

A CASE OF PROBABLE MACROGOL ALLERGY IN URTICARIA / ANGIOEDEMA**PATIENT****SHORT TITLE:** A CASE OF PROBABLE MACROGOL ALLERGY**WORD COUNT:** 597**TABLE COUNT:** 0**FIGURE COUNT:** 1Minna E Kubin¹ and Riitta Riekk¹¹Department of Dermatology, Oulu University Hospital, Oulu, Finland**Corresponding author:**

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e-mail: minna.kubin@ppshp.fi[Tel: +358 8 315 3508](tel:+35883153508)[fax: +358 8 315 3801](tel:+35883153801)**FUNDING:** None**AUTHOR CONTRIBUTIONS:** Both authors contributed extensively to the case report presented in this manuscript.**DISCLOSURES:** The authors have declared no conflicts of interest.**KEY WORDS:** *macrogol 6000, polysorbate 80, urticaria, angioedema*

Macrogols are used widely as dispersing agents, solvents and excipients in the production of pharmaceutical preparations as well as in food and cosmetic industry¹. Anaphylactic reactions to macrogols have been reported after intake of tablet-form drugs^{2,3}, injectable corticosteroid solutions^{4,5} and ingestion of bowel-cleansing preparations^{6,7}. We report here a patient who was at first suspected of having a more common hypersensitivity reaction to NSAIDs, but turned out to have macrogol allergy.

A 28-year-old healthy female was referred to our clinic due to angioedema and widespread urticaria. The patient had given birth a few months earlier, and during labor she had been given several drugs: lidocaine (Lidocain®), levobupivacaine (Chirocaine®), bupivacaine (Bicain®) and lidocaine spray (Xylocain®). Widespread urticaria and angioedema developed at the end of the labor. The patient was treated with hydrocortisone (Solu-Cortef®) and hydroxyzine (Atarax®). Previous anamnesis revealed a history of mild occasional urticaria and angioedema, which had exacerbated upon ingestion of ibuprofen (Burana®) and diclofenac (Voltaren rapid®). Non-allergic NSAID hypersensitivity was primarily suspected, but to exclude allergies, the patient was prick tested with the medications used. Prick tests with bupivacaine, levobupivacaine, lidocaine, chlorhexidine, latex and macrogol 6000 were done; ibuprofen and macrogol 6000 were positive (weal diameter, respectively, 9 mm and 9 mm + pseudopods; histamine weal 6 mm; Fig. 1a). An additional intradermal test with lidocaine and a prick test with lidocaine spray were performed; the tests were negative. Prick tests were then performed with diclofenac and macrogol 400 diluted 0.001%, 0.01%, 0.1% and pure; diclofenac was positive (weal diameter 8 mm + pseudopods; histamine weal 5 mm; Fig. 1b). Finally, since cross-reactivity has been suggested in the literature⁸, prick testing with polysorbate 20, polysorbate 80 and povidone were done; polysorbate 80 was positive (weal diameter 6 mm, histamine weal 5mm). Intradermal testing or oral challenge was not done for safety reasons, as systemic anaphylactic reactions have been reported following similar testing⁴. The patient was advised to systemically check drugs and products potentially containing macrogols, including personal hygiene products and preserved foods and to carry an epinephrine injector with her all the time due to the fact that systemic reactions to macrogols have been reported and complete avoidance can prove difficult.

The treatment of patients with macrogol allergy is rather challenging. Drugs that are used to treat allergic reactions, for example antihistamines, contain macrogols. Also, macrogols are not

necessarily mentioned in the ingredients of foods, making avoidance almost impossible. Little is known about the mechanism by which macrogols cause allergic reactions. As Shah et al. report in their literature review¹, several studies demonstrating a delayed hypersensitivity to macrogols have been performed, but studies on immediate hypersensitivity reactions are extremely rare. The true hypersensitivity to macrogols is, however, suspected to be higher than reported⁷.

Cross-reactivity with macrogol analogies, as in this case, macrogol 6000 and polysorbate 80 (a macrogol-derivative), has been reported⁸. Clinical allergy may also be dependent on both dose and route of administration. Lower molecular weight (200-700) macrogols are liquid, and have been reported to cause contact dermatitis or contact urticaria while higher molecular-weight macrogols (1000-7500) are solid, and have been implicated in cases of anaphylaxis⁹. It is unclear whether the molecular weight or route of administration could affect the allergic response in macrogol-sensitized patients¹⁰.

This case resembled the more common NSAID hypersensitivity, but the tests revealed an allergy to excipients. The patient had not used many medications during her life but had handled macrogol-containing powder in a fume hood during laboratory work. Thus, sensitization via inhalation cannot be excluded, and we can only speculate as to what caused her to be sensitized to macrogols.

REFERENCES

1. Shah S, Prematta T, Adkinson NF, Ishmael FT. Hypersensitivity to polyethylene glycols. *J Clin Pharmacol* 2013;**53**:352-355.
2. Hyry H, Vuorio A, Varjonen E, Skyttä J, Mäkinen-Kiljunen S. Two cases of anaphylaxis to macrogol 6000 after ingestion of drug tablets. *Allergy* 2006;**61**:1021.
3. Co-Minh HB, Demoly P, Guillot B, Raison-Peyron N. Anaphylactic shock after oral intake and contact urticaria due to polyethylene glycols. *Allergy* 2007;**62**:92-93.

4. Borderé A, Stockman A, Boone B *et al.* A case of anaphylaxis caused by macrogol 3350 after injection of a corticosteroid. *Contact Dermatitis* 2012;**67**:376-378.
5. Dewachter P, Mouton-Faivre C. Anaphylaxis to macrogol 4000 after a parenteral corticoid injection. *Allergy* 2005;**60**:705-706.
6. Pizzimenti S, Heffler E, Gentilcore E *et al.* Macrogol hypersensitivity reactions during cleansing preparation for colon endoscopy. *J Allergy Clin Immunol Pract* 2014;**2**:353-354.
7. Savitz JA, Durning SJ. A rare case of anaphylaxis to bowel prep: a case report and review of the literature. *Mil Med* 2011;**176**:944-945.
8. Yamasuji Y, Higashi Y, Sakanoue M *et al.* A case of anaphylaxis caused by polyethylene glycol analogues. *Contact Dermatitis* 2013;**69**:183-185.
9. Bommarito L, Mietta S, Nebiolo F, Geuna M, Rolla G. Macrogol hypersensitivity in multiple drug allergy. *Ann Allergy Asthma Immunol* 2011;**107**:542-543.
10. Pérez-Pérez L, García-Gavín J, Piñeiro B, Zulaica A. Biologic-induced urticaria due to polysorbate 80: usefulness of prick test. *Br J Dermatol* 2011;**164**:1119-1120.

FIGURES

Figure 1: (a) Positive prick reactions to ibuprofen (Burana® 600 mg), macrogol 6000 and (b) to diclofenac (Voltaren Rapid®).