

The eye does not see what the mind does not know

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Case report

A 64 year old gentleman with a 15 year history of type 2 diabetes presented to us with extremely poor glycaemic control in spite of being on escalating insulin doses (100 Units/day). Multiple medical consultations over the preceding six months resulted in further addition of oral agents. His fasting glucose was 22 mmol/L, postprandial glucose of 29 mmol/L with glycosylated haemoglobin of 13.5%. There was no reason to suspect non-compliance. Clinical examination revealed a large area of lipohypertrophy over the right arm (Figure 1). On further questioning, the patient admitted to injecting insulin at the same site for the past 3 years with no rotation of sites. He was educated about injection site rotation and subsequently, glycaemic control improved dramatically over the next few weeks. On a recent follow-up, his fasting glucose was 5.5 mmol/L with a postprandial glucose of 8.2 mmol/L.

Discussion

Patients on high doses of insulin, polypharmacy and poor glycaemic control need to be evaluated through a proper algorithm, prior to escalating treatment. Differential diagnoses in such a scenario includes non compliance with insulin, wrong type of insulin for the clinical scenario, confusion with 40 and 100 Unit vials and syringes (in India), reduced potency of insulin due to storage issues, poor injection techniques, true insulin resistance due to intercurrent illness or endocrinopathies and finally lipodystrophies. A step wise approach would be helpful to exclude obvious correctable causes that could be easily missed. Our patient had visited multiple diabetologists and, unfortunately, the insulin lipohypertrophy was completely missed due to inadequate history and examination.

The estimated prevalence of significant insulin lipohypertrophy is around 20-30% in type 1 diabetes and approximately 4% in patients with type 2 diabetes.¹ Insulin lipohypertrophy seems to be related to a cellular response of the adipocytes to the local effects of injected insulin. The lesions are entirely composed of

Figure 1. A large area of insulin lipohypertrophy over the right arm



fatty tissue. The hypertrophic adipocytes are twice as large as those from the subcutaneous area and contain numerous small lipid droplets,² possibly illustrating the *in vivo* effects of insulin on adipocytes. Suggested risk factors for insulin lipohypertrophy include titres of insulin antibodies,³ frequent injections in the same site (as in our case), type of insulin, re-use of needles and use of pen devices rather than syringes.^{1,4}

Insulin lipohypertrophy can lead to erratic glycaemic control by delaying insulin absorption causing hyperglycaemia, as well as unpredictable hypoglycaemia. In a study looking at the effect of insulin absorption from lipohypertrophic injection sites, the clearance of radiolabelled insulin was significantly slower in the hypertrophied site compared to complementary non-hypertrophied sites.⁵ In addition, the lipohypertrophied sites can be unsightly and socially embarrassing.

In a busy diabetes clinic, there is always a tendency for physicians to make cursory superficial examination and be phamaco-centric. In fact, organizations like Diabetes UK advise physicians to check for insulin lipohypertrophy at least once a year. All physicians and diabetologists should take some time in palpating the insulin injection sites, as insulin lipohypertrophy is easier felt than seen. It is also important to educate all patients about rotating insulin injection sites to prevent such complications from occurring. Once a lipohypertrophic area is found, avoiding the particular area and rotating the injection site is often helpful. Our

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patient also needed a 30% reduction in his insulin doses after site rotation. Patients should be warned of hypoglycaemia once they change the sites, owing to improved insulin absorption.

Learning points

- Think of insulin lipohypertrophy in patients with erratic glycaemic control in spite of being on large doses of insulin
- Take time to examine injection sites
- Rotation of insulin injection sites is mandatory to prevent this complication.

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