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Case Report
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Injection Site Reaction during Liraglutide Therapy

*Kamila Jaworecka[1], Marcelina Pojawa-Golab[1], Ewa Otto-Buczkowska[2] and Adam Reich[1]**

[1]Department of Dermatology, University of Rzeszow, Poland

[2]Medical Specialist Centre in Gliwice, Poland

Abstract

Liraglutide is used in the treatment of diabetes mellitus to improve the glucose level controlling, thus, improving the patient prognosis. Here, we have demonstrated a patient with injection site reactions after liraglutide which lead to treatment cessation.

A 43-year-old woman underwent treatment with subcutaneous liraglutide injections for type 2 diabetes. After about three weeks of the treatment initiation, several hours after drug administration, the patient observed an outbreak of oval, red erythemas with accompanying swelling, itchiness and excessive skin warmth around the injection site. The patient continued taking subcutaneous injections for the following four days, observing, after taking each dose, new erythemas. The patient stopped the treatment and contacted her doctor who recommended oral antihistamines with topical methylprednisolone aceponate. After several days the intensity of skin lesions decreased and eventually disappeared completely within 1 month.

To date, skin adverse reactions after liraglutide have been relatively rarely reported and data about injection site erythemas are missing. It seems, that similarly to other drugs, such adverse events after liraglutide are usually of mild severity, but patients have to be informed about their nature to reassure them, that they are not related with serious consequences and the treatment does not have to be stopped.

Keywords: Diabetes; Drug induced skin reaction; Glucagon-like peptide-1

Introduction

In the glucose metabolism disorders related to overweight or obesity, Glucagon-Like Peptide-1 analogues (GLP-1) are being used more and more widely. One of the drugs in this group is Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RA)-liraglutide. Liraglutide decreases the prevalence of both metabolic syndrome and pre diabetes in obese individuals and is used in the treatment of diabetes mellitus [1-4]. However, liraglutide may also cause side effects. The commonest ones are nausea and vomiting which are causes for withdrawal of therapy in approximately 8% of patients. Skin reactions are much more rare complications. They can be associated with immune reactions. Here, we have demonstrated a patient with severe injection site reaction which leads to treatment cessation.

Case Presentation

A 43-year-old woman undergoing treatment with subcutaneous liraglutide (Victoza®) injections for type 2 diabetes has come in due to redness and swelling on the skin. Liraglutide was administered for four weeks in an increasing dose starting from 0.6 mg/d till 1.8 mg/d according to the manufacturer's instruction. After about three weeks of the commencement of treatment, several hours after drug administration, the patient observed an outbreak of an oval, red erythemas with accompanying swelling, itchiness and excessive skin warmth around the injection site (Figure 1A-1D). The patient continued taking subcutaneous injections for the following four days, observing, after taking each dose, new erythemas, of which the largest was 12 cm in diameter. The patient decided to stop taking liraglutide and contacted her doctor who recommended fexofenadine orally in a daily dose of 180 mg and topical use of methylprednisolone aceponate. After several days the intensity of skin lesions decreased and eventually disappeared completely within 1 month, leaving no trace.

Discussion

Due to the increasing number of patients with type 2 diabetes and a failure of the therapies used so far (only a small percentage of patients reach the estimated therapeutic goals), new products

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Correspondence:
Adam Reich, Department of Dermatology, University of Rzeszow, Ul. Szopena 2, 35-055 Rzeszów, Poland, Tel: +48-605076722; E-mail: adi_medicalis@go2.pl

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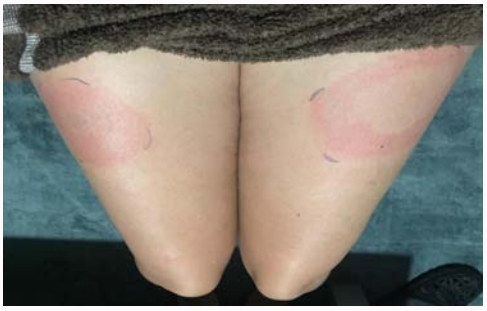

Figure 1A: Erythemas at the site of injection of liraglutid. Overview of the lesions located on the thighs.

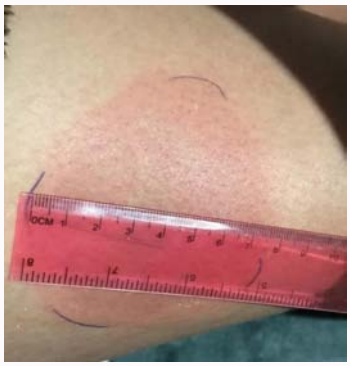

Figure 1B: Closer view of the lesions of both thighs.

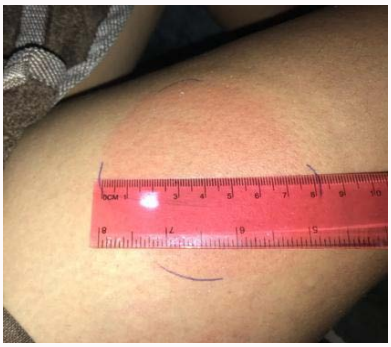

Figure 1C: Closer view of the lesions of both thighs.

have been launched to the pharmaceutical market, which are to optimize the treatment of diabetes [5]. However, introduction of new drugs results not only in better treatment of diabetes, but also in a potential risk of inducing new adverse reactions, which have not been properly described, yet. One of the new classes of drugs used to treat diabetes are Glucagon-Like Peptide-1 (GLP-1) analogues. Native GLP-1 is an incretin hormone which enhances the glucose-dependent insulin secretion in pancreatic beta cells. This class of drugs includes dulaglutide, exenatide, liraglutide and semaglutide. Liraglutide is characterized by 97% of homology to human GLP-1. Thanks to bonds between its own particles and albumins and a greater stability towards dipeptidyl peptidase 4 and neutral endopeptidase as compared with native GLP-1, the drug is characterized by a long-term effect, which makes possible to administer it once daily. In a way that is dependent upon glucose concentration, liraglutide regulates the pancreatic secretion of insulin and glucagon-when the glucose concentration in blood is high, the stimulation of insulin secretion

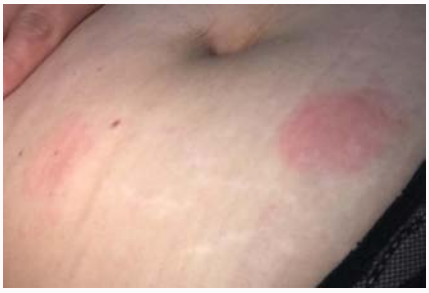

Figure 1D: Lesions on the abdomen.

and the inhibition of glucagon secretion ensue. The mechanism of decreasing the concentration of glucose in blood also comprises the inhibition of the stomach peristalsis, which causes a delay in its emptying. Moreover, liraglutide decreases body weight and body fat mass by inhibiting appetite and calorie intake.

Generally, GLP-1 analogues are well-tolerated drugs. The adverse reactions that are reported most often are alimentary tract ailments: nausea, vomiting, diarrhea, constipation, or dyspepsia. In most patients they occur at the beginning of therapy, are dose-dependent and their frequency and intensity decrease gradually during treatment. In order to reduce the risk of above mentioned side effects, it is advisable that treatment starts with small doses, which are increased gradually. Headaches, nasopharyngitis, and bronchitis were reported quite often, as well. In addition, the following adverse events may also occur during the drug use: anaphylactic reactions, bad mood, cholelithiasis, acute renal failure, dehydration, hypoglycaemia or acute pancreatitis [6].

Skin adverse reactions after liraglutide have been relatively rarely reported. The most frequent ones include an atypical rash, urticaria, or itchiness [7]. Here, we have described a case of severe injection site erythemas leading to treatment discontinuation. Although the literature data on this type of side effect is missing, such skin lesions may not be so unusual, although they are usually of mild intensity. Reactions of similar nature were reported during other biologic therapies administered subcutaneously, e.g. in patients treated with etanercept, adalimumab, or ixekizumab for plaque psoriasis [8,9]. Typically, changes like these are mild or moderate, they occur mostly at the initial stage of administering biologic drugs, and their intensity decreases gradually during therapy. Importantly, they rather do not constitute a cause for the cessation of biologic treatment, as they are local, do not cause major subjective discomfort like pain or itch and resolve over time [10]. However, patients have to be informed about their nature to reassure them, that they are not related with serious consequences in order not to stop the treatment by patients. Only in cases with severe side injection reactions as in the patient discussed, it may be necessary to consider treatment interruption or cessation. However, the decision about a possible stopping of therapy must take into account not only the presence of skin reactions, but also the advantages/disadvantages, which the patient has in terms of glycemia control in the course of diabetes.

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