Short report

Improvement of psoriasis during exenatide treatment in a patient with diabetes

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Abstract

Context and aim. – Psoriasis is an immune-mediated skin disorder frequently associated with obesity and type 2 diabetes (T2D). This report is of a clinically significant improvement in psoriasis lesions in a patient with T2D during treatment with a GLP-1 receptor agonist (exenatide).

Observation. – A 61-year-old male patient (BMI: 25.5 kg/m²) with T2D treated with metformin and sulphonylureas had also complained, since 1980, of extensive psoriasis that required multiple steroid-based treatments [Psoriasis Area and Severity Index (PASI) score: 11]. In September 2008, his diabetes treatment was intensified with exenatide (Byetta®) to improve poor glycaemic control. The patient, as expected, lost weight and reduced HbA1c levels from 65 mmol/mol to 56 mmol/mol. However, after just 1 month of treatment with exenatide, the patient also reported a dramatic improvement in psoriatic plaques that was confirmed at the 1-year follow-up (PASI: estimated at 3–4). Withdrawal of exenatide was associated with weight gain, deterioration of glycaemic control and deterioration of psoriasis (PASI: > 10). After reinstating exenatide treatment, the patient again reported a prompt improvement in psoriasis (PASI: 3.1).

Conclusion. – There was a major and rapid improvement in psoriasis in our patient with T2D following treatment with exenatide. A possible mechanism might be through direct modulation of the immune system by GLP-1 receptor agonists.

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Keywords: Psoriasis; Treatment; Improvement; Exenatide; Diabetes

Résumé

Amélioration d’un psoriasis chez un patient diabétique après traitement par exenatide.

Contexte et objectif. – Le psoriasis est une maladie cutanée inflammatoire liée à un désordre immunitaire et est souvent associé à l’obésité et au diabète de type 2. Nous souhaitons rapporter l’évolution d’un psoriasis chez un patient diabétique de type 2 traité par analogue du GLP-1 (exenatide) prescrit au vu d’un mauvais contrôle glycémique.

Observation. – Un sujet diabétique de type 2 (BMI 25.5 kg/m²), traité par metformine et sulfonylurées présente aussi, depuis1980, un psoriasis extensif qui a bénéficié d’applications locales récurrentes de corticoïdes. En septembre 2008, au vu du déséquilibre glycémique persistant, de l’exenatide (Byetta®) est rajouté à la bithérapie orale. Ceci s’accompagne d’une perte pondérale et d’une amélioration de l’HbA1c de 65 à 56 mmol/mol. Le tableau clinique est cependant dominé dès la fin du premier mois de traitement par une régression spectaculaire du psoriasis avec un score PASI (pour Psoriasis Area and Severity Index) diminuant de 11 à 3–4. L’interruption de l’exenatide amène une récidive des lésions cutanées. Sa réintroduction après six mois d’arrêt est à nouveau associée à une amélioration du psoriasis avec un score de sévérité à 3,1 après un an de traitement, sans qu’il n’y ait d’autres modifications thérapeutiques.

Conclusion. – Nous avons observé chez un diabétique de type 2 sous exenatide une régression majeure et rapide d’un psoriasis extensif. Ce bénéfice clinique pourrait faire suite aux effets immunomodulateurs des analogues du GLP-1.

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Mots clés : Psoriasis ; Amélioration ; Traitement ; Exenatide ; Diabète

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1. Introduction

Psoriasis is an immune-mediated skin disorder that is frequently associated with obesity and other metabolic disorders, such as type 2 diabetes (T2D) [1,2]. These are all clinical conditions characterized by chronic systemic inflammation [2,3]. Glucagon-like peptide-1 (GLP-1) receptor agonists (exenatide, liraglutide) are now increasingly being used in the treatment of patients with T2D to improve glycaemic control and reduce weight [4], as has also been found after the failure of metformin with sulphonlureas in daily clinical practice [5].

In a recent issue of Diabetologia, Hogan et al. [6] reported a clinically significant improvement of psoriasis lesions in three obese T2D patients after initiation of GLP-1 receptor agonist therapy. The present report describes a non-obese T2D patient with coexisting long-term psoriasis in whom a beneficial effect of exenatide on skin lesions was revealed during treatment with Byetta® for unsatisfactory glycaemic control.

2. Case report

A 61-year-old man with T2D for 14 years also complained, since 1980, of extensive refractory psoriasis that required multiple steroid-based treatments (clobetasol propionate in association with betamethasone dipropionate and calcipotriol) that also contributed to hyperglycaemia. In September 2008 (period T1, just prior to exenatide initiation for poor glycaemic control), the patient received metformin and sulphonylureas for managing his diabetes. He was also treated with perindopril (5 mg/day), moxonidine (0.4 mg/day) for high blood pressure and simvastatin (20 mg/day) for dyslipidaemia. His weight and height were 82.5 kg and 1.80 m, respectively; his body mass index (BMI) was 25.5 kg/m² and his waist circumference was 96 cm. Blood pressure level was 140/85 mmHg, and the Psoriasis Area and Severity Index (PASI) score was estimated at 11 [7].

Insulin sensitivity (IS) and beta-cell secretion (B), as assessed by homoeostatic model assessment (HOMA), were 43% and 29%, respectively, with an IS × B product of 13%. Glycated haemoglobin (HbA1c) was 65 mmol/mol (Table 1). Treatment of T2D was intensified with exenatide (2 × 5 μg/day) in combination with sulphonlureas and metformin. During follow-up, a higher dosage of Byetta was not tolerated because of gastrointestinal side-effects. At 1, 6 and 12 months after exenatide initiation, the patient had lost weight and significantly reduced HbA1c levels (Table 1). Also, his ultrasensitive (US) C-reactive protein (CRP) level was 0.03 mg/dL (vs 0.22 mg/dL before the T1 period). Then, unexpectedly and as early as the first follow-up visit at 1 month, the patient reported a dramatic clinical improvement in psoriatic plaques that was confirmed at the 12-month visit, with a PASI score that was retrospectively estimated to be around 3–4. Moreover, he had stopped all topical treatments.

However, exenatide had to be discontinued after 1 year in September 2009 for administrative reasons (no reimbursement by the National Health Insurance System). As shown in Table 1, withdrawal of exenatide was associated with weight gain and deterioration of glycaemic control, with an HbA1c level of 77 mmol/mol. In addition, the psoriatic lesions began to quickly recur, resulting in a 6-month PASI score greater than 10.

Exenatide treatment was eventually reinstated in April 2010 (period T2) with, as a consequence, weight loss and a reduction in HbA1c from 77 mmol/mol to 65 mmol/mol after 1 year. Interestingly, the patient again reported prompt improvement in the severity of psoriatic plaques immediately after exenatide reintroduction. His psoriasis further improved during exenatide treatment up to October 2011, by which time his PASI score had fallen to 3.1. This unexpected clinical benefit for psoriasis could be due to the anti-inflammatory and immune effects of GLP-1 receptor agonist treatment.

3. Discussion

There was a marked improvement in psoriasis following exenatide treatment at the low dosage of 2 × 5 μg/day in our non-obese T2D patient that deteriorated after stopping

<table>
<thead>
<tr>
<th>Visits</th>
<th>Weight (kg)</th>
<th>HbA1c (mmol/mol)</th>
<th>PASI</th>
<th>Exenatide (2 × 5 μg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[T1]a</td>
<td>9/2007</td>
<td>81.0</td>
<td>60 (7.6%)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>3/2008</td>
<td>82.0</td>
<td>63 (7.9%)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>9/2008</td>
<td>82.5</td>
<td>65 (8.1%)</td>
<td>&gt; 10</td>
</tr>
<tr>
<td></td>
<td>10/2008</td>
<td>80.5</td>
<td>60 (7.6%)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>3/2009</td>
<td>75.0</td>
<td>61 (7.7%)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>9/2009</td>
<td>78.0</td>
<td>56 (7.3%)</td>
<td>3 to 4</td>
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<tr>
<td>[T2]a</td>
<td>3/2010</td>
<td>81.0</td>
<td>77 (9.2%)</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>[Off]</td>
<td>9/2010</td>
<td>77.5</td>
<td>–</td>
<td>–</td>
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<td>3/2011</td>
<td>79.0</td>
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<td>–</td>
</tr>
<tr>
<td></td>
<td>10/2011</td>
<td>78.0</td>
<td>66 (8.2%)</td>
<td>3.1</td>
</tr>
</tbody>
</table>

PASI: Psoriasis Area and Severity Index Scores.

treatment, but improved again following retreatment with exenatide. No other changes of treatment were made during the follow-up. In particular, there was no intensification of conventional psoriasis therapy. Exenatide administration was associated, as expected, with weight loss (from 82.5 kg to 78.0 kg during T1, and from 81.0 kg to 78.0 kg during T2) and a reduction in HbA1c levels (from 65 mmol/mol to 56 mmol/mol during T1 and from 77 mmol/mol to 66 mmol/mol during T2). It is worth mentioning, however, that during the T2 period, glycaemic control, although improved, remained globally unsatisfactory compared with international recommendations.

The potential mechanism(s) accounting for the improvement in psoriasis during GLP-1 receptor agonist therapy remain(s) a matter of debate [8]. Glycaemic control per se does not appear to play a beneficial role, as was also suggested by our own HbA1c data, in particular, after the reintroduction of exenatide during T2, whereas weight reduction in itself can result in improvement in PASI scores in obese individuals [9,10]. In addition, it has been reported that a low-calorie diet can improve the severity of psoriasis independent of changes in BMI [11]. The data reported by Hogan et al. [6], as well as our present case report now, extend this observation, as the improvement of psoriasis was observed prior to any significant weight reduction.

One plausible scientific explanation for this is based on the extrapancreatic actions of GLP-1 receptor agonists. Invariant natural-killer T (iNKT) cells, considered to be potent drivers of innate and acquired immune responses, are present in psoriasis lesions [12,13], and it was recently shown by Hogan et al. [6] that these cells express functional GLP-1 receptors. The same authors also elegantly demonstrated that the administration of liraglutide for 6 weeks increased the number of iNKT cells in the circulation while reducing their numbers in psoriatic plaques. In addition, they found that liraglutide could also modulate iNKT-cell cytokine production.

Thus, the immunoregulatory actions of GLP-1 analogues on iNKT cells might account for (or contribute to) the improvement in clinical psoriasis reported by our patient. Furthermore, the fact that psoriasis has been shown to improve following bariatric bypass surgery may also be the consequence of increased GLP-1 levels rather than because of weight loss per se [14,15].

In conclusion, this is the first report of a major and rapid improvement in psoriasis in a non-obese T2D patient following treatment with low-dose exenatide. A possible mechanism of action could be direct modulation of the innate anti-inflammatory immune system by GLP-1 receptor agonists. Further clinical research is needed to investigate this potential beneficial effect of GLP-1 receptor agonists in psoriasis. To our knowledge, GLP-1 agonists are the first “non-psoriasis” medications to show, besides positive metabolic effects, such improvements in skin lesions in patients with T2D.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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References