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Long persistence of IgE antibody to cefaclor

R. Bernardini*, E. Novembre, E. Lombardi, N. Pucci, M. E. Rossi, A. Vierucci

Key words: cefaclor; child; IgE.

● ADVERSE drug reactions are a common clinical problem in childhood, and antibiotics are among the major contributors to drug hypersensitivity (1). Cefaclor, a second-generation oral

cephalosporin with a β -lactam ring, is used for a wide range of bacterial infections, especially in children. This antibiotic may cause various kinds of reactions (erythematous or papular eruptions, urticaria, serum sickness-like reactions, hypersensitivity myocarditis, and anaphylactic reactions) (1–3).

We describe a child who presented an adverse, IgE-mediated reaction to cefaclor and a long persistence of specific IgE to cefaclor.

At the age of 8 years, the patient had taken cefaclor suspension (5 ml) (trade name Panacef, Eli Lilly, Florence, Italy, 250 mg/5 ml) for infectious bronchitis. This drug had been previously taken by the child without adverse reactions; moreover, he had not experienced adverse reactions to other drugs. Five minutes after taking cefaclor, he presented angioedema with dyspnea and generalized urticaria; 10 min later, he was treated by a medical doctor with methylprednisolone 40 mg i.m., with clinical resolution in 1 h. Afterward, no determination of the cause of this adverse reaction was done.

Only 6 years later, the child was referred to our allergy clinic to determine the cause of this type of adverse reaction. He was now 14 years old, with allergic rhinitis to house-dust mite, but without family history of allergy. Panacef suspension contains excipients such as erythrosine and strawberry which might cause adverse reactions. Erythrosine (E127) is a coloring agent able to cause the appearance of clinical manifestations in subjects with hypersensitivity to this substance (4). Therefore, we did a test (double-blind vs placebo) with this agent, which was administered *per os* (capsules of 5 and 10 mg), according to the instructions of the manufacturer (Laboratorio Lofarma,

IgE antibody was detected up to 6 years after reaction.

Milan, Italy). No symptoms appeared after the administrations. A skin prick test (SPT) to erythrosine (10 mg/ml) was carried out on the volar side of the forearm with a plastic lancet (1-mm tip) made by Laboratorio Lofarma (Milan, Italy). A positive control with 10 mg/ml histamine was included. SPT results were assessed as positive (wheal response $\geq 2+$) according to the recommendations of the European Academy of Allergology and Clinical Immunology (5). The SPT result for erythrosine was negative (0+). This SPT was done because the presence of IgE to additives has been described (6). A skin test (prick+prick with fresh food) and a commercially available assay for specific IgE level (CAP System Pharmacia, Uppsala, Sweden) to strawberry were also performed with a negative result (0+ and <0.35 kUA/l, respectively). Specific IgE level (CAP System, Pharmacia) was then performed for cefaclor with a positive result (9.89 kUA/l), and for penicilloyl G, penicilloyl V, ampicilloyl, and amoxicilloyl with a negative result (<0.35 kUA/l). A SPT with a drop of Panacef (concentration 50 mg/ml) was also carried out. The SPT response to Panacef was 4+. In a control group of 20 children without family history of allergy, without appearance of adverse drug reactions, and with allergic rhinitis to house-dust mite, SPT and CAP to cefaclor were negative (0+ and <0.35 kUA/l respectively).

This report shows that cefaclor causes IgE-mediated reactions, and that it is possible to demonstrate the presence of specific IgE to cefaclor 6 years after the administration of this drug.

In the literature, there are no studies reporting the persistence of IgE to cefaclor for such a long period of time, whereas the evolution of skin test sensitivity in subjects allergic to benzylpenicillin, amoxicillin, and ampicillin has been investigated (7). We can propose some hypotheses to explain the long

persistence of specific IgE to cefaclor. We can exclude that the persistence of IgE to this drug was due to other drugs cross-reacting with cefaclor because during this period of time the child did not take any drugs. However, an uncontrolled or hidden contact, as with β -lactams, can occur in subjects with hypersensitivity to these drugs (7). Therefore, in our patient, an uncontrolled or hidden contact with cefaclor could have maintained the production of specific IgE to cefaclor. Other possible explanations for the persistence of IgE to cefaclor are

- 1) the ingestion of foods that might have allergenic peptides in common with cefaclor
 - 2) the presence of genetic factors which might be responsible for the continuous production of specific IgE to cefaclor without the presence of a specific stimulus
 - 3) the intrinsic peculiarity of cefaclor to induce a persistent IgE immune response.
- All these are only hypotheses because there are no studies on this matter.

In conclusion, this case shows that IgE to cefaclor may persist for many years after the last administration. It is thus important to advise the cefaclor-allergic patient strictly to avoid the administration of this drug in later years. Further studies are needed to evaluate the persistence of specific IgE to cefaclor in subjects with cefaclor allergy.

*Allergy and Clinical Immunology Unit
Department of Pediatrics
Anna Meyer Hospital
Via Luca Giordano 13
50132, Florence
Italy
Tel. (+39-055) 5662461
Fax: (+39-055) 570380

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MBP deposition in eosinophilic gastroenteritis

M. Koga*, M. Fujiwara, N. Hotta, T. Matsubara, E. Suzuki, S. Furukawa

Key words: eosinophil; eosinophilic gastroenteritis; major basic protein.

● A 6-YEAR-OLD boy, who had been suffering from bronchial asthma attacks several times a year, developed vomiting, loss of appetite, and generalized edema for 9 days before admission.

Laboratory studies revealed mild eosinophilia (9.0% of total white blood

cells), hypoproteinemia (3.6 g/dl), and hypoalbuminemia (1.6 g/dl). The serum IgE level was 580 IU/ml.

The serum specific IgE antibodies for milk, egg, house dust, and house-dust mite were positive.

Upper gastrointestinal endoscopy revealed broad geographic erosion in the gastric body and antrum (Fig. 1a). The patient was treated with an H_2 -blocker, and all clinical and laboratory parameters normalized within a month.

Microscopic examination of hematoxylin-eosin stained sections of biopsy specimens revealed heavy eosinophil infiltration in the gastric and duodenal mucosae. Immunostaining with monoclonal antibody against eosinophil granule major basic protein (MBP) (Monosan, Uden, the Netherlands) and eosinophil peroxidase (EPO) (Oncogene, Cambridge, UK) was performed. Heavy MBP-positive eosinophil infiltration and massive extracellular deposition of MBP were observed in the gastric and duodenal mucosae (Fig. 1b). No deposition of extracellular MBP was observed in the control specimens. No extracellular deposition of EPO was observed in either the patient or the control specimens.

A few studies of adult cases indicate that in eosinophilic gastroenteritis (EOG), eosinophils become activated and release cytotoxic proteins (1). This is the first report of EOG in a young child in which massive extracellular deposition of eosinophil granule MBP was demonstrated. MBP may have played an important role in damaging the gastrointestinal mucosa.

MBP is known to stimulate histamine release from mast cells (2). In this case, histamine release stimulated by deposited MBP may have increased the secretion of gastric acid, which could have increased the

A young boy with major basic protein deposits in the mucosae.