



# Insulin-induced Lipoatrophy in a Patient on Insulin Analogue Therapy: a Case Report

Vesselina Yanachkova<sup>1</sup>, Radiana Staynova<sup>2</sup>

<sup>1</sup> Dr Shterev Hospital, Sofia, Bulgaria

<sup>2</sup> Faculty of Pharmacy, Medical University of Plovdiv, Plovdiv, Bulgaria

**Corresponding author:** Vesselina Yanachkova, Dr Shterev Hospital, 25-31 Hristo Blagoev St., Razsadnika quarter, Sofia, Bulgaria; E-mail: v\_ess@abv.bg; Tel.: +359 886 436 963

**Received:** 15 Jan 2020 ♦ **Accepted:** 13 Mar 2020 ♦ **Published:** 30 Sep 2020

**Citation:** Yanachkova V, Staynova R. Insulin-induced lipoatrophy in a patient on insulin analogue therapy: a case report. *Folia Med (Plovdiv)* 2020;62(3):597-600. doi: 10.3897/folmed.62.e50166.

## Abstract

Insulin-induced lipoatrophy is a rare skin complication in patients with diabetes mellitus. It is characterized primarily by localized subcutaneous atrophy of the fatty tissue at the site of frequent insulin injection. We report a clinical case of a 38-year-old woman with lipoatrophy, developed during treatment with insulin analogues. Lipoatrophic zone formation began 3 months after the treatment was initiated. A lipoatrophic defect developed on the thighs and the upper outer arms, resulting from repeated insulin injections at the same site. Regarding lipoatrophic areas, treatment with topical administration of corticosteroids was attempted but without a significant clinical effect. The best prevention from lipoatrophy development is education of patients regarding rotation of insulin injection sites and more frequent needle change.

## Keywords

diabetes mellitus, insulin analogues, lipoatrophy

## INTRODUCTION

Insulin therapy is one of the iatrogenic causes of localized acquired lipoatrophy. In addition, acquired lipoatrophy may be a complication of local action due to other injectable agents such as corticosteroids, antibiotics, heparin, vaccines, and growth hormone. It may also occur as a result of an abscess, recurrent trauma (lipoatrophy semicircularis), localized scleroderma (morphea), cutaneous systemic lupus erythematosus, dermatomyositis, etc. Insulin-induced lipoatrophy is a rare skin complication in patients with diabetes mellitus.<sup>1-3</sup> In past years, when bovine and porcine insulin was used, its incidence used to be significantly higher, between 10-55%.<sup>4</sup> However, in the era of human insulin and insulin analogues, lipoatrophy occurred in approximately 3.6% of treated patients.<sup>3,5,6</sup> It is most common in young women with type 1 diabetes mellitus.<sup>4,7</sup> The reason for its occurrence may be: the use of the same insulin

injection site over a long period of time, irregularly changing needles of injection devices, applying different analogue insulin to the same patient.<sup>1,4,5</sup>

## CASE REPORT

We present a case of a 38-year-old woman with a 5-year history of type 1 diabetes mellitus. The disease occurred three months after the woman gave birth. It debuted with hyperglycemia, blood glucose levels up to 20 mmol/L and ketonuria. The patient did not perform an oral glucose tolerance test during pregnancy. It is therefore unknown if any disorder in carbohydrate metabolism had been present previously. She gave birth to a fetus with weight of 3850 g. Under the conditions of hospitalization, insulin therapy was initiated. The patient was on multiple dose injection therapy, using combination of regular human insulin and intermediate-acting in-

sulin. Six months later the therapy was switched to one with a short-acting insulin analogue (aspart) and long-acting insulin analogue (detemir).

In the endocrinology consulting room, the patient presented in July 2015 with severe hypoglycemia, with registered blood sugar level of 1.9 mmol/L. Based on medical history and physical examination, it became clear that the type of diabetes had not been classified correctly. The patient reported that she had gained 30 kg in two years and used to be having frequent episodes of hypoglycemia, including ones with loss of consciousness. The patient had never been educated on insulin dose titration, therefore she was using the constant dose prescribed by the endocrinologist as a definitive and fixed one. In addition, the patient had another endocrine di-

sease – autoimmune thyroiditis in a hypothyroid phase. At the time of examination, she was being treated with 75 µg of levothyroxine once daily for substitution. She reported a family history of thyroid disease and diabetes mellitus. There was no evidence for diabetic complications.

Data from physical examination included: Obesity class I (BMI=34 kg/m<sup>2</sup>), and four areas of lipoatrophy with a diameter of about 10 cm each, located on thighs and upper outer arms (Figs 1, 2). Lipoatrophic zone formation began 3 months after initiation of treatment with insulin analogues. The patient had not been instructed to rotate the injection sites and continuously administered insulin in the same area until lipoatrophy occurred, the zone then deepened and enlarged. It was not until then when she changed the location.



**Figure 1.** Lipoatrophy located on the front of the thighs.



**Figure 2.** Lipoatrophy located on the upper outer arms.

Following the examination, several laboratory tests were recommended and performed (Table 1).

**Table 1.** Results of laboratory tests

Test	Results	Normal range
Blood glucose (fasting)	3.8 mmol/L	2.8 – 6.1 mmol/L
HbA1c	5.1%	<7%
C-peptide	0.78 nmol/L	0.26-1.39
GAD-65/IA-2	3.1 (Negative)	0-4 IU/L
Zn-transporter 8	Normal	-
TSH	1.8 $\mu$ IU/L	0.27 – 4.20 $\mu$ IU/L
Anti-TPO	>900 IU/ml	< 35 IU/ml
Creatinine	58 $\mu$ mol/L	44 – 80 $\mu$ mol/L
Triglycerides	Normal	-
ALAT	20 U/L	<33 U/L
ASAT	21 U/L	<32 U/L
Albumin	Normal	-
GGT	15 U/L	5-35 U/L

HbA1c: glycated haemoglobin; GAD: glutamic acid decarboxylase; TSH: thyroid-stimulating hormone; Anti-TPO: anti-thyroid peroxidase; GGT: gamma-glutamyltransferase

Before the results of the immunological tests were obtained, the insulin doses had been reduced. Hypoglycaemia was recorded even when 2E fast-acting insulin was administered. Having the negative antibody levels detected, insulin therapy was discontinued. The patient was treated with metformin 850 mg 3 times daily. Gradually, the patient reduced 25 kg of her body weight and achieved good glycemic control (HbA1c 5.52 % and blood glucose profile – 4.4/5.5/6.5/5.9 mmol/L, results from January 2019). Regarding the lipoatrophic areas, treatment with topical administration of corticosteroids was administered, but no significant clinical effect was achieved.

## DISCUSSION

Insulin-induced lipoatrophy is considered an immunological side effect during the course of insulin therapy.<sup>1,5,7</sup> The pathogenesis is still not clear enough. It is characterized by the local formation of complexes between the injected agent and circulating antibodies, activation of the complement system and infiltration of inflammatory cells.<sup>4</sup>

The local accumulation of immune complexes is followed by vascular changes. Overproduction of cytokines and TNF- $\alpha$  by mast cells inhibit adipocyte differentiation. Besides, the presence of anti-insulin antibodies is also associated with cutaneous atrophy.<sup>1,2,6</sup>

The lipoatrophic areas of the skin appear in a period of time that varies between 4 weeks and 2 years after initiation of insulin therapy. It is crucial to recognize and treat this condition as early as possible. Insulin absorption at these

sites is unpredictable, which creates the prerequisites for hyperglycemia or hypoglycemia.<sup>1-6,8,9</sup>

A key element in prevention of this complication is the education of patients with diabetes. They should be instructed to alternate the injection sites, to observe the skin, and not to use the same needle for a long period of time (up to 12 times).<sup>9,10</sup> In case of lipoatrophy, attempts to treat the affected areas include topical corticosteroid injections. A positive reversal is recorded in some of the treated patients.<sup>11</sup>

## CONCLUSION

The present case report is intended to draw attention to one of the rare complications of diabetes mellitus, in particular one related with insulin therapy. Even treatment with insulin analogues may cause skin changes. Patient's education is very important in regard of titration of insulin doses depending on blood glucose values, as well as on the diet and the physical activity. Patients on insulin therapy should be advised on rotation of insulin injection sites and the need for more frequent needle change. This will minimize the occurrence of local skin reactions as an insulin treatment complication.

## REFERENCES

1. Reeves WG, Allen BR, Tattersall RB. Insulin-induced lipoatrophy: evidence for an immune pathogenesis. *Br Med J* 1980;280(6230):1500–3.
2. Richardson T, Kerr D. Skin-related complications of insulin therapy. *Am J Clin Dermatol* 2003;4(10):661–7.
3. Radermecker RP, Pierard GE, Scheen AJ. Lipodystrophy reactions to insulin. *Am J Clin Dermatol* 2007;8(1):21–8.
4. Murao S, Hirata K, Ishida T, et al. Lipoatrophy induced by recombinant human insulin injection. *Internal Med* 1998;37(12):1031–3.
5. del Olmo MI, Campos V, Abellán P, et al. A case of lipoatrophy with insulin detemir. *Diabetes Res Clin Practice* 2008;80(1):e20–1.
6. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes – 2018. *Diabetes care* 2018;41(Suppl 1):S13–27.
7. Griffin ME, Feder A, Tamborlane WV. Lipoatrophy associated with lispro insulin in insulin pump therapy: an old complication, a new cause? *Diabetes Care* 2001;24(1):174.
8. Ampudia-Blasco FJ, Hasbum B, Carmena R. A new case of lipoatrophy with lispro insulin in insulin pump therapy: is there any insulin preparation free of complications? *Diabetes Care* 2003;26(3):953–4.
9. Mokta JK, Mokta KK, Panda P. Insulin lipodystrophy and lipohypertrophy. *Indian J Endocrinol Metab* 2013;17(4):773.
10. Blanco M, Hernández MT, Strauss KW, et al. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. *Diabetes Metab* 2013;39(5):445–53.
11. Chantelau EA, Praetor R, Praetor J, et al. Relapsing insulin-induced lipoatrophy, cured by prolonged low-dose oral prednisone: a case report. *Diabetol Metab Syndr* 2011;3(1):33.

# Инсулин-индуцированная липоатрофия у пациента на терапии аналоговым инсулином: клинический случай

Веселина Яначкова<sup>1</sup>, Радиана Стайнова<sup>2</sup>

<sup>1</sup> Больница „Д-р Щерев“, София, Болгария

<sup>2</sup> Факультет фармации, Медицинский университет – Пловдив, Пловдив, Болгария

**Адрес для корреспонденции:** Веселина Яначкова, Больница „Д-р Щерев“, ул. „Христо Благоев“ 25-31, район „Разсадника“, София, Болгария; E-mail: v\_ess@abv.bg; Tel.: +359 886 436 963

---

**Дата получения:** 15 января 2020 ♦ **Дата приемки:** 13 марта 2020 ♦ **Дата публикации:** 30 сентября 2020

---

**Образец цитирования:** Yanachkova V, Staynova R. Insulin-induced lipoatrophy in a patient on insulin analogue therapy: a case report. *Folia Med (Plovdiv)* 2020;62(3):597-600. doi: 10.3897/folmed.62.e50166.

---

## Резюме

Инсулин-индуцированная липоатрофия является редким кожным осложнением у пациентов с сахарным диабетом. Она характеризуется главным образом локальной подкожной атрофией жировой ткани в месте частых инъекций инсулина. Мы сообщаем о клиническом случае 38-летней женщины с липоатрофией, которая развилась во время лечения аналогами инсулина. Формирование липоатрофической зоны началось через 3 месяца после начала лечения. Липоатрофический дефект развился на бёдрах и верхних частях руки после нескольких инъекций инсулина в одно и то же место. Что касается липоатрофических областей, было проведено лечение местными кортикостероидами, но не было значительного клинического эффекта. Лучшая профилактика против развития липоатрофии – информирование пациентов о ротации участков инъекции инсулина и более частой смене иглы.

---

## Ключевые слова

сахарный диабет, аналоги инсулина, липоатрофия

---