Case Report

Improved therapeutic response to biologic treatment after bariatric surgery: Experience from an obese patient with psoriasis

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Abstract
Psoriasis is an inflammatory skin disease with a well-established link to obesity. Excess body weight is associated with higher psoriasis severity. Besides, obesity reduces the effectiveness of systemic therapy. Herein, we reported a morbidly obese patient with severe psoriasis who had only partial response to adalimumab, achieved satisfactory clearance of psoriatic lesions after bariatric surgery in combination with adalimumab therapy. Since bariatric surgery is effective for reducing weight as well as improving psoriasis severity, morbidly obese psoriasis patients who failed noninvasive weight reduction strategies may consider bariatric surgery as a potential adjuvant treatment.

Keywords: Adalimumab, bariatric surgery, biologic treatment, obese, psoriasis

Introduction
Psoriasis is a multisystem inflammatory disease characterized by skin inflammation and epidermal hyperplasia, as well as increased risk of a destructive arthritis and cardiovascular morbidity. Obesity is an important risk factor for psoriasis. Excess body weight was associated with not only higher psoriasis incidence but also higher disease severity.¹,² Furthermore, obesity reduced the effectiveness of systemic treatment for psoriasis. Therefore, treating psoriasis in obese individuals appears to be more challenging. Herein, we reported a morbidly obese woman with severe psoriasis achieved satisfactory clearance of psoriatic lesions after bariatric surgery in combination with adalimumab therapy.

Case Report
A 24-year-old obese female, weight 98.7 kg, height 148 cm (body mass index [BMI] 45.1), presented with severe plaque-type psoriasis (psoriasis area and severity index (PASI) score 28.5) with psoriatic nail changes and arthralgia in 2013 [Figure 1a]. She had been affected by psoriasis since she was 15. Previous treatments, including methotrexate (MTX), acitretin, phototherapy, and topical steroids, all showed limited effects. Besides, MTX-related hepatitis was also noted. With a PASI score of 28.5 and >45% of body surface area affected, she received treatment with adalimumab, the fully human

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anti-tumor necrosis factor (TNF)-alpha monoclonal antibody, since December 2013. Adalimumab was administered with an initial dose of 80 mg, followed by 40 mg every other week starting 1 week after the initial dose. The PASI scores reduced from 28.5 to 13.0 in the first 6 months of treatment [Figures 1b and 2]. However, the therapeutic effect reached a plateau without further reduction in PASI during the subsequent 5 months. The patient received laparoscopic sleeve gastrectomy (LSG) for bodyweight control in November 2014. Biologics treatment was stopped during the perioperative period, and a mild flare of disease was noted. Adalimumab therapy was restarted at a dosage of 40 mg every other week in January 2015. No other systemic treatment was administered along with adalimumab therapy after bariatric surgery. After the surgery, she lost 8 kg in the 1st month and then continued to lose weight at a rate of 3 kg/month until maintaining at 52.8 kg (BMI: 24.1) [Figure 2]. The patient experienced dramatic improvement along with weight reduction and concomitant adalimumab therapy in the following year. Her PASI scores reduced from 15.6 to 8.8 in the first 6 months after re-treatment and kept improving to around 5 after another 12 months of adalimumab treatment in August 2016 [Figure 1c and d]. However, after discontinuing adalimumab, disease flared with a PASI of 12.1 without regain of body weight was noted in June 2017.

**DISCUSSION**

Psoriasis is an immune-mediated inflammatory skin disease with a well-established link to obesity (BMI ≥ 30). Excess body weight is associated with higher psoriasis incidence and severity. The mechanism proposed for this association includes the proinflammatory effects derived from excess body fat. More specifically, adipose tissue can release adipokines involved in the regulation of metabolic processes and produce a variety of proinflammatory cytokines, including TNF-α, monocyte chemoattractant protein-1, and interleukin-6. In obesity, the distribution and function of adipose tissue as well as the adipokine profile are altered. The unbalanced production of pro- and anti-inflammatory adipokines contribute to the worsening of psoriasis lesions. In addition, obesity may compromise the effectiveness of systemic treatments for psoriasis, including conventional and biologic therapy. It has been suggested that adipose tissue can dramatically alter the volume of drug distribution and limit drug efficacy. Although biologics frequently induce dramatic responses in psoriasis patients, it is reported obesity reduced the effectiveness of biologic as measured by changes in PASI score. The
certain therapeutic dilemma was encountered in the presented case. Conventional treatment, including MTX, acitretin, phototherapy and topical steroids, resulted in limited effects, even when used in combination. Furthermore, the response to 11-month adalimumab treatment was only achieving around PASI 50. Specifically, adalimumab is the anti-TNF-α agents given at a fixed-dose independent of body weight. It is reported that other weight-based dosing anti-TNF-α agents, such as infliximab, also associate with a delay in response and overall lower efficacy in obese patients.\[9]\ The result supports that body weight modifies the pharmacokinetics of anti-TNF-α agents biologic drugs to compromise their effectiveness for psoriasis.

Conversely, weight reduction by diet or exercise has been demonstrated to associate with reduction in the severity of psoriasis in obese patients in a meta-analysis study consisting of five randomized controlled trials.\[10]\ A review of seven prospective trials on the effect of combining a low calorie diet with other therapies for treating obese psoriasis patients concluded that weight reduction could decrease the severity of psoriasis.\[11]\ Similarly, the loss of visceral fat was proposed to decrease the inflammatory cytokine load and potentially contribute to the reduction of psoriasis inflammation.\[12]\ Dietary weight loss by diet control was also demonstrated to increase the efficacy of cyclosporine and anti-TNF-α biologic therapy for moderate-to-severe psoriasis in obese patients.\[12,13]\ These nonsurgical weight reduction studies highlight the benefits of lifestyle behavior changes in managing obese psoriasis patients.

However, weight reduction may not be achieved easily in some obese patients with eating disorders or psychiatric problems. Bariatric surgery, performed by Roux-En-Y gastric bypass, LSG or laparoscopic adjustable gastric banding, is found to be effective for losing weight as well as reducing the severity of psoriasis. A randomized controlled trial examining the efficacy of bariatric surgery is still lacking. Several retrospective cohort studies,\[14-16]\ describing the positive effects of bariatric surgery on psoriasis, although not all psoriasis patients who underwent bariatric surgery showed clinical improvement. The case series of 10 obese psoriasis patients who underwent bariatric surgery reported 70% of the patients stayed in remission 6 months after surgery, while the quality of life of those patients also significantly improved after surgery.\[14]\ A retrospective study conducted on 34 psoriasis patients who had undergone bariatric surgery reported 62% improvement in psoriasis after surgery, 9% reported no change, and 12% reported worsening of their psoriasis.\[15]\ Another retrospective study reported improvement of psoriasis in 40% of 33 morbidly obese psoriasis patients who underwent bariatric surgery, except one patient became worse several months after the surgery.\[16]\ Importantly, the clinical improvement of psoriasis is directly related to the degree of postoperative weight loss.\[10]\ Deterioration of psoriasis in some patients after bariatric surgery was considered to associate with physiological and psychological stress accompanied with surgery.\[17]\ In the presented case, mild flare-up of disease was considered due to discontinuation of adalimumab treatment during the perioperative period. After adalimumab treatment was restarted, it is found that improvement in PASI scores is positively correlated to the degree of weight loss after bariatric surgery.

In summary, we reported a morbidly obese patient with severe psoriasis, who had only partial response to adalimumab after 11 months, achieved optimal clearance of psoriatic lesions after bariatric surgery in combination with adalimumab therapy. Although the delayed response to biologic treatment may be considered in this situation, it is less likely that psoriasis patients gain maximal therapeutic effect after <1 year of treatment.\[18]\ Although noninvasive weight reduction strategies and healthy lifestyle should be promoted, morbidly obese psoriasis patients who failed noninvasive weight reduction strategies may consider bariatric surgery as a potential adjuvant treatment to control the activity of their psoriasis.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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