



Imagens em Endocrinologia

## Angioedema Secondary to Exenatide



Mariana Esteves <sup>a,\*</sup>, Sandra Alves Morais <sup>a</sup>

<sup>a</sup> Serviço de Medicina Interna, Centro Hospitalar de Trás-os-Montes e Alto Douro, Vila Real, Portugal

### INFORMAÇÃO SOBRE O ARTIGO

#### Historial do artigo:

Received/ Recebido: 2022-11-06

Accepted/Aceite: 2022-12-18

Publicado / Published: 2023-01-18

© Autor (es) (ou seu (s) empregador (es)) e Revista SPEDM 2022. Reutilização permitida de acordo com CC BY-NC. Nenhuma reutilização comercial.

© Author(s) (or their employer(s)) and SPEDM Journal 2022. Re-use permitted under CC BY-NC. No commercial re-use.

#### Keywords:

Angioedema/chemically induced;  
Diabetes Mellitus, Type 2/drug therapy;  
Exenatide/adverse effects.

## Angioedema Associado ao Exenatide

#### Palavras-chave:

Angioedema/induzido quimicamente;  
Diabetes Mellitus Tipo 2/tratamento farmacológico;  
Exenatide/efeitos adversos.

Exenatide extended release is a weekly subcutaneous injectable glucagon-like peptide-1 (GLP-1) receptor agonist approved by European Medicines Agency (EMA) in 2011.<sup>1</sup> The mechanism of action involves the enhancement of insulin secretion from pancreatic beta-cells, the delaying of gastric emptying and the suppression of glucagon secretion which is known to be inappropriately elevated in patients with type 2 diabetes, leading to lower glucagon concentrations and therefore to decreased hepatic glucose output. The most frequently reported adverse reactions were nausea, diarrhea and injection site reactions (such as pruritus, nodules, erythema). Interestingly, angioedema is documented as a potential side effect of exenatide by its manufacturer however its frequency of occurrence remains unknown<sup>1</sup> and only one case has been reported in literature.<sup>2</sup> Angioedema is a self-limited subcutaneous or submucosal swelling caused by a localized increase in microvascular permeability. Angioedema subdivides in three main categories: histamine-, leukotriene-, and bradykinin-mediated. Allergic angioedema (or histamine-mediated) is one of the most common causes of angioedema and can be triggered by exposure to certain foods, drugs or insect bites.<sup>3</sup>

A 43-year-old woman with a history of diabetes mellitus admitted to the emergency room with an exuberant progressive swelling of the lips and periorbital region, associated with pruritic rash on the chest and abdomen with a reported 3 days of evolution. She had no history of allergies, trauma or family history of angioedema. No other alterations on examination were found. The patient initiated an extended release exenatide 13 days before admission and had her second dose 6 days prior. The diagnosis of angioedema secondary to exenatide was assumed and she was treated with antihistamines and corticosteroids, with resolution of symptoms. The patient was discharged the following day with a course of corticosteroids and antihistamines, given the prolonged half-life of exenatide, and an indication to discontinue exenatide. She made a full recovery.

Regarding our patient's symptoms (angioedema associated with pruritic rash), the temporal sequence (2 weeks post-first injection, which concurs with the first peak plasma concentration of exenatide),<sup>4</sup> the resolution with conventional treatment (antihistamines and steroids) and the negative family history, allergic angioedema secondary to exenatide was assumed. The underlying mechanism for the development of drug-associated angioedema is multifactorial<sup>5</sup> and since GLP-1 agonists induced angioedema is a rarely reported adverse effect, this mechanism remains uncertain.

\* Autor Correspondente / Corresponding Author.

E-Mail: [mariana.martins.esteves@hotmail.com](mailto:mariana.martins.esteves@hotmail.com) (Mariana Martins Esteves)

Centro Hospitalar de Trás-os-Montes e Alto Douro  
Avenida da Noruega, 5000-508 Vila Real, Portugal

<https://doi.org/10.26497/ie220065>

1646-3439/© 2022 Sociedade Portuguesa de Endocrinologia, Diabetes e Metabolismo. Publicado por Sociedade Portuguesa de Endocrinologia, Diabetes e Metabolismo. Este é um artigo Open Access sob uma licença CC BY-NC (<https://creativecommons.org/licenses/by-nc/4.0/>).



**Figure 1.** Angioedema – Front view: Exuberant swelling of the lower lip, right-side of upper lip and face.



**Figure 2.** Angioedema – Lateral view: Exuberant swelling of the lower lip, right-side of upper lip and face.

This case aims to raise awareness to the extremely rare potential adverse effect of angioedema secondary to exenatide, which has only been reported once in literature. Moreover, this case reminds us to a fundamental detail, the necessity of prolonging the course of treatment due to the prolonged half-life of exenatide.

#### Contributorship Statement / Declaração de Contribuição:

ME: responsible for writing and revising the article / responsável pela redação e revisão do artigo.

SAM: responsible for reviewing the article / responsável pela revisão do artigo.

#### Responsabilidades Éticas

**Conflitos de Interesse:** Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

**Fontes de Financiamento:** Não existiram fontes externas de financiamento para a realização deste artigo.

**Confidencialidade dos Dados:** Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

**Consentimento:** Consentimento do doente para publicação obtido.

**Proveniência e Revisão por Pares:** Não comissionado; revisão externa por pares.

#### Ethical Disclosures

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

**Financing Support:** This work has not received any contribution, grant or scholarship.

**Confidentiality of Data:** The authors declare that they have followed the protocols of their work center on the publication of data from patients.

**Patient Consent:** Consent for publication was obtained.

**Provenance and Peer Review:** Not commissioned; externally peer reviewed.

#### References / Referências

1. European Medicines Agency. European Public Assessment Report for Bydureon (exenatide weekly). EMEA/H/C/002020 - II/0074. [accessed in October 2022] Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/bydureon>.
2. Mahfooz F, Aylor K, Mathew J Jr, Reichmuth M. Extending our understanding of exenatide: a rare case of angio-oedema. *BMJ Case Rep.* 2021;14:e235663. doi: 10.1136/bcr-2020-235663.
3. Tarbox JA, Bansal A, Peiris AN. Angioedema. *JAMA.* 2018;319:2054. doi: 10.1001/jama.2018.4860.
4. Bhavsar S, Mudaliar S, Cherrington A. Evolution of exenatide as a diabetes therapeutic. *Curr Diabetes Rev.* 2013;9:161-93. doi: 10.2174/1573399811309020007.
5. Weldon D. Differential diagnosis of angioedema. *Immunol Allergy Clin North Am.* 2006;26:603-13. doi: 10.1016/j.iac.2006.09.006.