

## Obesity and Psoriasis: Can Bariatric Surgery Trigger Psoriasis?

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### Abstract

Psoriasis is a chronic disfiguring incurable skin disease. It has been associated with comorbidities under the skin such as obesity, multiple metabolic, cardiovascular diseases and psychological disorders. Previous research reported that bariatric surgery for obese psoriatic patients can improve psoriasis and its comorbidities. In contrast, we report a case of morbidly obese diabetic patient who develop psoriasis after having a bariatric surgery to reduce his weight and review the association between psoriasis and obesity.

**Keywords** Psoriasis; Obesity; Bariatric surgery

### Introduction

Psoriasis is no longer a skin problem; it is a chronic immune inflammatory condition associated with multiple comorbidities under the skin and up to a third of the patients develop psoriatic arthritis (PsA) [1]. The disease has been associated with obesity, dyslipidaemia, diabetes mellitus, hypertension, cardiovascular diseases, stroke, cancer and mental distress or depression [1,2]. There is no current cure for psoriasis and although the global prevalence of psoriasis is around 2% the disease incurs long term financial strain on the patient and on the health provider. International studies associated obesity with psoriasis incidence, severity and with diminish response to psoriasis systemic therapy [3,4]. Clinical trials and bariatric surgery conducted on obese psoriasis patients showed that weight reduction can improve psoriasis and its associated comorbidities [3]. We present a case report of morbidly obese diabetic patient who developed psoriasis after having bariatric surgery and review the association between psoriasis and obesity and the impact of weight reduction on obese psoriasis patients.

### Case report

A 52 year old obese diabetic electrician was referred to the dermatology department with psoriasis. The patient's obesity evolved since his childhood. In January 2009, he underwent Roux-en-Y gastric bypass surgery to improve his uncontrolled diabetes and morbid obesity. Few days after the surgery the patient developed a large psoriasis plaque at the site of his abdominal surgical wound (Figure 1).

More larger plaques then appeared on the extensor surface of his elbows, knees and shins. The patient's comorbidities prior to the surgery include Insulin dependent diabetes mellitus since 1992, hypertension since 2005, and diabetic neuropathy and retinopathy since 2007. In 2008, the patient developed right foot Charcot arthropathy and multiple toes ulcerations which subsequently led to amputation of a toe from each foot. Over the past ten years the patient's antihypertensive medication included ramipril, amlodipine, losartan, doxazosin and his current antihypertensive was hydralazine. The patient's current medications include atorvastatin, furosemide, tramadol, pregabalin and forceval.



**Figure 1:** Site of abdominal surgical wound.

Within 6 months of bariatric surgery the patient lost 40 kilograms (kg) of his weight (from 129 kg to 89 kg). His insulin therapy discontinued after surgery and was switched to gliclazide and metformin. His recent clinical examination showed a large psoriasis plaque crossing the longitudinal scar on his abdomen and a smaller one around his umbilicus (Figure 1) and larger psoriasis plaques covering the extensor surface of his forearms, elbows and shins. He had no joint pain or nail changes. His psoriasis area and severity index (PASI) was 5.4 and his dermatology life quality index (DLQI) was 10. His weight was 96 kg and height was 177 centimetres, giving him a body mass index (BMI) of 30.6. The main side effect of the bariatric surgery was diarrhoea mainly after drinking milk. The positive findings of his recent routine blood tests: Urea 13.9, Creatinine 199, Haemoglobin 112, and his Glycosylated haemoglobin 7.3. Because of his neuropathy, nephropathy and retinopathy the patient was under regular follow up with the endocrinology, nephrology, and ophthalmology's teams, respectively. Despite having multiple comorbidities the patient was enjoying his full-time work as an electrician. He never smoked a cigarette and drinks a few units of

alcohol over weekends. After discussing the treatment options for psoriasis the patient agreed to try Dithranol ointment and Coal tar cream. Within a week his psoriasis plaques improved and he was pleased to wear T-shirt and short trousers outdoor without feeling embraced from his visible skin rash (Figure 2).

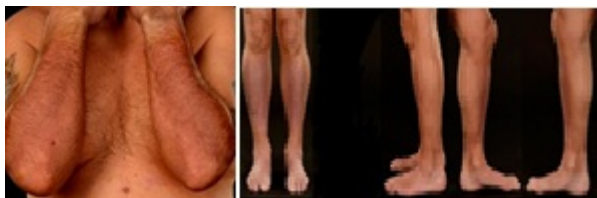


Figure 2: psoriasis plaques improved after the treatment.

## Discussion

### Psoriasis and obesity; nature or nurture?

The association between psoriasis and obesity was reported in a large population-based study. It included 44,715 individuals (4,065 with psoriasis and 40,650 controls) and identified metabolic syndrome (obesity, hypertriglyceridemia, and hyperglycaemia) in 34% of psoriasis patients versus 26% in the matched controls with odds ratio (OR) 1.50 (95% confidence interval (CI) 1.40-1.61) [2]. Further, a meta-analysis of 16 observational studies on the epidemiological associations between psoriasis and obesity included a total of 2.1 million patients (201,831 psoriasis patients) identified OR for obesity among patients with mild psoriasis was 1.46 (95% CI: 1.17-1.82) and 2.23 (95% CI: 1.63-3.05) for severe psoriasis [5]. Additionally, obesity was found more common in children with psoriasis than in controls in two recent large population studies [6,7].

However, there is no sufficient evidence to relate the onset of psoriasis to obesity or vice versa. Not all psoriasis patients are obese and not all obese individuals develop psoriasis [4]. Although the above population studies related psoriasis to obesity, they miss assessing other environmental factors that may contribute to the onset of psoriasis such as; trauma, medications, infections, smoking, alcohol, stress or mental health disorders. Equally, they miss assessing patient's lifestyle behaviour, daily physical activity or eating habits, which could contribute to obesity [2,5]. Our patient was obese since childhood and he developed psoriasis after having a surgery to reduce his weight. Obesity has been associated with a wide spectrum of dermatoses including acanthosis nigricans, hirsutism, lymphedema, chronic venous insufficiency, and hidradenitis suppurativa, and not only with psoriasis [8]. Further, obesity was found not only a risk of psoriasis (OR 1.48-6.46), but a major environmental factor contributing to the onset of autoimmune diseases such as rheumatoid arthritis (RA) (OR 1.2-3.4), multiple sclerosis (OR 2), and PsA (OR 1.48-6.46). It also worsens the course of RA, IBD, PsA and impairs the treatment response of RA, IBD, PsA, as well as psoriasis [4].

Genetically, the concordance rate in monozygotic twins (35% to 72%) for psoriasis and not 100%, [9] reflecting the potential role of environmental factors in triggering psoriasis. The gene-environment interaction and a polymorphism in IL12B and IL23R genes were suggested in one study as a risk for adiposity or obesity in psoriasis [10]. However, obesity is a growing global epidemic and a behaviour

problem affecting psoriasis and nonpsoriasis individuals. The imbalance between food intake and calorie burn associated with sedentarism can trigger obesity [11]. A reduced level of physical activity in psoriasis patients compared with non-psoriasis patients was reported with an odds ratio of 3.42 (95% CI 1.47-7.91) [12]. Other environmental variables may contribute to obesity in psoriasis is eating disorders. A case control study suggested that psoriasis is associated with psychopathological traits, which are frequently found in eating disorders (ED). The study assessed 100 psoriatic patients and 100 matched controls by PASI score, the Eating Disorder Inventory (EDI) and the Symptom Checklist-90 Revised. The results showed an association between the progressive weight increase and an impairment on most of EDI subscales in psoriasis patients [13].

### Which comes first; obesity or psoriasis?

The answer to this question is still unknown as the precise mechanism underlying the association between psoriasis and obesity remains elusive [4]. Interestingly, two longitudinal prospective cohort studies found weight gain or obesity, particularly from the age of 18 years was a risk for developing psoriasis in women. The first study found increased adiposity and weight gain are strong risk factors for incident psoriasis. During a 14 years follow-up period (1991-2005) of 78,626 women, the study identified 892 self-reported incident cases of psoriasis and a linear correlation between BMI and the risk of incident psoriasis in adult women. The multivariate relative risks (RRs) of psoriasis were 1.40 (95% CI, 1.13-1.73) for a BMI of 25.0 - 29.9; 1.48 (95% CI, 1.15-1.91) for a BMI of 30.0 - 34.9; and 2.69 (95% CI, 2.12-3.40) for a BMI of 35.0 or greater (P for trend, < 0.001) [14]. The second study is more recent one and also reported that higher BMI and weight gain are risk factors for incident psoriasis in women gaining weight since the age 18 years. The study followed-up 67,300 female nurses over a 12-year period (1996-2008). The authors identified 809 incident psoriasis cases and positive association between BMI and the risk of psoriasis (P < 0.0001). Compared to women with updated BMI of < 25, the multivariate RRs of incident psoriasis were 1.21 (95% CI, 1.03-1.43) for a BMI of 25.0-29.9, 1.63 (95% CI, 1.33-2.00) for a BMI of 30.0-34.9 and 2.03 (95% CI, 1.58-2.61) for a BMI of 35.0 or greater [15].

In contrast, a cohort study compared 44,164 patients with a first-time diagnosis of psoriasis from both genders with 219,784 age, sex and index date matched nonpsoriasis controls and found that patients with psoriasis had higher risks of incident for obesity, diabetes and other cardiovascular disease (CVD) risk factors. The study used General Practice Research Database and identified 2,760 (6.3%) new diagnosis of obesity during cohort follow-up. The hazard ratio (HR) for new onset obesity in psoriasis patient was of 1.18 (95% CI 1.14-1.23) compared with a matched cohort without psoriasis [16].

### Which causes comorbidities; obesity or psoriasis?

Obesity is considered a chronic, low-grade inflammatory condition associated with high levels of proinflammatory cytokines, particularly TNF-alpha and IL-6. It was suggested that these cytokines can inhibit the synthesis of adiponectin (an anti-inflammatory adipokine) by the subcutaneous and visceral adipose tissue and can trigger psoriasis, metabolic syndrome and cardiovascular diseases [8]. In contrast, psoriasis patients found to have higher risks of incident obesity (HR 1.18; 95% CI 1.14-1.23), diabetes [HR 1.33; 95% confidence interval (CI) 1.25-1.42], hypertension (HR 1.09; 95% CI 1.05-1.14), and hyperlipidaemia (HR 1.17; 95% CI 1.11-1.23), myocardial infarction

(HR 1.21; 95% CI 1.10-1.32), angina (HR 1.20; 95% CI 1.12-1.29), atherosclerosis (HR 1.28; 95% CI 1.10-1.48), peripheral vascular disease (HR 1.29; 95% CI 1.13-1.47) and stroke (HR 1.12; 95% CI 1.00-1.25) [16].

Metabolically, both psoriasis and obesity are associated with hypo adiponectinemia and hyperleptinemia, at statistical significance [17,18]. Adiponectin acts as anti-inflammatory adipokines involves in the regulation of numerous physiological functions and immune response. Leptin acts as a regulator of appetite, energy expenditure and as proinflammatory adipocytokine plays a major role in the chronic inflammatory state present in metabolic syndrome and atherosclerosis. Leptin, adiponectin, resistin, tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6) and C-reactive protein (CRP) levels appear to be correlated with psoriasis severity and patient BMI. Serum levels of TNF- $\alpha$ , IL-6, leptin, and resistin were found significantly higher ( $P < 0.05$ ) and serum adiponectin levels were significantly lower in patients with psoriasis than in controls ( $P < 0.0001$ ). Further, serum leptin level in men and women with psoriasis correlated positively with obesity ( $P < 0.05$ ) and was the only adipokines significantly decreased after TNF- $\alpha$  inhibitors treatment ( $P = 0.0003$ ) [17].

In nonpsoriasis obese individuals a case control study was conducted on bariatric surgery candidates found similar results. Serum leptin level was correlating positively with BMI, and was higher while serum adiponectin level was lower in obese individuals than in non-obese controls. The study suggested that weight loss rather than the type of bariatric surgery procedure is responsible for adipokines variation as the percentage of total weight loss correlated positively with adiponectin levels and negatively with leptin levels [18]. The results of above two recent studies match in the positive correlation between leptin and BMI in psoriasis and nonpsoriasis individuals, and in the reduction of serum leptin level after psoriasis treatment and weight reduction, respectively. They however mismatched in the serum level of adiponectin in both cohorts. Future research may clarify the role of adipokines and other cytokines in the pathogenesis of psoriasis and metabolic syndrome.

## Impact of weight reduction in obese psoriasis patients

### Nonsurgical weight loss and psoriasis

A meta-analysis showed that nonsurgical weight loss intervention was associated with reduction in the severity of psoriasis in overweight or obese patients. The analysis included 5 Randomised controlled trials (RCTs) reported a greater improvement of psoriasis rash in patients receiving weight loss intervention than in controls. More participants in the intervention group than in the control group achieved a 75% reduction in the PASI score, with a pooled odds ratio of 2.92 (95% CI, 1.39-6.13;  $P < 0.005$ ) [19]. Equally, 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 psoriasis severity. Even in those who did not lose significant weight the calorie restriction group showed more significant decrease in psoriasis severity and in serum lipids compared to the control group and the improvement in serum lipids seems more significant in improving psoriasis than the decrease in body weight [3].

These nonsurgical weight reduction studies highlight the benefits of lifestyle behaviour changes in managing psoriasis. However, they were limited by the short follow up period, which can impair proper assessment of the long-term compliance and impact of lifestyle

behaviour changes on psoriasis. They also deficient in assessing personal, social and environmental barriers in maintaining a healthy lifestyle or long-term lifestyle behaviour changes.

### Surgical weight loss and psoriasis

Bariatric surgery found to be beneficial for obese psoriasis patients. A case series on 10 obese psoriasis patients underwent bariatric surgery reported 100% improvement of insulin resistance, 75% improvement in diabetes, and 57% improvement in hypertension among the study population [20]. However, not all psoriasis patients undergo bariatric surgery have improved. A retrospective study conducted on 34 patients with psoriasis that had undergone weight loss surgery reported 62% improvement in psoriasis after surgery, 9% reported no change, and 12% reported worsening of their psoriasis [21]. A recent study reported improvement of psoriasis in 40% of a 33 obese psoriasis patients underwent bariatric surgery several months after surgery and one person became worse after the surgery [22].

The cause of worsening of psoriasis in some patients after bariatric surgery needs is still unclear [20-22]. Physiological and psychological stress may contribute to the deterioration of psoriasis or indeed to the onset of psoriasis as in our case. Koebner phenomenon after having surgical incision and/or the stress of major surgery may trigger psoriasis in genetically susceptible patients [9]. Nonetheless, regardless the triggering factor for psoriasis, bariatric surgery is not routinely indicated as a first-line treatment for the obese psoriasis management unless the patient has other comorbidities [3]. Furthermore, not all patients undergo bariatric surgery were successful in maintaining a healthy lifestyle or regular body weight. Six years after having a bariatric surgery our patient's BMI is still struggling with his obesity and a BMI of 30.6. Preoperative cognitive behaviour therapy and/or psychiatric treatment may be needed in individuals with morbid obesity and eating disorders to cope with postoperative eating problems [20-22].

In conclusion, we may present the first case of psoriasis developed in morbidly obese individual underwent bariatric surgery, a single case report however, is not sufficient to relate bariatric surgery to the onset of psoriasis. Further studies are needed to affirm the mechanism behind the association between psoriasis and obesity.

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