

## BRIEF ARTICLES

## Successful Treatment of Granuloma Annulare with Certolizumab

Aidan Martinez<sup>1</sup>, Joseph Han<sup>2</sup>, Nahla Shihab, MD<sup>3</sup>, Mark Lebwohl, MD<sup>4</sup><sup>1</sup>Research Assistant, Icahn School of Medicine at Mount Sinai, New York, NY<sup>2</sup>Medical Student, Icahn School of Medicine at Mount Sinai, New York, NY<sup>3</sup>Clinical Dermatology Fellow, Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY<sup>4</sup>Professor and Chairman, Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY

## ABSTRACT

Generalized granuloma annulare (GA) is a subtype of GA that consists of widespread annular papules and plaques varying in size. There are no randomized trials of treatment for GA, however topical treatment, phototherapy, and various systemic therapies, have been reported to be effective. We report the first case of generalized GA that is successfully treated with certolizumab pegol.

## INTRODUCTION

Granuloma Annulare (GA) is a common skin disorder, classically presenting as annular erythematous papules and plaques.<sup>1</sup> The most common type of GA is the localized form, accounting for about 75% of all reported cases. This form is usually self-limited, treatment is primarily indicated for cosmetic reasons and associated impact on self-image and quality of life.<sup>2</sup> A less common type is generalized GA, which can be diagnosed by the presence of generalized skin-colored plaque and papules varying in sizes.<sup>3</sup> Unlike the localized form, generalized GA is often pruritic. In addition, this subtype rarely resolves spontaneously and is fairly unresponsive to treatment.<sup>3,4</sup> The characteristic features of GA in histopathology consist of lymphohistiocytic infiltrate, degeneration of collagen, and mucin deposition.<sup>4</sup> Certolizumab pegol is a PEGylated tumor necrosis factor alpha (TNF- $\alpha$ ) antagonist commonly used as a treatment for various autoimmune diseases including

psoriatic and rheumatoid arthritis.<sup>5</sup> We report a case of a patient with generalized GA who was successfully treated with certolizumab.

## CASE REPORT

A 73-year-old woman presented to our clinic with multiple itchy red rashes on the trunk and extremities that were first noticed three years earlier. She had no other comorbidities, and her family medical history was unremarkable. Upon physical examination, there were numerous erythematous annular papules and plaques on her trunk, arms, legs, and feet. The patient refused biopsy, however since her clinical presentation was very characteristic, we were pretty confident with our diagnosis. The patient was diagnosed with granuloma annulare and was previously prescribed topical treatments including potent topical corticosteroids and topical calcineurin inhibitors. However, lesions gradually increased in size and extent to involve her entire body, hence she was prescribed phototherapy with NBUVB. She

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underwent 28 sessions of phototherapy, but the skin lesions kept spreading. We then prescribed her adalimumab, which resulted in minor improvement. After four months with unsatisfactory result, we decided to treat her with certolizumab 400 mg every two weeks. By week eight of initiating certolizumab, we saw major clinical improvement. The patient was then instructed to continue treatment with certolizumab for another six months to prevent reoccurrence of GA.

**Figure 1.** Patient at week 0 before certolizumab treatment



## DISCUSSION

Generalized Granuloma Annulare (GA) is an extensive type of GA that consists of grouped of annular papules and plaques varying in sizes that can present anywhere on the body surface.<sup>1,3</sup> Histologically GA can show lymphohistiocytic infiltrates and collagen degeneration.<sup>2</sup> Furthermore, GA is considered a Th1-type delayed hypersensitivity reaction.<sup>6</sup>

**Figure 2.** Patient at 12 weeks of certolizumab treatment



Tumor necrosis factor-alpha (TNF- $\alpha$ ) has also been known as an important cytokine in a granuloma formation, which is the logic behind the use of TNF- $\alpha$  antagonists for GA.<sup>7</sup> Few studies have reported the successful treatment of GA using adalimumab and infliximab.<sup>7,8</sup>

We present the first case of a patient with generalized GA who failed topical treatment, phototherapy, and adalimumab, but was able to achieve complete resolution with certolizumab. Certolizumab pegol is a PEGylated Fab portion of a human monoclonal antibody indicated for inflammatory and autoimmune diseases.<sup>5</sup> It works by binding to and neutralizing TNF- $\alpha$ , thereby reducing the elevated levels of TNF- $\alpha$  that propagate inflammation. In addition, PEGylation serves to enhance its pharmacokinetic behavior to include improving solubility, drug stability and

decreasing immunogenicity.<sup>9,10</sup> Although no studies exist on the efficacy of certolizumab on GA, the excellent response of this patient demonstrates that certolizumab may be an effective treatment for generalized GA.

## CONCLUSION

Generalized granuloma annulare (GA) is often resistant to a variety of treatments and may take a chronic course. Certolizumab can be an alternative treatment for persistent generalized GA.

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**Corresponding Author:**

Nahla Shihab, MD  
 Department of Dermatology  
 Icahn School of Medicine at Mount Sinai  
 5 E 98<sup>th</sup> Street, NY, NY 10029  
 Email: [nahla.shihab@gmail.com](mailto:nahla.shihab@gmail.com)

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