

# Angioneurotic edema: a rare case of hypersensitivity to metoclopramide

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## Abstract

The case of a 30-year-old woman who had already experienced two incidents of angioneurotic edema and urticaria caused by drugs during the acute gastroenteritis. The allergological workup revealed hypersensitivity to metoclopramide. This case documents that metoclopramide, a drug commonly used to inhibit the vomiting, may cause not only bronchospastic reaction in an asthmatic patient but also angioneurotic edema of the tongue and larynx as well as urticaria. No similar cases in the literature were found.

**Key words:** metoclopramide, angioneurotic edema, hypersensitivity to drugs.

## Introduction

Despite the permanent progress of knowledge in undesirable drug after-effects, they still pose a serious and difficult diagnostic problem in everyday medical practice. The number of undesirable drug after-effects is still growing and is closely linked with the growing number of therapeutic substances placed on the market. However, applying the drugs which are popular and have been universally used for decades can be a reason for rare and not previously described hypersensitivity of such drugs.

The paper presents the case of a woman who experienced the recurrent edema of the tongue and urticaria after applying metoclopramide. The presented case is an example of a probably allergic or pseudo-allergic drug after-effect which cannot be foreseen [1].

## Case report

The paper presents the case of a 30-year-old woman admitted to the Department of Infectious Diseases and Allergology, Military Institute of Medicine, who had already experienced two incidents of face and tongue angioneurotic edema and generalized urticaria but without accompanied breathlessness. The first incident occurred in 2002 and the second one in 2011. The patient had negative family and ontogenetic past history of atopy. She had never been diagnosed for illnesses requiring long-term phar-

macologic therapy. She had linked these incidents with receiving the drugs being used during the acute gastroenteritis. In both cases, metoclopramide and nifuroxazide were used and the symptoms of urticaria and angioneurotic edema appeared during the second day of treatment with these drugs.

The patient's past history was confirmed by the medical documentation delivered by her. Beside the previously described incidents, other symptoms of hypersensitivity to drugs or food were not observed. Within the physical examination at the time of admission, no significant deviations from the normal condition were found. Additional laboratory tests did not reveal any abnormalities. During the hospitalization the skin tests – epidermal and intradermal with metoclopramide – were performed. The test results were negative. The single blank test with metoclopramide was also performed. During the second day of the oral provocation angioneurotic edema occurred. The skin tests included prick tests with the common inhalant allergens aimed at determining potential co-occurrence of atopy. Positive results were obtained only for the tree pollen of birch, alder and hazel. The obtained information was not reflected in the patient's past history.

## Discussion

According to most authors, allergic reactions being the cause of undesirable drug after-effects constitute

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**Table 1.** Drug groups which are most frequently linked to the pseudo-allergic symptoms and mechanisms of these reactions [3]

Pathomechanism of pseudo-allergic reactions	Drugs causing pseudo-allergic reactions
Direct degranulation of mastocytes – release of mediators	Antibiotics, atracurium, D-tubocurarine, opiates, contrast mediums, dextran
Activation of complement	Immunoglobulins, heparin-protamine complexes, roentgenological contrast media, protamine
Activation of the kinin system	Angiotensin-converting-enzyme inhibitor
Stimulation of vegetative and free receptors	Metabisulfite, local anesthetics drugs
Release of neurotransmitters	Erythrosine, glutamate

around 10-15% of all undesirable reactions. Despite the common pathogenetic characteristic, which is the involvement of the immunocompetent cells, the drug after-effects are characterized by broad diversity of the clinical picture. The immunological mechanism of a given drug after-effect can constitute each of the listed types of effects according to the Gell and Coomb Classification. Moreover, the occurrence of two or more mechanisms active simultaneously or sequentially is typical of some of the hypersensitivity effects. The diagnostic difficulties can be caused by the fact that as regards the clinical picture, the pseudo-allergic and idiosyncrasy effects can be similar to the allergic effects. For obvious reasons, among all four types listed within the classification the most important is type I of hypersensitivity related to the IgE which can be a cause of serious, life-threatening, generalized immediate effects. The most common clinical drug after-effect is macular and popular rash. As regards frequency of occurrence, the second clinical effect is urticaria, particularly its acute form. In 40% of all the cases it is accompanied by angioneurotic edema. The isolated edema can be admittedly a clinical effect of the hypersensitivity to the drug but it is mainly related to the congenital or acquired dysfunction of C1 complement inhibitor. The studies available in the European centers show that urticaria and angioneurotic edema occur in 21-25% of patients being hospitalized because of undesirable drug after-effects [2-4]. The presented case of the patient is a very good example of difficulties in determining the mechanisms responsible for the release of mediators of inflammatory reaction to skin and subcutaneous tissue. Taking into account that the skin tests of the prick type as well as intradermal type performed for the patient brought clear negative results and attempt of oral provocation brought a clear positive result, it is justified to suspect that the observed effects resulted from the pseudo-allergic reaction. Unfortunately, it was not possible to determine the detailed mechanism of reaction in this case. Many drugs and sorts of food are active as the so-called direct histamine release factor causing degranulation of mastocytes and basophilic granulocytes without IgE participation [5]. It should be added that some sort of drugs can be a reason for a pseudo-allergic

reaction as well as allergic and allergic IgE-dependent reactions. In the presented case, the IgE-dependent allergy could be excluded because of the negative results of the skin tests (Table 1).

In conclusion, currently the problem of drug allergy is one of the most complex issues of contemporary medicine. It is because the mechanisms of many drug after-effects have not been sufficiently examined. Each physician applying drugs in the therapeutic process should know their undesirable effects, which can occur after their administration. However, many of them are rarely used and their clinical picture is so atypical that a physician who is applying them cannot recognize their effects. Because of that it should be possible to consult a specialist allergist specially trained in this area. Any additional reason for the high complexity of the issue is the fact that the pseudo-allergic reactions, clinically similar to the allergic reactions, can occur. Both types of reactions belong to the kind of reactions which cannot be predicted. Even in the case of drugs which have been commonly used for years and they did not cause any hypersensitivity reactions as in the case of metoclopramide, such possibility should be taken into account as a part of the analysis of undesirable effects.

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