

CASE REPORT

Insulin Lipohypertrophy: A Non-Fatal Dermatological Complication of Diabetes Mellitus Reflecting Poor Glycemic Control

Ishrat H. Dar, Showkat H. Dar, Sumayya Wani¹

Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, ¹Endocrinology and Metabolism, AIIMS, New Delhi, India

Correspondence: Dr. Ishrat Hussain Dar, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir - 190 010, India. E-mail: dardrshrathussain@yahoo.com

ABSTRACT

Lipohypertrophy has been a recognized complication of insulin therapy. Despite improvements in insulin purity and the introduction of recombinant human insulin, its prevalence has remained high particularly in those with a poor glycemic control. Injection of insulin into a site of lipohypertrophy, although painless, may lead to erratic absorption of insulin, with the potential for poor glycemic control and unpredictable hypoglycemia. Rotation of injection sites can reduce the frequency of the problem but does not abolish it. The importance of this complication is not only cosmetic but also in its impact on insulin absorption, and hence glycemic control. Lipohypertrophy is characterized by a benign “tumor-like” swelling of fatty tissue secondary to subcutaneous insulin injections. A strong association of lipoatrophy and lipohypertrophy with insulin antibodies might suggest that autoimmune phenomena with insulin play a role in the development of both. Presented here is a young type 1 diabetic on human insulin with poor glycemic control who developed lipohypertrophy at the injection sites around the umbilicus.

Key words: Adipocytes, diabetes, dystrophy, insulin, insulin antibodies, lipohypertrophy

هذه دراسة حالة لمريض سكري من النوع الأول يعاني من تضخم شحمي في موضع حقن الأنسولين حول السرة ورغم أن حقن الأنسولين في موضع تضخم شحمي ليس مؤلماً إلا أنه ربما يؤدي إلى زيادة في امتصاص الأنسولين مما قد يتسبب في نقص التحكم وربما نقص معدل السكر في الدم. ولذا فإن تغيير موضع الحقن قد يقلل من هذه المشكلة.

INTRODUCTION

Lipohypertrophy is a potential clinical adverse effect associated with intensive insulin therapy. Insulin-induced lipohypertrophy is the loss of subcutaneous fat at the site of insulin injection. Lipohypertrophy seems to be due to a cellular response of adipocytes to the local effects of injected insulin. Despite change of insulin from bovine or porcine to human recombinant insulin, the problem of lipohypertrophy has remained

a major concern. Clinically the problem is seen more in type 1 than type 2 diabetics using insulin, and immunological factors seem to be important in its development.

CASE REPORT

A 26-year-old young man detected with type 1 diabetic at the age of 19 years and who was on subcutaneous insulin [recombinant human regular insulin and neutral protamine Hagedorn (NPH)] was admitted to the hospital with frequent fluctuations in his blood sugar levels and appearance of unsightly painless swellings at the injection sites. On examination the patient was of lean build with a body weight of 63 kg and a height of 1.58 m with a body mass index (BMI) of 25.23 kg/m². Blood pressure was 128/84 mm Hg. Pulse was 74/min regular with good volume. No pedal or sacral edema was noted and no lymphadenopathy was found. Chest

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and the cardiovascular system was normal and central nervous system examination showed absence of deep tendon reflexes in the lower limbs bilaterally suggestive of possible diabetic motor neuropathy. Fundus examination showed evidence of proliferative retinopathy with bilateral lenticular changes. Abdominal examination revealed the presence of two large masses one on each side of the umbilicus [Figures 1-3]. Both the masses were soft, rounded and movable about 8 cm in diameter with scars on the surface of the skin representing needle pricks of the insulin use. No other clinical abnormality was evident. Hematological and some biochemical investigations were practically normal (complete blood count, kidney function tests, liver function tests, electrolytes, thyroid function tests). Glycosylated hemoglobin (HbA_{1c}) was 8.5% and fasting blood glucose was 276 mg/dL. Lipid profile revealed cholesterol of 220, triglycerides 288, high density lipoproteins 34 and low density lipoproteins 158. Electrocardiogram (ECG), X-ray chest and ultrasound abdomen were normal. Routine urine examination and 24-h urinary protein were normal. Fine needle aspiration cytology (FNAC) of the swellings showed presence of mature adipocytes only. A diagnosis of type 1 diabetes with retinopathy and motor neuropathy with insulin-induced lipohypertrophy was made in view of the historical, clinical and investigative background. The patient was advised to avoid the abdominal sites for injecting insulin and was instructed to use the multiple rotation method in other sites as well. The glycemic control improved with HbA_{1c} falling to 7% and fasting blood glucose to 134 mg/dL. Requirement of insulin also showed a decrease reflecting the possible poor and erratic absorption of insulin from the lipohypertrophy site. Regular follow up of the patient showed a marginal decrease in the size of the swellings.

DISCUSSION

The incidence and prevalence of diabetes is increasing at an alarming rate and secondary failure of oral hypoglycemic agents is shifting the focus of treatment towards the use of insulin for better control of blood sugar but nonetheless has given rise to newer complications with its use. In the United Kingdom Prospective Diabetes Study (UKPDS) with over 10 years of observation, 38% of patients needed insulin to reduce fasting plasma glucose concentrations to <6 mmol/L.^[1] Insulin therapy is associated with skin-related complications like lipoatrophy, lipohypertrophy, edema or allergy.^[2] Lipoatrophy is the loss of subcutaneous fat at the site of insulin injection and occurred in patients who used porcine/bovine insulin. Use of highly purified



Figure 1: Showing the presence of two moderate sized swellings as seen in the forward bending position



Figure 2: Showing the presence of two well defined rounded masses in the erect position on either side of the umbilicus



Figure 3: Lateral view of the swellings as seen from the side

recombinant human insulin has made this complication rare. Lipohypertrophy is the most common cutaneous complication characterized by a tumor-like swelling of the fatty tissue around subcutaneous insulin injection sites

and reported prevalence ranges from 27 to 49% (Type 1 diabetes) and 4% (Type 2 diabetes) in different studies.^[3-7] Lipohypertrophy occurs because patients inject the same site day after day and frequently occurs on both sides of the umbilicus or in the mid thigh areas, as these are the most convenient places to inject and where the patient's hands reach most naturally.^[8] Sites are often asymmetrical as the dominant hand tends to inject one side preferentially. Eventually the area becomes hyposensitive and the patient feels less pain injecting the same area leading to erratic insulin absorption and poor glycaemic control.^[9-12] The pathophysiology of insulin-induced lipohypertrophy is generally thought to be the result of lipogenic effects of insulin and adipocytes enlarge and hypertrophy due to stimulation of proliferation and differentiation of preadipocytes as explained in a classic paper from Japan by Fujikura *et al.* Microscopic examination of a resected insulin-induced lipohypertrophy lump showed nests of mature adipocytes expanding toward the dermal reticular layer. The hypertrophic adipocytes were twice as large as those from normal subcutaneous areas and contained numerous small lipid droplets. Electron microscopic analysis also revealed a minor population of small adipocytes, suggesting active differentiation or proliferation.^[10] Lipohypertrophy seems to be due to a cellular response of the adipocytes to the local effects of injected insulin. But susceptibility to this complication varies significantly and therefore immunological factors may be more important. A study of lipohypertrophy in children and young adults with type 1 diabetes found that the titre of insulin antibodies correlated directly with the degree of lipohypertrophy and lipoatrophy in these patients thus suggesting that autoimmune phenomena with insulin play a role in their development but requires further longitudinal exploration.^[11] Other risk factors suggested for lipohypertrophy include young age, low body mass index, missing rotation, frequent injection at the same site, type of insulin, number of injections per day, total daily dose of insulin, reuse of needles and use of pen devices rather than syringes.^[7] Other than looking unsightly and causing frequent dysglycemia including hypoglycemia, the lipohypertrophied areas may not cause any life-threatening event.^[12] It has been suggested that the clinicians examine and palpate each case of erratic glycaemic control to look for lipohypertrophy.^[9] Change of sites and change of insulin may lead to regression in the size of the swellings but in extreme cases liposuction and even surgical removal may be mandatory.^[8,10] Insulin lispro has been reported

to resolve cases of lipohypertrophy caused due to short acting human recombinant insulin and may provide the much needed relief in susceptible individuals.^[13]

CONCLUSIONS

Look for lipohypertrophy in all patients being treated with insulin particularly in those with poor or erratic glycaemic control.

REFERENCES

1. UK Prospective Diabetes Study {UKPDS} Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:857-53.
2. Richardson T, Kerr D. Skin related complications of insulin therapy: Epidemiology and emerging management strategies. *Am J Clin Dermatol* 2003;4:661-7.
3. McNally PG, Jowett NI, Kurinczuk JJ, Peck RW, Hearnshaw JR. Lipohypertrophy and lipoatrophy complicating treatment with highly purified bovine and porcine insulin's. *Postgrad Med J* 1988;64:850-3.
4. Kordonouri O, Lauterborn R, Deiss D. Lipohypertrophy in young patients with type 1 diabetes. *Diabetes Care* 2002;25:634.
5. Vardar B, Kizilci S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. *Diabetes Res Clin Pract* 2007;77:231-6.
6. Schiazza L, Occella C, Bleidl D, Rampini E. Insulin lipohypertrophy *J Am Acad Dermatol* 1990;22:148-9.
7. Hauner H, Stockhamp B, Haastert B. Prevalence of lipohypertrophy in insulin treated patients and predisposing factors. *Exp Clin Endocrinol Diabetes* 1996;104:106-10.
8. Chowdhury TA, Escudier V. Poor glycaemic control caused by insulin lipohypertrophy. *BMJ* 2003;327:383-4.
9. de Villiers FP. Lipohypertrophy – a complication of insulin injections. *S Afr Med J* 2005;95:858-9.
10. Fujikura J, Fujimoto M, Yasue S, Noguchi M, Masuzaki H, Hosoda K, *et al.* Insulin induced Lipohypertrophy: Report of a Case with Histopathology. *Endocr J* 2005;52:623-8.
11. Raile K, Noelle V, Landgraf R, Schwarz HP. Insulin antibodies are associated with lipoatrophy but also with lipohypertrophy in children and adolescents with type 1 diabetes. *Exp Clin Endocrinol Diabetes* 2001;109:393-6.
12. Young RJ, Hannan WI, Frier BM, Steel JM, Duncan JP. Diabetic lipohypertrophy delays insulin absorption. *Diabetes Care* 1984;7:479-80.
13. Roper NA, Bilous RW. Resolution of lipohypertrophy following change of short acting insulin to insulin lispro (Humalog). *Diabet Med* 1998;15:1063-4.

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