Human Insulin–Induced Lipoatrophy

A successful treatment with glucocorticoid

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Before the development of purified insulin in the 1970s, lipoatrophy was a common complication of insulin therapy (1,2). With the arrival of human insulin, lipoatrophy has decreased dramatically, becoming a rare problem in clinical practice. Lipoatrophies are considered an adverse immunological side effect of insulin therapy, and in some cases they are mediated by a local high production of tumor necrosis factor-α, which leads to a dedifferentiation of adipocytes in the subcutaneous tissue. The treatment with corticosteroids is useful because of its immunomodulating properties and also because it is able to produce a differentiation of adipocytes (2–4).

In most reported cases of insulin-induced lipoatrophies, there were attempts of changing the injection areas without any evidence of improvement (5–8). Kumar et al. (9) in a single-blind study used small amounts of dexamethasone, adding 4 μg/unit to insulin injections, in nine patients with marked lipoatrophy in both thighs. A mix of insulin and dexamethasone was injected into one thigh and insulin without dexamethasone was injected into the other. This way, each patient was her own control subject. Six patients showed significant improvement. None used human insulin (9).

We report a case of localized lipoatrophy in a patient treated with human insulin since the onset of type 1 diabetes when the application of betamethasone was effective in stopping and reversing this abnormality.

RESEARCH DESIGN AND METHODS — We studied a 6-year-old multiethnic girl who was diagnosed with type 1 diabetes when she was 5 months old and then presented a glycemic level >600 mg/dl, ketoacidosis, and sepsis. She has been, since then, intermittently followed at the Endocrinology and Diabetes Unit at Alcides Carneiro University Hospital.

RESULTS — On the first medical appointment after hospital discharge, the patient was between the 20th and 30th percentiles for weight and between the 10th and 20th percentiles for height, according to the National Center of Health Statistics criteria. She was receiving 13 units daily of recombinant DNA human insulin (NPH associated with regular insulin), with an HbA_{1c} (A1C) level of 15.1% (reference value 4.0–6.2%). The patient's mother has participated effectively in the treatment by monitoring her daughter's glycemic levels (15 glycemic tests per month) at home and doing partial rotation of injection sites.

When she was 32 months, she returned to our care to investigate abdominal distention and growth rate reduction. She was using 10 units daily of NPH human insulin (unique dose) with an A1C of 7.5%. She was under the 2nd percentile for weight and height, according to the National Center of Health Statistics. The lab tests were compatible with celiac disease and a dietetic treatment was then applied.

She then came back only when she was 4.5 years old, in May 2004. She was using 10 units daily of NPH insulin with two circumscribed localized lipoatrophic areas of ~5 cm in diameter on both arms (Fig. 1*A*). She was presenting an A1C of 10.4%. According to her mother's report, the patient had been presenting atrophic lesions on injections areas for a year, at which point she looked for medical assistance in the city where she lives. Many treatments were tried, mainly the change of injections sites. However, there were also lipoatrophic lesions in these areas. Her mother tried to return to the first sites of injections because of the smaller intensity of pain the patient felt.

The chosen treatment was the injection on lipoatrophic areas of a mix of insulin and betamethasone, using 0.075 mg of corticoid in each injection. This had been tried successfully in the 1970s (10). She returned to our care after 1 month of hospital discharge, with an A1C of 8.8%, using 14 units daily of NPH insulin mixed with betamethasone. In November 2004, 6 months following this treatment, a total remission of lipoatrophy occurred (Fig. 1*B*).

CONCLUSIONS — We report a case of complication when following a recombinant DNA human insulin treatment, a rare observation in current clinical practice. Due to the rarity of this phenomenon it is difficult to find a sufficient number of cases to make a more extensive evaluation. This is the second case of lipoatrophy of 328 people with type 1 diabetes in

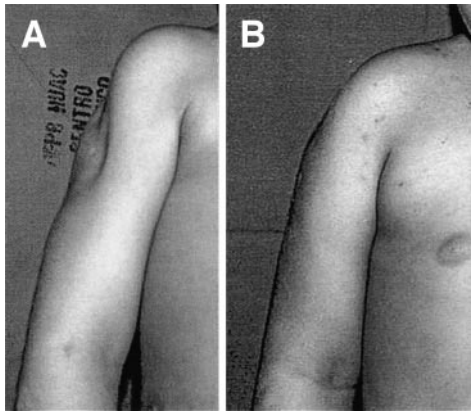

Figure 1—A*: Lipoatrophic area in the right arm.* B*: Total remission of lipoatrophic area.*

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

our care. In both cases, the use of betamethasone associated with insulin was effective. Due to the natural anxiety of the reported patient's parents and the child being too young—unlike the subjects in Kumar et al. (9)—we have chosen the treatment of all areas with lipoatrophy at the same time. Also unlike Kumar et al. (9), we have chosen the use of fixed doses of corticoids (0.075 mg/dose). It is possible that the use of corticoid doses per unit, in cases in which the patients use high insulin doses, can cause hypercortisolism; even so, this did not occur on the patients followed by Kumar et al., probably because of the lower insulin doses required by his patients (36.7 ± 18 units/day [means ± SD] before and 38.2 ± 18 units/day during the therapy) (9).

Since the advent of human insulin and insulin analogs, an important reduction in the number of people with lipoatrophy caused by insulin therapy occurred. We need other reports like this one as well as multicentric controlled studies to establish which is the best treatment for this rare but mutilating insulin therapy complication.

References

1. Hulst SG: Treatment of insulin lipoatrophy. *Diabetes* 25:1052–1054, 1976
2. Reeves WG, Allen BR, Tattersall RB: Insulin induced lipoatrophy: evidence for an immune pathogenesis. *Br Med J* 280: 1500–1503, 1980
3. McNally PG, Jowett NI, Kurinczuk JJ, Peck RW, Hearnshaw JR: Lipohypertrophy and lipoatrophy complicating treatment with highly purified bovine and porcine insulins. *Postgrad Med J* 64:850–853, 1988
4. Atlan-Gepner C, Bongrand P, Farnarier C, Xerri L, Choux R, Gauthier JF, Brue T, Vague P, Grob JJ, Vialettes B: Insulin-induced lipoatrophy in type I diabetes: a possible tumor necrosis factor-alpha–mediated dedifferentiation of adipocytes. *Diabetes Care* 19:1283–1285, 1996
5. Arranz A, Andia V, López-Guzmán A: A case of lipoatrophy with lispro insulin without insulin pump therapy (Letter). *Diabetes Care* 27:625–626, 2004
6. Griffin ME, Feder A, Tamborlane W: Lipoatrophy associated with lispro insulin in insulin pump therapy (Letter). *Diabetes Care* 24:174, 2001
7. Ampudia-Blasco FJ, Hasbum B, Carmena R: A new case of lipoatrophy with lispro insulin in insulin pump therapy (Letter). *Diabetes Care* 26:953–954, 2003
8. Jaap AJ, Horn HM, Tidman MJ, Walker JD: Lipoatrophy with human insulin. *Diabetes Care* 19:1289–1290, 1996
9. Kumar D, Miller LV, Mehtalia SD: Use of dexamethasone in treatment of insulin lipoatrophy. *Diabetes* 26:296–299, 1977
10. Arduino F: Complications of insulin use: allergy, resistance, lipodystrophy and hypoglycemia. In *Diabetes Mellitus.* 2nd ed. Arduino F, Ed. Rio de Janeiro, Brazil, Guanabara Koogan, 1980, p. 225–245