Insulin-Induced Distant Site Lipoatrophy

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A 46-year-old Japanese woman with type 2 diabetes noticed a depression in her right anterior abdomen where she had previously injected insulin for approximately 9 months (human neutral protamine Hagedorn insulin and insulin lispro), and this lesion expanded to her right groin. About 18 months after the insulin injections were stopped, a second depression lesion appeared on her left buttock where she had never injected insulin (Fig. 1*A–C*). Computed tomography showed lipoatrophy of the right submandibular region, right anterior abdomen, and left buttock sites (Fig. 1*D* and *E*). Laboratory data

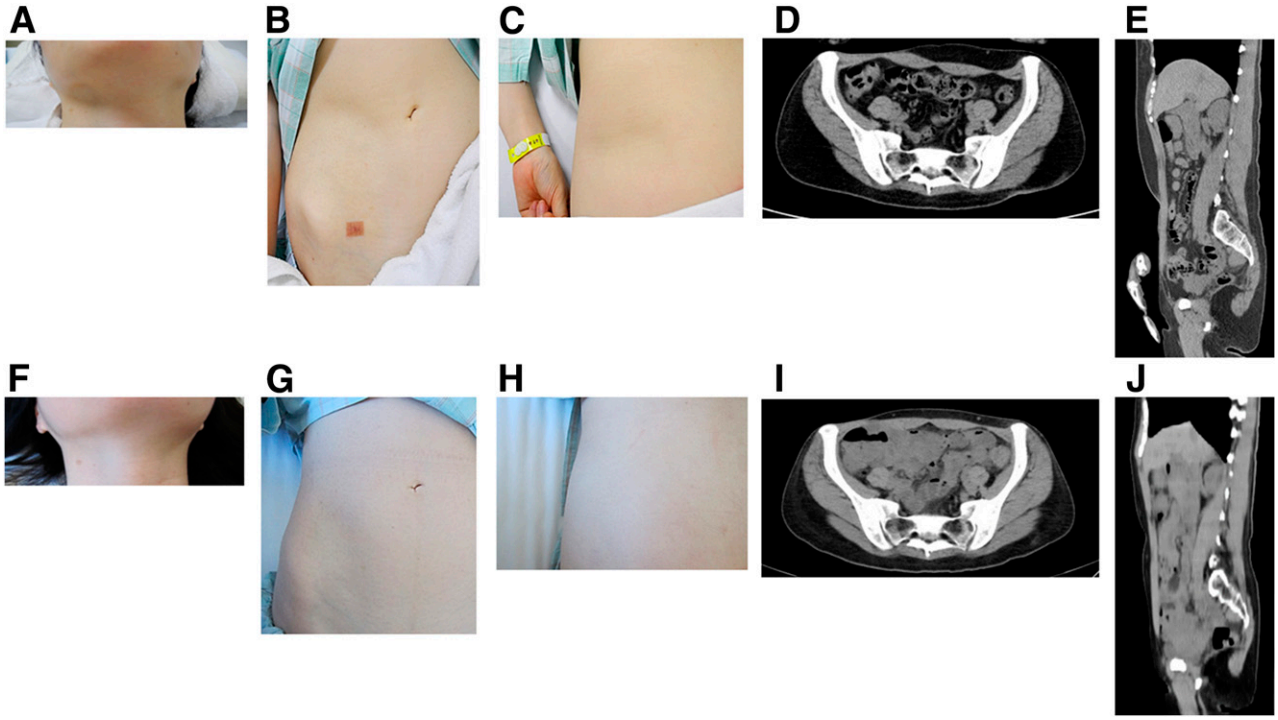

Figure 1—Areas of lipoatrophy in the right submandibular region (*A*, *F*), right anterior abdomen (*B*, *G*), and left buttock (*C*, *H*) and computed tomography imaging of the right anterior abdomen and left buttock (*D*, *I*) and over the groin (*E*, *J*) before (*A–E*) and after (*F–J*) improvement of lipoatrophy.

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showed high values of HbA_{1c} (8.9% [73 mmol/mol]) and fasting insulin levels (1,163 μU/mL). The insulin antibody titer was over 5,000 nU/mL, and the binding rate was 86.7%. Insulinoma was negative, with no increase in her fasting C-peptide level, and there was no hypoglycemia. The glucose infusion rate was 3.03 mg/kg/min as measured by the glucose clamp technique, a level that shows insulin resistance in Japanese subjects. A skin biopsy from the lipoatrophic area of her right anterior abdomen revealed that subcutaneous fat was absent and was replaced by fibrous connective tissue. Accordingly, the patient was diagnosed with insulin-induced lipoatrophy. Pioglitazone was given, followed by metformin, in the expectation of improvement of insulin resistance. HbA_{1c} (6.0% [41 mmol/mol]) and fasting insulin levels (23.1 μU/mL) were reduced and insulin resistance also improved (glucose infusion rate 6.57 mg/kg/min) after starting the insulin sensitizers. Interestingly, the lipoatrophy partially reversed (Fig. 1*F–J*).

Insulin-induced lipoatrophy is a rare complication of insulin therapy. Insulin-induced distant site lipoatrophy is even rarer. To the best of our knowledge, there are only a few reports of insulin-induced distant site lipoatrophy (1–3). It has been hypothesized that insulin-induced lipoatrophy is the result of an immunological reaction. Raile et al. (4) reported that there was a strong association between insulin antibody levels and lipoatrophy, which is consistent with our case. Regarding insulin-induced distant site lipoatrophy, Chakraborty and Biswas (3) speculated that it could be caused by a local lymphatic spread of the antigens from the injection site. However, we could not show the pathogenesis by histopathological analysis in our case.

Treatment options for local insulin-induced lipoatrophy include stopping insulin injections and changing injecting sites and insulin preparation. We chose the use of pioglitazone, followed by metformin, for the following reasons: *1*) the patient did not necessarily need insulin therapy because of her non–insulin-dependent state, and *2*) the main cause of her glucose intolerance was insulin resistance. As a result, her glucose tolerance improved with the administration of these agents. Interestingly, insulin-induced lipoatrophy also improved not only at the insulin injection site but also at the distant site. It has been reported that one of the adipose tissue–specific effects of thiazolidinediones is the stimulation of adipocyte differentiation (5); thus, pioglitazone might reverse the dedifferentiated adipocytes of the subcutaneous tissue. However, there is not enough evidence to state that insulin sensitizers reversed the lipoatrophy.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.
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