Persistent injection site nodules from exenatide: Successful treatment with intralesional triamcinolone

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Key words: exenatide; intralesional triamcinolone; persistent injection nodules.

INTRODUCTION

Exenatide extended release is a once-weekly injectable medication used for the treatment of type II diabetes mellitus. The long-acting formulation consists of the original twice-daily formulation encapsulated in 0.06-mm-diameter microspheres.1 The subcutaneously injected exenatide microspheres then diffuse the medication slowly over time, reaching therapeutic range by 2 weeks and steady state by 6 to 7 weeks.1 Pharmacologically, it acts as an incretin analogue that activates glucagon-like peptide 1 receptors causing a glucose-dependent insulin secretion.2 Exenatide reduces Hgb-A1C, fasting and postprandial glucose, and bodyweight.2 The most commonly reported adverse events include nausea, vomiting, diarrhea, and headache.4 Common adverse reactions at the injection site include pruritus, erythema, and subcutaneous nodules, which have reportedly resolved without intervention or limiting treatment.1,3 These reactions are thought to be either an inflammatory foreign body reaction or an antiexenatide antibody response.1,4 A handful of cases have also identified eosinophil-rich granulomatous panniculitis at the exenatide injection site, along with more persistent, nonresolving nodules.5-8 For these rarer, persistent nodules, hospitalization and surgical intervention have been reported.8 We report a case of persistent exenatide extended release panniculitis nodules successfully treated with serial intralesional triamcinolone injections.

CASE REPORT

A 60-year-old man presented to the dermatology clinic with 6 large, persistent nodules of the abdomen and left thigh, occurring after each of his exenatide extended release weekly injections. The patient denied fevers, chills, lymphadenopathy or systemic allergic symptoms. The patient’s medical history was significant for diabetes mellitus type II, hypertension, dyslipidemia, and nonalcoholic steatohepatitis (NASH). Before starting exenatide, he had been on metformin, liraglutide, and dulaglutide for treatment of his diabetes.

The first nodule occurred 8 weeks prior, without any improvement over time. The nodules were extremely pruritic, with mild discomfort because of the size of the lesions and induration.

Fig 1. Two firm subcutaneous nodules with overlying erythema on the right abdomen.

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examination found a large, firm 5.5-cm × 4-cm subcutaneous nodule on the left side of the abdomen with 5 other 2.0- to 4.0-cm deep nodules palpated from the right and left sides of the abdomen as well as the left thigh. Slight erythema and warmth was noted from the overlying skin of each nodule. Because of the patient’s discomfort, exenatide was discontinued by the prescribing physician for approximately 2 weeks, and the nodules were treated with betamethasone 0.5% cream and Zyrtec for 1 week without improvement. The patient requested excision of each of these large nodules, as the pruritus was no longer bearable.

An excisional biopsy was taken from a nodule on the right side of the abdomen, and we elected to inject a separate superior right abdominal nodule with intralesional triamcinolone (10 mg/mL, 1 mL injected; Fig 1). Pathology findings from the specimen showed a lobular and septal panniculitis with mononuclear cells and prominent admixed eosinophils (Fig 2, A and B). A dermal hypersensitivity reaction was also present with moderate predominantly perivascular lymphohistiocytic infiltrate with admixed eosinophils and occasional plasma cells. Periodic acid–Schiff and acid-fast bacilli stains were negative.

During a telephone call 2 weeks after his visit, the patient described worsening erythema surrounding the biopsy site with yellow, thickened drainage. Thus, he was started on doxycycline, 100 mg twice daily for a week. After this course, the patient was started on a 6-week prednisone course (starting at 50 mg) with the addition of 50 mg of dapsone to treat the nodules. The patient reported, however, that he discontinued both medications after approximately 1 week because of worsening of his lower extremity edema.

The patient followed up in the dermatology clinic 6 weeks after his initial evaluation, with great improvement within the nodule on the right side of the abdomen that was treated with intralesional triamcinolone. This nodule now measured 0.8 cm and showed greater than 50% improvement in size. The remaining nodules were similar in size, but the overlying erythema was no longer appreciated. Each nodule was injected with 10 mg/mL of triamcinolone, placed 1 mL deep within the subcutaneous tissue of each involved area. He then returned 6 weeks later with significant improvement of all of his nodules. There were 2 subtle, less than 0.5 cm persistent nodules from the right and left sides of the abdomen that were injected again, with just 0.5 mL of triamcinolone (10 mg/mL) at this visit. The patient was extremely relieved that the pruritus and discomfort of the nodules had resolved. No skin atrophy developed from the triamcinolone injections, and they were well tolerated by the patient.

**DISCUSSION**

Local, transient injection site reactions are common among injectable medications. However, rarer, atypical persistent nodules, panniculitis, and even morphea-like changes of the skin have been reported with various subcutaneous injected medications, and prescribing physicians need to be aware of this.5–10 As the number of subcutaneously injected medications expands, we suspect the number of more atypical, persistent cutaneous reactions will follow. Proper patient education is imperative, along with prompt cessation of the drug. Depending on the patient’s history and the reaction involved, consideration of immediate systemic intervention or intralesional steroid injections is warranted. As reported in our case, patients can have significant improvement with serial intralesional triamcinolone injections in lieu of undergoing multiple surgical procedures.
REFERENCES
1. DeYoung MB, MacConell L, Sarin V, Trautmann M, Herbert P. Encapsulation of exenatide in poly-(D,L-lactide-co-glycolide) microspheres produced an investigational long-acting once-weekly formulation for type 2 diabetes. Diabetes Technol Ther. 2011;13(11):1145-1154.
2. Gentilella R, Bianchi C, Rossi A, Rotella CM. Exenatide: a review from pharmacology to clinical practice. Diabetes Obes Metab. 2009;11(6):544-556.
3. Grimm M, Han J, Weaver C, et al. Efficacy, safety, and tolerability of exenatide once weekly in patients with type 2 diabetes mellitus: an integrated analysis of the DURATION trials. Postgrad Med. 2013;125(3):47-57.
4. Bhavsar S, Mudaliar S, Cherrington A. Evolution of exenatide as a diabetes therapeutic. Curr Diabetes Rev. 2013;9(2):161-193.
5. Shan SJ, Guo Y. Exenatide-induced eosinophilic sclerosing lipogranuloma at the injection site. Am J Dermatopathol. 2014;36(6):510-512.
6. Boysen NC, Stone MS. Eosinophil-rich granulomatous panniculitis caused by exenatide injection. J Cutan Pathol. 2014;41(1):63-65.
7. Andres-Ramos I, Blanco-Barrios S, Fernandez-Lopez E, Santos-Briz A. Exenatide-induced eosinophil-rich granulomatous panniculitis: a novel case showing injected microspheres. Am J Dermatopathol. 2015;37(10):801-802.
8. Jones SC, Ryan DL, Pratt VS, Niak A, Brinker AD. Injection-Site nodules associated with the use of exenatide extended-release reported to the U.S. Food and Drug Administration Adverse Event Reporting System. Diabetes Spectr. 2015;28(4):283-288.
9. Domingos J, Ricotti V, Martinez AE, Muntoni F. Severe persistent injection site reactions after subcutaneous 2’-O-methyl phosphorothioate oligonucleotide therapy for Duchenne muscular dystrophy. Neuromuscul Disord. 2018;28(2):176-177.
10. Ho J, Rothchild YH, Sengelmann R. Vitamin B12-associated localized scleroderma and its treatment. Dermatol Surg. 2004;30(9):1252-1255.