Injection site reaction secondary to GLP-1 analogue therapy

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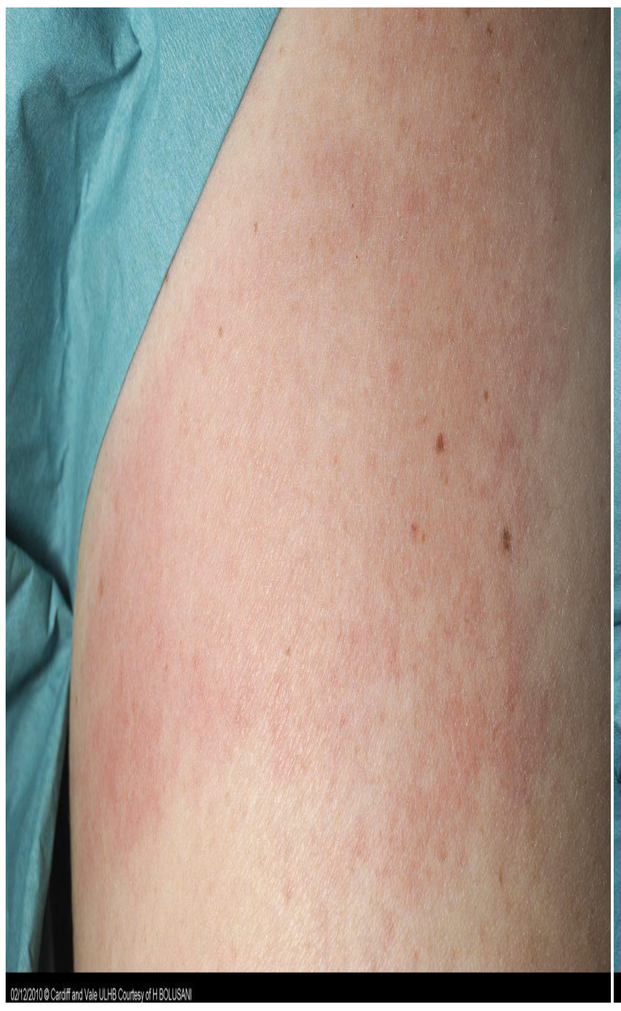
Introduction

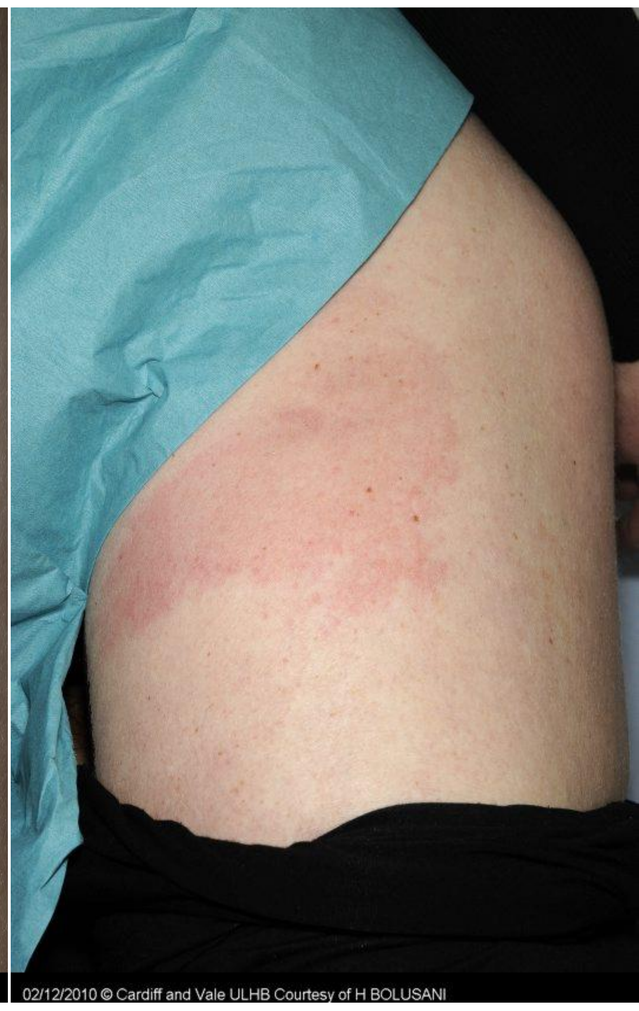
- The Glucagon like peptide -1 (GLP-1) or incretin effect is significantly reduced or absent in individuals with Type-2 diabetes.
- GLP -1 analogues are widely used in the management of Type -2 diabetes in the last decade.
- Exenatide was the first GLP-1 analogue to be approved in the treatment of obese Type 2 diabetes individuals with poor glycaemic control.
- Gastrointestinal adverse effects are well recognised with the use of GLP-1 analogues. However, hypersensitivity reactions including injection site reactions, generalized pruritus and or urticaria, macular or papular rash, angioedema, anaphylactic reactions have also been reported.
- We report a patient who developed allergic reaction at the injection site to exenatide.

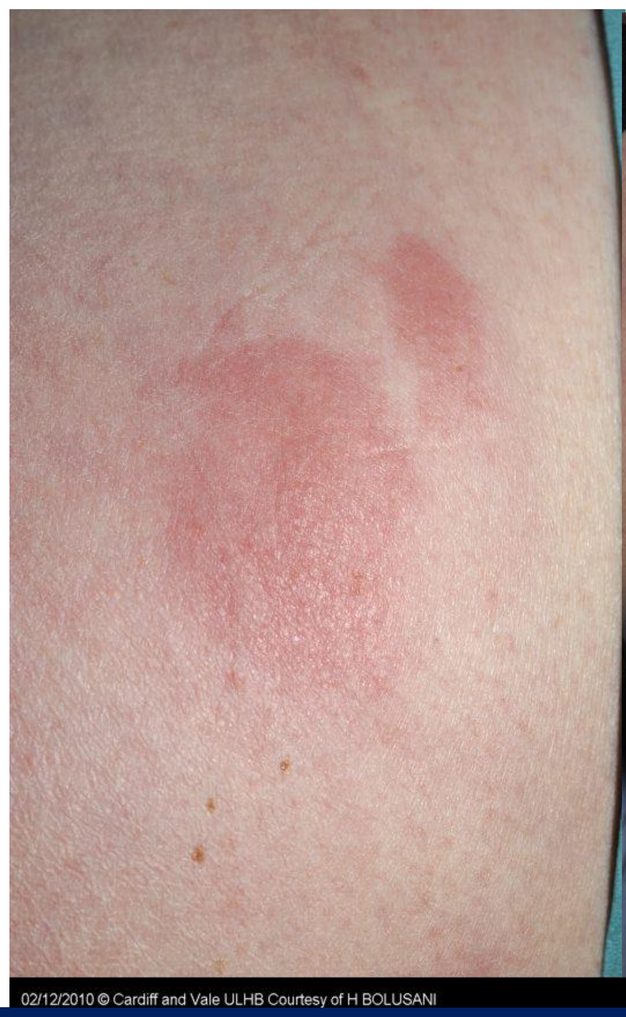
The Case

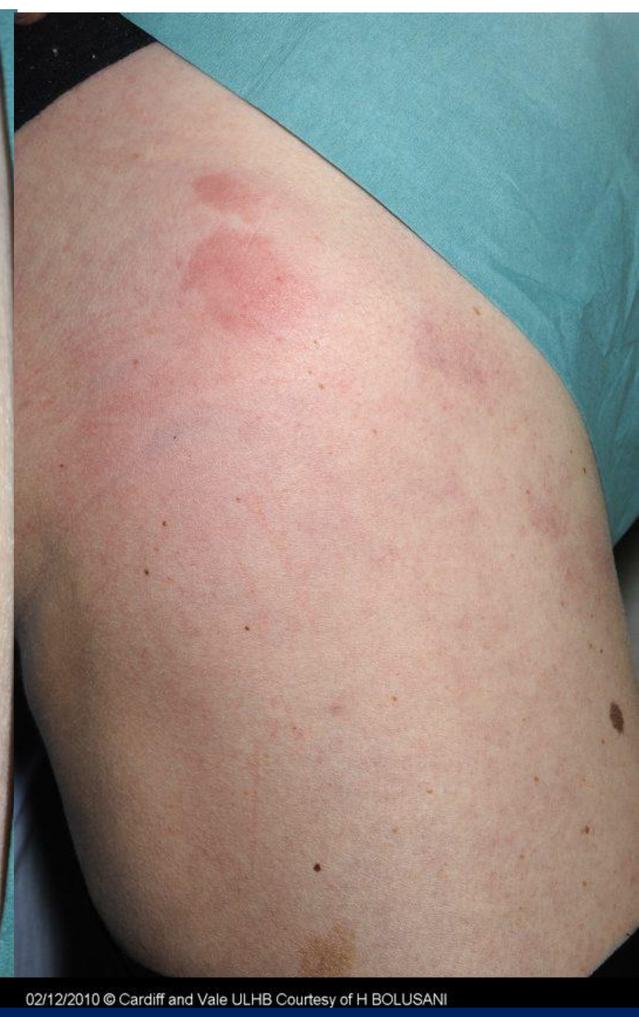
- A 54 years old lady with 12 years history of Type-2 diabetes and BMI of 33, was initiated on exenatide, as her glycaemic control was poor despite being on maximum oral hypoglycaemic therapy.
- She was started with 5 mcg twice a day and the dose was increased to 10 mcg after 4 weeks.
- She tolerated it well with no gastro intestinal side effects and showed satisfactory response in terms of weight and HbA1c
- About 4 to 6 weeks after initiating exenatide therapy, she started developing a rash at the injection site.
- The rash was mildly pruritic, diffuse, erythematous, urticated plaque with few papular lesions.
- She developed similar rashes at each injection site
- She was treated with oral antihistamines and topical steroids to relieve the symptoms and exenatide was discontinued.
- The rashes at all sites of injection gradually diminished over a 3 month period.

Injection site reaction









Discussion

- The precise pathogenesis of injection site reaction remains unclear, but possible mechanisms include immune reaction to GLP1 or excipients of the injection solution
- GLP-1 analogues are peptides, therefore antibody formation may occur triggering adverse effects ranging from mild injection reaction to anaphylaxis.
- This is supported by the fact that injection-site reactions were observed in 14.2% of antibody-positive patients in comparison to 3.1% of antibody-negative patients treated with Bydureon[1].
- The head to head studies have demonstrated that antibody formation is higher with the use of exenatide compared to liraglutide; likely to be due to the fact that exenatide shares only 53% of native GLP-1 peptide sequence, where as liraglutide shares 97% of the native sequence.
- Injection site reaction to long acting preparations like bydureon is also due to the dissolvable suture material in the formulation.
- Although most injection site reactions tend to decrease in frequency with continued treatment, a persistent or worsening reaction has been described.
- The antibody formation may potentially result in attenuation of the GLP-1 response with resultant failure to achieve gycemic control.
- It is important to recognise injection site reaction to GLP-1 analogues and stop the treatment apart from treating rashes, as they are not going to be effective in achieving adequate glycaemic control due to possible presence of neutralizing antibodies.

1. Fineman MS, Mace KF, Diamant M, et al. Clinical relevance of anti-exenatide antibodies: safety, efficacy and cross-reactivity with long-term treatment. Diabetes Obes Metab 2012;**4**:546–54**.**