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 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 exams 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 insulin (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 1980. 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/m²), and HbA₁c 9.8% (reference values 4.7-5.9%). C-peptide antibodies were negative, and no insulin autoantibodies were found at diagnosis. The follow-up of the patient demonstrated satisfactory metabolic control, with HbA₁c determinations always <6.3%. After 2 years, lipoatrophy occurred around injection sites (left arm, abdominal wall, thigh, 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 HbA₁c of 5.9% and plasma anti-insulin antibodies of 21% (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, while areas of fibrosis. In the immunohistochemical analysis, neither inflammatory reaction nor immunoglobulin deposition was found.

Clinical course
Considering our findings, our patient scored to administer insulin using a jet injector (Precject-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 HbA₁c <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 titre, the dermatologic appearance 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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Received for publication 16 August 1995 and accepted in revised form 12 October 1995.

Diabetes Care, Volume 19, Number 3, March 1996

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short half-life, and is thus less degraded (7,8). 2) The insulin is not contaminated by silicone 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 lipodystrophy.

References


