CASE REPORT

Human Insulin-Induced Lipoatrophy

Successful treatment using a jet-injection device

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OBJECTIVE — To evaluate the efficacy of the administration of insulin by a jet-injector device in stopping and reversing severe human insulin–induced lipoatrophy.

CASE — We report a case of a woman with severe human insulin–induced lipoatrophy who has been treated exclusively with recombinant DNA human insulin since the onset of IDDM.

RESULTS — The loss of subcutaneous tissue in the injection areas was demonstrated and measured by high-frequency ultrasound. Dermatologic exam demonstrated a severe reduction of fat tissue. After 8 months of administration of human insulin by a jet injector, there were no more new lesions of lipoatrophy and those affected areas were substantially ameliorated.

CONCLUSIONS — Jet-injection devices might constitute a helpful method to treat those patients affected by severe human insulin–induced lipoatrophy.

Since the introduction of highly purified insulins, lipoatrophy, a common complication associated with less purified forms of insulin, has rarely been seen. This secondary effect was considered to be an immunological reaction to the use of impure animal insulins (1). To our knowledge, there are very few reports describing lipoatrophy in patients treated with human insulin (2,3). In addition, there is only one case report in which this adverse effect was successfully treated by continuous subcutaneous infusion of insulin (4).

We report the case of a woman with severe insulin-induced lipoatrophy who has been treated exclusively with recombinant DNA human insulin since the onset of IDDM and in whom administration of the hormone by a jet injector was effective in stopping and reversing this abnormality.

CASE — A 21-year-old woman developed IDDM with mild ketosis in August 1990. She was treated with a thrice-daily dose of insulin: regular insulin (Actrapid HM, Novo-Nordisk, Bagsvaerd, Denmark) before breakfast and lunch delivered by a pen injector and a mixture of NPH (Insulatard HM, Novo-Nordisk) and regular insulin before dinner delivered by a syringe. Her weight was 54.6 kg, height 1.64 m (BMI 21 kg/m^2), and HbA_{1c} 9.8% (reference values 4.7–5.9%). Islet-cell antibodies were positive, and no insulin autoantibodies were found at diagnosis. The follow-up of the patient demonstrated satisfactory metabolic control, with HbA_{1c} determinations always <6.5%. After 2 years, lipoatrophy occurred around injection sites (left arm, abdominal wall, thighs, and buttocks), and it was especially severe at the left arm (Fig. 1).

RESULTS — Injection techniques were evaluated and no mistakes were found. Laboratory findings included an HbA_{1c} of 5.9% and plasma anti-insulin antibodies of 2+% (reference value <3%). A high-frequency ultrasound study (7.5 MHz) demonstrated a loss of subcutaneous tissue in the above-mentioned areas. Measurements were performed to evaluate the evolution of the lipoatrophic lesions. At the same time, a dermatologic evaluation of the lipotrophic areas was performed. Muscle tissue was completely normal, and fat tissue was clearly reduced, with areas of fibrosis. In the immunohistochemical analysis, neither inflammatory reaction nor immunoglobulin deposition was found.

Clinical course

Considering our findings, our patient started to administer insulin using a jet injector (Precijet-50, Advanced Medical Technologies, Charlottetown, P.E.I., Canada), avoiding those areas more severely affected. After 8 months of using the jet injector, there were no more new lesions of lipoatrophy and substantial amelioration of previously affected areas was demonstrated by ultrasound and physical exam. Metabolic control remained within satisfactory levels, with HbA_{1c} <6.2%, and anti-insulin antibody levels remained unchanged.

CONCLUSIONS — We report a further case of lipoatrophy complicating recombinant DNA human insulin treatment, an extremely rare observation. This secondary effect has commonly been described with less purified animal insulins, and an immunological basis for this condition has been suggested (1,5). On other occasions, the release of silicone oil from insulin-pen injectors has also been implicated in the etiology of such lesions (6).

In our case, in spite of a moderately high circulating insulin antibody titer, the dermatologic analysis of subcutaneous tissue was negative for inflammatory reaction or immunoglobulin deposition. Taking this finding into account, we did not attempt treatment with immunomodulators and an alternative therapy was selected. We opted for jet-injection insulin for several reasons: *1*) with jet injection, the insulin microjet stream penetrates and insulin is deposited subcutaneously in a dispersed way, has a relatively

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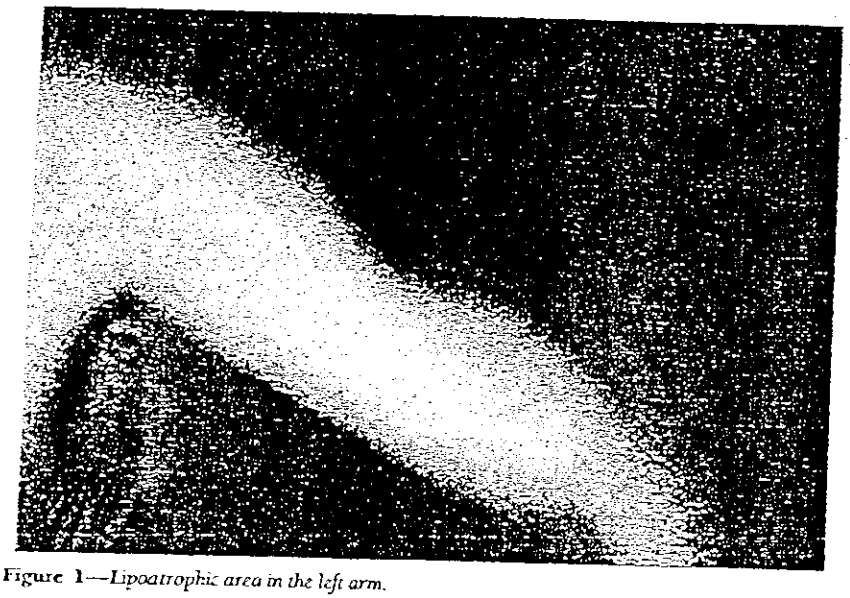

Figure 1—*Lipoatrophic area in the left arm.*

short half-life, and is thus less degraded (7,8); 2) the insulin is not contaminated by silicon oil; and 3) some studies have demonstrated that jet injection is associated with a diminished antibody response in short-duration insulin treatment (9).

In summary, we propose that jet-injection devices might constitute a helpful method to treat those rare cases of human insulin–induced lipoatrophy.

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