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CASE REPORT

Pyoderma Gangrenosum Paradoxical Reaction to Adalimumab, Efficacy of Golimumab

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Abstract

We report clinical observation of a patient who received Adalimumab for ankylosing spondylitis and he developed a pyoderma gangrenosum. The severity of this dermatosis required the interruption of Adalimumab and the introduction of Golimumab. This work will expose the effectiveness of Golimumab on this unexpected and particularly rare paradoxical reaction.

Keywords: Golimumab; Pyoderma Gangrenosum; Paradoxical Reaction

Introduction

Golimumab is a humanized IgG1 monoclonal antibody TNF-α inhibitor. Its indication in rheumatology among others is ankylosing spondylitis (AS). Pyoderma gangrenosum (PG) is a rare idiopathic inflammatory disease classified as neutrophilic dermatosis. This exceptional paradoxical reaction can be induced by Adalimumab. We report the second case in literature having PG successfully improved under Golimumab.

Observation

A 41-year-old male followed since 2012 for ankylosing spondylitis. After failure of conventional treatment, Adalimumab was introduced in 2015 at the dose of 40 mg every two weeks with a BASDAI remission. In March 2020, the patient presented skin ulcers in the right wrist and the left hand. The lesion on the right wrist is ulcerative, necrotic, and surrounded by an erythematous halo, the edges are purplish, hypertrophic, and well defined (Figure 1). The lesion of the left hand is bullous, tense with serohematic content, the surrounding skin tissue is erythematous and infiltrated. Adalimumab was stopped. Probabilistic antibiotic treatment was started after bacteriological analysis of lesions. The patient developed bilateral anterior uveitis. Local microbiological analysis was sterile, and biological inflammatory syndrome (CRP at 162 mg/L, procalcitonin at 0.42 ng/ml, VS at 128 mm, hyperleukocytosis at 14 890) was found. Skin biopsies were performed on the right wrist. The anatomopathological analysis revealed a dermal infiltrate of inflammatory cells predominantly of neutrophil polynuclear without signs of vasculitis. The patient was diagnosed with adalimumab induced pyoderma gangrenosum. An etiological research eliminated a malignant hemopathies. A digestive exploration did not find any signs of chronic inflammatory bowel disease. A chest-abdominal-pelvic CT scan did not detect any tumor syndrome.

The immunological check-up was negative.

Corticosteroids at the dosage of 1mg/kg/day and a switch to Golimumab at a dose of 50 mg/month have been initiated. A significant clinical improvement was observed with a rapid decreased of corticosteroid therapy. Complete healing of the lesions occurred within six weeks (Figure 2). After two months of Golimumab, the patient had no skin lesions, no uveitis. At three months, the SA is in remission.

Figure 1: Pyoderma gangrenosum lesions in the right wrist

Figure 2: The right wrist after treatment with Golimumab (at two months)

Discussion

PG is a rare female-predominant auto inflammatory dermatitis [1]. PG is idiopathic in 25-50% of cases [1]. It is typically a painful ulcerative lesion wrongly attributed to an ischemic or infectious lesion [2]. Skin ulceration may be unique or multiple with erythematous, purplish and poorly delineated borders [1]. In 75% of cases, PG is associated with chronic inflammatory bowel disease (20.2%), rheumatoid arthritis (11.8%), hematology malignancy (3.9%) or cancer (8.5%) [3].

Its physio pathological mechanism remains unknown. A malfunction of the neutrophil polynuclear was suggested [4,5]. Marzano et al. demonstrated significant overexpression of cytokines and molecules amplifying pro-inflammatory cytokines and so the inflammatory response and recruitment of neutrophils compared to healthy skin [5,6]. This suggests that PG, like other neutrophilic dermatoses, should be classified as an autoinflammatory disease [5].

Multiple factors, such as genetic predisposition, undefined infectious agents, or paraneoplastic phenomena could initiate or maintain these anomalies [5]. PG could be a skin paradoxical reaction to anti-TNFα [7]. The pathophysiology of paradoxical PG is not yet well determined. Inhibition of TNF would stimulate the synthesis of interferon alpha and interleukin 23 (IL23), responsible for paradoxical reactions [7].

In our case report, all additional tests eliminated systemic pathologies usually associated with PG. The switch from Adalimumab to Golimumab allowed the resolution of the symptomatology. No new lesions have appeared with the new treatment confirms the paradoxical character of this dermatosis. The causal link of Adalimumab was thus retained.

The management of PG is not codified [5]. The induction treatment remains systemic corticosteroids at a dose of 1 mg/kg/day [10], in monotherapy or in combination with other immunosuppressive treatments [5].

Currently, biologics treatments appear to be promising as a therapeutic of refractory PG [5]. The efficacy of anti-TNFα has been demonstrated in the PG [5,8]. Infliximab and Adalimumab were the first to be tested, with response rates ranging from 21% to 100% according to studies [5].

For our patient, Golimumab allowed complete healing of ulcers and uveitis. SA also responded well to this therapeutic. This efficacy has already been reported for the treatment of PG during an ulcerative colitis in a 68-year-old patient with comorbidities [8]. This is the only observation found in the literature.

Conclusion

This observation comes to enrich the indications of Golimumab. In our case, Golimumab showed an interesting efficacy as a second line therapeutic. Dermatologists should consider the efficacy of Golimumab on the auto inflammatory profile of PG.

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