab, peristomal pyoderma gangrenosum, Infliximab-resistant

1. INTRODUCTION

Initially described in 1930 by Brunsting[3], Pyoderma Gangrenosum (PG) is a rare but serious ulcerating skin condition. It is characterized by a painful, chronic, and recurrent lesion that most commonly affects the legs but could potentially occur on any skin surface. It usually starts with a small papule, which then develops into a large deep ulcer with a well-defined, undermined edge. Classical, pustular, Bullous, vegetative, and peristomal are all variants of pyoderma gangrenosum, with the classical being the most common.

Peristomal Pyoderma Gangrenosum, which occurs near abdominal stomas, is a rare subtype of PG comprising about 15% of all cases [4]. Peristomal PG can occur in patients who have had an ileostomy or colostomy for Inflammatory bowel disease, malignancy, and diverticular disease. A large questionnaire-based study found a 0.6% annual incidence of peristomal pyoderma among all patients with abdominal stomas regardless of etiology [5]. Treatment of PG is mostly empirical, often requiring a combination of local wound care and systemic medications. Long term immunosuppression with corticosteroids, cyclosporine, and tacrolimus has been the mainstay of treatment. Recently, TNF inhibitors such as infliximab has also been shown to be effective in treating pyoderma gangrenosum.
Ustekinumab, sold under the brand name “Stelara”, is a human monoclonal antibody that was first used to treat psoriasis. In September, 2016 FDA approved the use of Ustekinumab for the treatment of IBD. Ustekinumab is designed to interfere with the triggering of the body's inflammatory response through the suppression of certain cytokines. Specifically, it blocks interleukin IL-12 and IL-23 which have been implicated as an important contributors to the chronic inflammation that is a hallmark of Crohn’s disease. Ustekinumab now provides another option of treatment for both psoriasis and IBD patients.

2. CASE REPORT

This patient is a 58-year-old female with a past medical history of crohn’s since 1999, and a past surgical history of ileocolic resection and a robotic Abdominoperineal Resection (APR) for rectal cancer. The patient is not a smoker and does not have a family history of crohn’s or colorectal cancer. Her crohn’s disease started in 1999 when the patient was 39 years old. The disease was controlled on Mesalamine, Azathioprine, Budesonide until 2006 when infliximab was needed as an add-on therapy to control her symptoms. Many attempts were made to stop Azathioprine but she had recurrent symptoms in terms of RLQ pain, loss of appetite, and feeling ill. In 2013, our patient was diagnosed with rectal cancer. Chemotherapy was started but she did not tolerate treatment due to severe pancytopenia with sepsis. Her adverse reaction to treatment required the cessation of chemotherapy and to proceed with surgery. A robotic assisted APR with a permanent colostomy on mid left abdomen was performed. She tolerated the procedure well and had regular follow up afterwards. Her stoma worked well for two years after surgery, until she started experiencing discomfort and ulceration over the stoma site, biopsy was consistent with Pyoderma Gangrenosum. The patient was started on oral steroids and infliximab. Over the course of two years, even though Infliximab dose was increased to 10-mg/kg and to a frequency of 6 per week, along with regular local Triamcinolone injections, and supervised wound care, only a mild improvement was noted. Her recent reaction to chemotherapy was worrisome in terms of choosing the best next option of treatment. A decision was made to avoid using cyclosporine, tacrolimus and alkylating agents for the possible bone marrow suppression. Ustekinumab “Stelara”, a new FDA approved biologic for the treatment of Crohn’s was then started. Stelara 90 mg injections were given every 8 weeks. On two months follow up and after two years of failed attempts to slightly reduce the size of the ulcer, the patient’s Peristomal PG was improving. The skin around the ulcer was less inflamed and the ulcer was more dried out. In a period of 4 months, the ulcer started getting smaller with new healthy skin building up towards the stoma and a healthier ulcer bed. (figure1), (figure2), (figure3).

Figure 1: demonstrates the pyoderma gangrenosum before Ustekinumab

Figure 2: demonstrates the pyoderma gangrenosum before Ustekinumab
Glucocorticoids are the most common systemic drugs because of their rapid action. Systemic cyclosporine can also be used as an alternative first-line treatment for patients who cannot tolerate systemic glucocorticoids. Other systemic medications can be used as alternative or adjunctive treatments for PG that fail to respond sufficiently to first-line therapies. Examples include biologic drugs, conventional immunosuppressants, dapsone, and minocycline. Intravenous immune globulin (IVIG) and the alkylating agents cyclophosphamide and chlorambucil are also options for patients with severe pyoderma gangrenosum that is refractory to first and second line treatments. The use of these agents is limited though due to their cost and adverse effects [6]. Surgery remains a controversial but a valid option in the management of PG. It is only considered in select cases because of the risk of pathergy.

Our patient’s risk of developing severe bone marrow suppression with sepsis has narrowed our options of treatment. Since most of the agents used have an association with inducing pancytopenia. Ustekinumab “Stelara”, a new FDA approved biologic for the treatment of Crohn’s was then started. Stelara 90 mg injections were given every 8 weeks. On two months follow up, the patient’s Peristomal PG was eventually improving. The skin around the ulcer started to show less inflammation and the ulceration started to heal. over a period of 4 months, the overall appearance of the lesions around the stoma has improved dramatically.

4. CONCLUSION

Peristomal Pyoderma gangrenosum is a rare entity. It usually exists in conjunction with a systemic inflammatory diseases or malignancy. The approach to such ulcers requires a combination of careful clinical examination, local wound care and systemic medications. While treatment with oral or systemic glucocorticosteroids seems to be the optimum first-line therapy, Pyoderma gangrenosum can be difficult to heal. Ustekinumab offers an additional line of treatment that is now available for the treatment of refractory pyoderma gangrenosum.
REFERENCES