Eosinophilic Panniculitis Following the Subcutaneous Injection of Exenatide Extended-Release

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Exenatide extended-release was recently developed as an antidiabetic drug; it acts as a glucagon-like peptide-1 receptor agonist. A 54-year-old male visited our clinic complaining of a subcutaneous tender nodule on his left thigh that had developed over the course of 1 week. The patient had received exenatide extended-release injections for 5 months to treat diabetes. A histopathologic examination showed septal and lobular panniculitis with lymphohistiocytic and eosinophil infiltration. The patient was diagnosed with eosinophilic panniculitis (EP) due to exenatide extended-release injection. EP is a rare type of panniculitis characterized by a prominent infiltrate of eosinophils in the subcutaneous fat layer. It is a histologic reaction pattern that is associated with various clinical conditions. Among the injection-site reactions reported in exenatide extended-release users, injection-site nodules occur infrequently. Clinicians who treat diabetics who use exenatide extended-release should be aware of the possible occurrence of injection-site nodules. (Ann Dermatol 32(3) 230 ~ 232, 2020)

Keywords
Diabetes mellitus, Exenatide, Panniculitis

INTRODUCTION
Exenatide, a glucagon-like peptide-1 receptor agonist, is effective in the treatment of type 2 diabetes. In particular, exenatide extended-release (BYDUREON®; AstraZeneca, Cambridge, England, UK) is a long-acting antidiabetic drug that only requires administration once per week. This drug is convenient but can sometimes cause cutaneous injection-site reactions1. Here, we describe a case of eosinophilic panniculitis (EP) induced by exenatide extended-release at the injection site.

CASE REPORT
A 54-year-old male complained of a slowly enlarging nodule on his left thigh that had occurred 1 week previously. A physical examination revealed a solitary 2-cm skin-colored nodule without pain but with some tenderness (Fig. 1). The patient had been a type 2 diabetic for 17 years and had received exenatide extended-release injections. He had experienced no side effects during the course of treatment and was injected in his thigh once per week over a period of 5 months. The nodule was excised and sent for histopathologic examination, which revealed lobular and septal panniculitis with fat necrosis along with lymphohistiocytic cells and some eosinophils (Fig. 2). Multinucleate giant cells with vacuoles and spaces were also observed. He was diagnosed with EP due to exenatide extended-release injection. No relapse has occurred after changing to an oral medication for the last 2 years.
DISCUSSION

EP is a rare type of panniculitis that was initially described by Burket and Burket in 1985. Histopathologically, it is characterized by a prominent infiltrate of eosinophils in the subcutaneous fat layer, and it presents with both septal and lobular patterns. A granulomatous inflammatory infiltrate and fat necrosis can sometimes be observed. Clinically, although the morphology of EP-associated skin lesions is diverse, nodular lesions are the most common manifestation, as in our case. EP is considered to be a histologic reaction pattern that is associated with a variety of conditions such as arthropod bites, erythema nodosum, leukocytoclastic vasculitis, lupus panniculitis, gnathostomiasis, and substance injections, including sodium heparin.

Exenatide extended-release was developed to encapsulate exenatide in poly-(D,L-lactide-co-glycolide) (PLG) microspheres, which can extend its duration of action. Foreign body-like reaction could occur in response to these PLG microspheres. Shan and Guo speculated that the eosinophilic reaction after exenatide extended-release injection might be associated with a lack of the enzyme that hydrolyzes PLG to lactic acid and glycolic acid. Moreover, previous reports identified the histopathologic appearance of the microspheres of PLG in exenatide-induced eosinophilic granulomatous panniculitis. Injection-site reactions in exenatide extended-release users were observed more frequently (17.1%) compared to exenatide (12.7%) and insulin glargine (1.8%) users. Pruritus is the most common local injection-site reaction, while nodules are relatively frequent and benign. Patient withdrawal rates because of injection-site nodules are only 0.5% in exenatide extended-release users.

In the US Food and Drug Administration Adverse Event Reporting System, 27 nodule cases, including abscess (22.2%; 6/27), were reported from 27 January 2012 to 31 December 2013. Among these, biopsy of the nodules was performed in only two cases and one of them was diagnosed as necrotizing adipose tissue. In other studies, four case reports of exenatide extended-release-induced injection-site granuloma were identified. In these cases, the nodule occurred at the injection site. The histopathologic features revealed fat necrosis with eosinophils and mixed cell infiltration, similar to our case.

To the best of our knowledge, our present case is the first report of EP following the injection of exenatide extended-release in the Korean literature. As more patients are using exenatide extended-release, clinicians who care for patients with diabetes who use exenatide extended-release should be aware of the possible occurrence of injection-site nodules.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Fig. 1. A solitary, tender skin-colored subcutaneous nodule on the left thigh is shown (dotted line).

Fig. 2. (A) Low-power view showing lobular and septal panniculitis. (B) High-power view showing fat necrosis with a mixed inflammatory cell infiltrate containing abundant eosinophils (H&E staining; original magnification: A, ×40; B, ×200).
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