

A case of anaphylaxis caused by macrogol 3350 after injection of a corticosteroid

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Macrogols are polymers of ethylene glycol, and are widely used in food and food packaging, and also in cosmetics and pharmaceutical preparations as solvents, softening agents, and lubricants. There are different types of macrogols, according to their molecular weight (e.g. macrogol 400, 3350, 4000, and 6000). There have been reports of anaphylactic reactions to macrogol

after injection of a corticosteroid solution (1), use of electrolyte lavage solutions (2), use of a throat lozenge (3), ingestion of tablet-form drugs (4), and use of topical corticosteroids (5).

Case Report

We report a case of an anaphylactic reaction to macrogol 3350 (CAS No. 25322-68-3) after an intra-articular injection of Depo-Medrol Lidocaine[®] (methylprednisolonacetate, macrogol 3350, benzyl alcohol 8.7 mg/ml, lidocaine 10 mg, myristyl-gamma-picolinium chloride, sodium chloride, and water for injection).

A 54-year-old woman gave a history of an anaphylactic reaction after an intra-articular injection with Depo-Medrol Lidocaine[®] in her shoulder. She reported respiratory distress, generalized erythema, itch, and hypotension, a few minutes after the injection. Her general practitioner immediately treated her with an intramuscular injection of Solu-Medrol[®] (methylprednisolone sodium succinate), and this gave relief of the symptoms. No adrenaline was injected.

The patient has a history of atopy (allergic rhinoconjunctivitis and eczema), urticaria (mild dermatographism), lichen planus, migraine, and fibrocystic breast disease. In addition, she mentioned sneezing when handling wheat flour and erythema after eating lobster.

Prick tests with a panel of inhalation allergens, Depo-Medrol and wheat flour were positive for tree pollen, dermatophagoides farinae, cat, wheat flour, and Depo-Medrol.

We were not able to obtain the separate constituents of Depo-Medrol from the manufacturing laboratory; components of Depo-Medrol that were commercially available were ordered and prepared for skin testing by the pharmacy of our hospital.

Prick tests with macrogol 3350 diluted 0.01%, 0.1%, 1% and 10% and pure were slightly positive for 10% and the pure solution (weal diameter, respectively, 3 and 5 mm; histamine weal 7 mm).

To differentiate between an irritant test result and allergy, the patient was admitted to perform intradermal testing with macrogol 3350 in increasing concentrations (CFR prick tests) while being monitored. Thirty minutes after intradermal injection of the 10% solution of macrogol 3350, the patient developed rhinitis, and itching in her mouth and throat. Ten minutes later, she developed anaphylactic shock with a general itch with weals on her legs, hypotension, and lowered consciousness. She was treated with 0.5 ml of 1/1000 intramuscular adrenaline and two tablets

Table 1. Drugs containing macrogol 3350⁽⁹⁾

KLEAN-PREP [®] powder	TROBALT [®] 50-mg tablets
MOVICOL [®] oral powder	TROBALT [®] 100-mg tablets
MOVICOL-HALF [®] oral powder	TROBALT [®] 200-mg tablets
MOVICOL PAED PLAIN [®] 6.9 g/sachet	TROBALT [®] 300-mg tablets
MOVIPREP [®] oral powder sachets	TROBALT [®] 400-mg tablets
MOVICOL PLAIN [®] 13.7 g/sachet powder	TROBALT [®] tablet initiation pack
LAXIDO ORANGE [®] oral powder sachet	MEDIKINET XL [®] 10-mg m/r capsules
MOVICOL CHOCOLATE [®] 13.9 g/sachet	MEDIKINET XL [®] 20-mg m/r capsules
COMPOUND MACROGOL [®] s/f oral powder	MEDIKINET XL [®] 30-mg m/r capsules
MOLAXOLE [®] oral powder sachets	MEDIKINET XL [®] 40-mg m/r capsules
MOVIPREP ORANGE [®] oral powder sachet	MEDIKINET XL [®] 5-mg m/r capsules
MOVICOL [®] orange concentrated solution 500 ml	KALETRA [®] 200 mg/50-mg tablets
VOLIBRIS [®] 5–10-mg tablets	KALETRA [®] 100 mg/25-mg tablets
SEVIKAR [®] 20/5-mg tablets	PREZISTA [®] 300-mg tablets
SEVIKAR [®] 40/5-mg tablets	PREZISTA [®] 400-mg tablets
SEVIKAR [®] 40/10-mg tablets	PREZISTA [®] 600-mg tablets
SEVIKAR [®] HCT 20/5/12.5-mg tablets	PREZISTA [®] 75-mg tablets
SEVIKAR [®] HCT 40/5/12.5-mg tablets	PREZISTA [®] 150-mg tablets
SEVIKAR [®] HCT 40/10/12.5-mg tablets	CELESTRIN [®] 150-mg tablets
SEVIKAR [®] HCT 40/5/25-mg tablets	CELESTRIN [®] 300-mg tablets
SEVIKAR [®] HCT 40/10/25-mg tablets	ATRIPLA [®] 600/200/245-mg tablets
XARELTO [®] 10-mg tablets	ISENTRESS [®] 400-mg tablets
XARELTO [®] 15-mg tablets	BONEFOS [®] 800-mg tablets
XARELTO [®] 20-mg tablets	JANUVIA [®] 100-mg tablets
NU-SEALS ASPIRIN [®] 75-mg e/c tablets	ONGLYZA [®] 5-mg tablets
HEMOFIL M [®] 250 iu inj + solv	ONGLYZA [®] 2.5-mg tablets
HEMOFIL M [®] 500 iu inj + solv	JANUMET [®] 50/1000-mg tablets
HEMOFIL M [®] 1000 iu inj + solv	TOVIAZ [®] 4-mg m/r tablets
UNIFLU PLUS GREGO C [®] tablets 2 × 6	TOVIAZ [®] 8-mg m/r tablets
ATARAX [®] 10-mg tablets	NASTROSA [®] 1-mg tablets
ATARAX [®] 25-mg tablets	LYSODREN [®] 500-mg tablets
INVEGA [®] 3-mg m/r tablets	NEXAVAR [®] 200-mg tablets
INVEGA [®] 6-mg m/r tablets	ADENURIC [®] 80-mg tablets
INVEGA [®] 9-mg m/r tablets	ADENURIC [®] 120-mg tablets
INVEGA [®] 12-mg m/r tablets	BACTROBAN [®] 2% ointment 15 g
NU-SEALS ASPIRIN [®] 300-mg e/c tablets	LAXAGOL [®] sachet 20
CODIPAR [®] caplets	LAXAGOL [®] sachet 30
VEGANIN [®] tablets	LAXIDO ORANGE [®] s/f powder sachet 30
ZAPAIN [®] caplets	LAXIDO ORANGE [®] s/f powder sachet 20
PALEXIA [®] 50-mg tablets	LAXIDO ORANGE [®] s/f powder sachet 8
PALEXIA [®] 75-mg tablets	LAXAGOL [®] powder lemon/lime 20
TARGINACT [®] 10/5-mg m/r tablets	LAXAGOL [®] powder lemon/lime 30
TARGINACT [®] 20/10-mg m/r tablets	
TARGINACT [®] 5/2.5-mg m/r tablets	
TARGINACT [®] 40/20-mg m/r tablets	

m/r, modified release; e/c, enteric-film coated; s/f, suspension forte; g/sachet, gram per sachet; iu, international unit; inj, injection; solv, solvent

of levocetirizine, and completely recovered. She was discharged on the same day.

She was seen the following day because she had developed erythematous swellings where the 1% and 10% solutions were injected on the previous day (diameter, respectively, 10 and 20 mm). The lesions disappeared after treatment with ebastine, but reappeared several hours later. Treatment with two tablets of ebastine daily was continued for 1 week, with complete resolution of the lesions.

Additional tests (prick test, intradermal tests, and provocation tests) with lidocaine and methylprednisolone were performed to rule out additional allergies. These tests gave negative results. **A basophil activation test (BAT) for macrogol 3350 gave a negative result.**

Discussion

Anaphylaxis after injections with corticosteroids can be caused by an allergy to the corticosteroid itself, or to additives such as carboxymethylcellulose (6, 7), or, less frequently, to macrogols. There have been only a few case reports of anaphylactic reactions to macrogols. Our patient had an anaphylactic reaction to macrogol 3350. As macrogols are so widely used in the food industry and medicines (e.g. antihistamines; see Table 1), management of hypersensitivity to macrogols is challenging. It is unclear whether the hypersensitivity response depends on the route of administration (oral versus parenteral). An allergic response to oral administration of macrogols after anaphylactic reaction to parenteral macrogols has been described (8). **It is unclear whether the hypersensitivity reaction is specific for macrogols of a certain**

molecular weight. Cross-allergies are possible, but have only occasionally been investigated. **Our patient tolerated medication containing macrogol 400.**

Also, little is known about the mechanisms causing hypersensitivity to macrogols.

The fact that the skin test gave a positive result is suggestive of an IgE-mediated reaction. Knop et al. suggest that complement activation is responsible, causing hypersensitivity reactions that may lead to anaphylactic shock (10).

The **BAT** for macrogol 3350 gave a negative result (11, 12). Basophils have high-affinity IgE receptors, and can be **used as indicator cells for IgE-mediated reactions.** Upon allergen challenge, basophils upregulate intracellular markers and activation markers on their surface. In the BAT, these alterations can be detected by multicolour flow cytometry with specific monoclonal antibodies. With this technique, one can prove the IgE dependence of a drug reaction. However, false-negative reactions are also possible.

In this case report, a patient with hypersensitivity to macrogol 3350 has been described. Macroglols are widely used as additives in medications, and should not be overlooked in the work-up of anaphylactic reactions following the use of medication. **Intradermal tests should only be performed in a unit fully equipped to promptly treat anaphylaxis, because patients can develop anaphylaxis during this type of testing.**

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