Diabetes Vignette

Lipoatrophy associated with insulin aspart in continuous subcutaneous insulin infusion

AH was diagnosed with gestational diabetes in the 28th week of her first pregnancy seven years previously. She was treated with insulin from diagnosis until delivery. Six weeks post-partum an oral glucose tolerance test confirmed diabetes (F 10.7, 2hr 18.9mmol/L). Anti-GAD antibodies were positive at 71 units/ml (normal range 0–1). She was commenced on a basal bolus regimen of aspart and glargine.

Due to recurrent hypoglycaemia, principally at night, her basal bolus regimen was replaced by continuous subcutaneous insulin infusion (CSII) delivering aspart three years previously. After two years of stability, blood glucose became erratic, with recurrent nocturnal hypoglycaemia. Examination of her infusion site revealed marked lipoatrophy in the right lower abdomen (Figure 1). She found use of her thighs cumbersome leading to cannulae dislodgement with resultant hyperglycaemia. She was advised to revert to the abdomen 11 months ago, this time on the left, with advice to stop if any skin dimpling was noted. So far no problems have been reported.

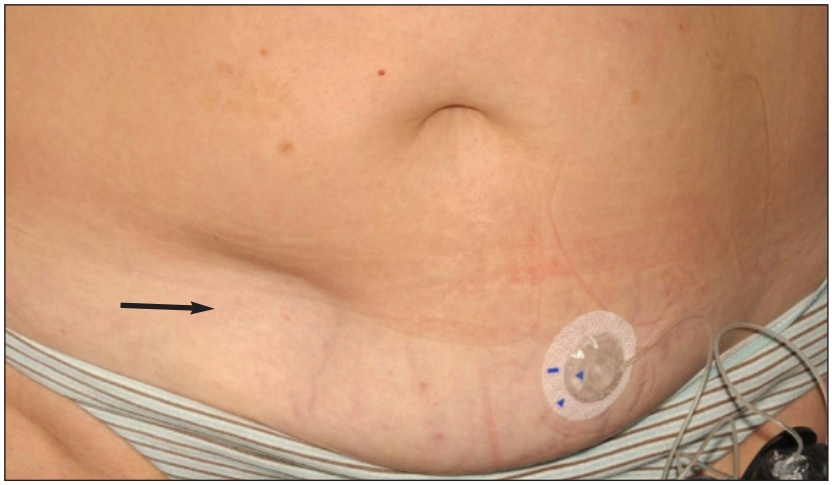

Figure 1. Examination of the infusion site revealed marked lipoatrophy in the right lower abdomen

Lipoatrophy was a common problem with impure insulin, e.g. NPH and zinc preparations. Chromatographic purification techniques allowed the production of highly purified animal insulin in the 1970s and this, together with mass production of human recombinant insulin in the 1980s, markedly reduced the incidence of lipoatrophy.

With early insulins (e.g. Lente), it was thought lipoatrophy resulted from immunological reaction to impurities. Some reports suggested impurities constituted almost 25% of the mixture.[1]

In vitro studies of patients who developed lipoatrophy in the presence of insulin have shown an increase in TNF-α and IL-6 by macrophages. A small series of biopsies of those with lipoatrophy showed degrees of atrophy and fibrosis, with variable lymphocytic, eosinophilic and mast cell infiltration. Histological examination of a subject who developed significant lipoatrophy, revealed small de-differentiated adipose cells.[2]

In 2001, Griffin *et al*. reported the first two cases of lipoatrophy associated with insulin lispro in a CSII.[3] There was no progression of atrophy when switched to human buffered Insulin. Lispro has also been reported to cause lipoatrophy when used as part of a basal bolus regimen.

Aspart (Novorapid) was found to cause lipoatrophy when part of a biphasic insulin mix.[1] To our knowledge there have been no accounts of lipoatrophy as a result of aspart when used as part of a continuous infusion as presented here.

The development of lipoatrophy in our patient, given no previous problem with aspart as part of a multiple daily injection regimen, suggests that her lipoatrophy could result from trauma from recurrent catheter insertions or possibly the Teflon-coated catheter surface, as in her case. A study of intravenous Teflon catheters revealed that native catheters, as opposed to catheters modified with ethyl hydroxyethyl cellulose, were associated with increased skin blood flow resulting in catheter-associated tissue reaction.[4]

Several therapeutic approaches on small numbers of patients with lipoatrophy have proved successful. Topical sodium cromoglycate, a mast cell stabiliser, was used in four out of five patients with lipoatrophy. After 12 weeks, significant reduction of lipoatrophy was observed. Non-resolution was observed in more chronic lesions.[2] Several groups have described resolution of lipoatrophy by injecting a mixture of glucocorticoids and insulin into the affected tissue.[5–7]

Areas of lipoatrophy can cause significant emotional distress to patients and may affect insulin absorption. Where blood glucose is variable one should consider lipoatrophy as a potential explanation, even with analogue insulin delivered as CSII.

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Declaration of interest

There are no conflicts of interest.

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