First Reported Case of Allergy to Somatostatin

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Somatostatin is an oligopeptide hormone discovered in 1973 as a neurotransmitter that is secreted naturally in humans. It inhibits the secretion of growth hormone by the hypophysis and insulin and glucagon by the pancreas. Furthermore, it induces hepatic and splenic arterial vasoconstriction with no major systemic hemodynamic effects [1]. Therefore, somatostatin has been demonstrated to be an effective treatment in the acute management of esophageal variceal bleeding [2].

Despite its extended use, reported cases of allergy to this drug are scarce, with most of them related to an analogue of the natural hormone somatostatin. Two of the cases were associated with octreotide. The first report involved a 12-year-old boy who had had 2 episodes of apparent allergy symptoms after an octreotide infusion (positive intradermal test results) that necessitated desensitization treatment [3]. The second one involved a 42-year-old man who experienced 2 episodes of a generalized rash after a subcutaneous octreotide injection. No allergy study was performed [4]. The third case was related to somatostatin. However, the symptoms consisted of hyperthermia and pancytopenia, which are more suggestive of adverse effects, as the authors report, than of an allergic reaction. Moreover, since no allergy tests were performed, it may be considered a doubtful allergic reaction [5].

We present the case of a 56-year-old man with a previous history of alcoholic hepatic cirrhosis, which had previously been stable, and esophageal varices. No previous allergy history was reported. He was treated at the emergency department after an episode of suspected upper digestive bleeding. He was hemodynamically stable, with no anemia or thrombopenia, and received an initial infusion bolus of somatostatin (GP-Pharm). A few minutes later, he developed itchy hives on his chest and neck, facial angioedema, dyspnea, dizziness, and, subsequently, cardiorespiratory arrest. He required cardiopulmonary resuscitation maneuvers and intravenous treatment with methylprednisolone 80 mg,

dexchlorpheniramine 10 mg, and epinephrine 0.5 mg. His symptoms improved, and his hemodynamic status stabilized. The tryptase level during the reaction was 13.3 µg/L. No other treatments or food had previously been taken. It was the first time he received treatment with exogenous somatostatin.

The allergology study was initiated 3 months later, after the patient provided his written informed consent. The study comprised a skin prick-by-prick test with somatostatin 1/1, which was immediately positive in the patient (eliciting a hive of 8×7 mm in 10 minutes) and negative in 4 controls (2 atopic and 2 nonatopic). The baseline tryptase level was 3.9 µg/L. We performed a basophil activation test (BAT, BasoFlowEx Exbio) using somatostatin at 4 × 10-fold concentrations with the patient's blood sample and blood from a nonatopic healthy control. The population of basophils was defined as CD203cpos/SSClow by flow cytometry. The results are expressed as the percentage of CD63-positive basophils (activated basophils). Dose–response curves were constructed using serial 1:10 dilutions of the drug, starting at 3 mg/mL in phosphate-buffered saline solution. A cross-linking anti-IgE antibody mixed with a stimulating peptide, N-formyl-Met-Leu-Phe (fMLP), was used as a positive control. The diagnostic reliability of this test was inconclusive in the present case owing to the absence of basophil activation in the positive control and for the drug in the patient, in contrast with the results for the nonatopic healthy control.

Allergic sensitivity to endogenous hormones has previously been addressed, with a wide variety evaluated, including progestogen [6], estradiol [6], and insulin [7]. Individual cases of allergy to the analogue of somatostatin have also been reported [3,4]. To date, no cases of allergy to somatostatin have been published, and the only data available are for an adverse effect [5].

In 1983, somatostatin was demonstrated to be a potent histamine secretagogue [8]. It was later shown to have a secretory and inhibitory impact on histamine production, mainly affecting gastric receptors, by acting as a regulatory hormone [9]. In the present case, a positive prick-by-prick test with somatostatin (4 negative controls), together with a significative increase in tryptase level during the reaction (to 9.4 µg/L, ie, 3-fold), objectively demonstrated an anaphylactic reaction. The absence of basophil activation in the BAT has been demonstrated in 10%-20% of the general population, and multiple external factors can alter the accuracy of the BAT. A negative BAT result does not exclude allergy [10]. Components and excipients other than somatostatin and sodium hydroxide have not been reported in the summary of product characteristics (somatostatin GP-Pharm), leaving the possibility of allergy to other substances. We report the first case of allergy to somatostatin.

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Conflicts of Interest

Dr. Betancor was supported by a Rio Hortega Research Contract from Instituto Carlos III, Spanish Ministry of Science. Dr. Valverde has received lecture fees from GSK and sits on advisory boards for Organon. Dr. Rial reports receiving personal fees from GSK, Allergy Therapeutics, and AstraZeneca outside the submitted work. Dr. Sastre reports grants and personal fees from Sanofi, GSK, Novartis, AstraZeneca, Mundipharma, and Faes Farma outside the submitted work. The remaining authors declare that they have no conflicts of interest.

References

1. Olias G, Viollet C, Kusserow H, Epelbaum J, Meyerhof W. Regulation and function of somatostatin receptors. J Neurochem. 2004;89(5):1057-91.
2. Huaringa-Marcelo J, Huaman MR, Brañez-Condorena A, Villacorta-Landeo P, Pinto-Ruiz DF, Urday-Ipanaqué D, et al. Vasoactive Agents for the Management of Acute Variceal Bleeding: A Systematic Review and Meta-analysis. J Gastrointestin Liver Dis. 2021;13;30(1):110-21.
3. Azkur D, Yoldas T, Toyran M, Kocabas CN. A pediatric case of anaphylaxis due to octreotide. Asian Pac J Allergy Immunol. 2011;29(4):361-3.
4. Priyotosh B, Tarun K, Phrang S, Kupar P, Devi S, Pfuzia A. Octreotide induced hypersensitivity reaction: a rare case report. Int J Adv Res. 2017;5;1921-3.
5. Wu C, Gu F, Cong X, Li J, Li X. Severe Allergic Reaction Caused by Pre-Operative Somatostatin Analog Treatment of Tsh- and Gh- Secreting Pituitary Adenoma: A Case Report. Am J Biomed Sci Res. 2019;6;322-6.
6. Chiarella SE, Buchheit KM, Foer D. Progestogen Hypersensitivity. J Allergy Clin Immunol Pract. 2023;12:S2213-2198
7. Caballero ML, Quirce S. Delayed Hypersensitivity Reactions Caused by Drug Excipients: A Literature Review. J Investig Allergol Clin Immunol. 2020;30(6):400-8
8. Diel F, Bethge N, Oprée W. Histamine secretion in leukocyte incubates of patients with allergic hyperreactivity induced by somatostatin-14 and somatostatin-28. Agents Actions. 1983;13(2-3):216-8.
9. Vuyyuru L, Schubert ML, Harrington L, Arimura A, Makhlouf GM. Dual inhibitory pathways link antral somatostatin and histamine secretion in human, dog, and rat stomach. Gastroenterology. 1995;109(5):1566-74.
10. Kleine-Tebbe J, Erdmann S, Knol EF, MacGlashan DW Jr, Poulsen LK, Gibbs BF. Diagnostic tests based on human basophils: potentials, pitfalls and perspectives. Int Arch Allergy Immunol. 2006;141(1):79-90.

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