

Multiple Antibiotic Allergy of a Young Woman - Fact or Fiction?

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ABSTRACT

A 20-years-old female was referred to Dermatology Clinic due to multiple common antibiotic allergy appearing as wide urticaria based on urticarial episode 5 years earlier. After investigations, no antibiotic allergy was confirmed.

It is important to make at the local Health Care site case descriptions and recordings to the patient files accurately as facts without making an overestimation of the etiology based on only clinical picture. The false positive allergy diagnosis hampers the later treatments and cause avoiding the use of optimal and appropriate medications; dismissing of these results later from the patient's Medical Risk File is laborious.

Keywords: Dermatology clinic; Antibiotic allergy; Misdiagnosis; Urticaria; Medical risk file

Introduction

Suspicions and beliefs of antibiotic allergies are common in general population, based on various skin reactions at the time of use of antibiotics. Also, the description and recording of symptoms may also be poorly or inaccurately documented and the estimations even by health care personnel may be inaccurate. Also, documentation may also be based on patient's or his/her parent's oral information or phone call to health care unit where, f. ex., a nurse has documented the data.

Here a young 20-year-old woman is described to be suspected to be allergic for the most used and common antibiotics. The GP doctor referred Dermatology clinic about the problem what antibiotics could be used in the future.

Case Report

A-20-year-old student female was sent by a GP at Primary Health Care Center of her student time city for investigations

of suspicions of multiple antibiotic allergy. The suspected antibiotics were penicillin, erythromycin, sulfadiazine, trimethoprim and cephalosporin, appearing as wide urticaria.

The patient had no allergic rhinitis nor asthma. Years earlier there was a short episode of dermatitis treated by topical 1% hydrocortisone. Family history included brother with hay fever. At elementary school level she once had taken acetylsalicylic acid for flu and experienced oedema in lower lip and plantar feet, but no diagnostics measures were carried out and paracetamol (i.e., acetaminophen) was used since then. Once as child she had experienced mild itchy dermatitis after taken colored candies and red soft drink.

Years later at age 15, the patient had experienced some itch and dermatitis in lower extremities starting after a few days of phenoxymethylpenicillin intake for purulent right otitis media. The GP doctor set the diagnosis of urticarial adverse reaction for penicillin. The antibiotic was changed to sulfa-trimethoprim

combination followed by similar wide skin reaction within a few days followed by with the same skin reactions to erythromycin again after a few days. Thus, the 4th antibiotic cephalexin was prescribed with positive outcome. About 4 years later in connection of tooth removal, 2 hours after taken cefadroxil (Duracef) she experienced slight lip swelling and eye lid skin rash.

At polyclinical examinations, wide Prick-tests revealed positive reactions to birch and alder and small test reactions to apple and home dust mites. Epicutaneous test of antibiotics were negative. Serum IgE-antibodies for phenoxymethylpenicillin and benzylpenicillin were negative. Serum IgE was 137 kU/L (ref. range 0-100 kU/L).

Based on the information available from the referring GP doctor and patient, we selected for oral exposure first erythromycin (100 to 400 mg), then trimethoprim (50 to 150 mg) and finally sulfadiazine (50 to 150 mg) with negative results. Cephalosporin was not tested since patient's medical files were now obtained from home Health Care Center where the otitis media with parallel urticarial reactivity was treated by cephalexin ruling out the earlier urticaria diagnosis from cephalosporin. Also, in these circumstances oral penicillin was decided not to challenge.

Patients Medical Files revealed that the patient was prescribed for her purulent right-side otitis media first phenoxymethylpenicillin (V-Pen) 800.000 IU 3x/day, 2 days later urticarial diagnosis was set and drug was changed to erythromycin acistrate (Erasid) 400 mg 3x/day. Three days later again urticarial rash was diagnosed leading to the drug change to sulfadiazine-trimethoprim (Ditrim Duplo) and paracentesis to eardrum was performed with thick blood-containing secretion obtained and also left-side eardrum was slightly reddish. Five days later urticarial reaction re-appeared and cephalexin (Kefexin) 500 mg 2x/day was prescribed leading to positive outcome without a description of urticaria.

The home Healthcare Center, however, provided additional medical records about later time treatments. About 3 months later - after the urticarial episode - the patient was treated 3 times in one-month intervals for 7 to 10 days for tonsillitis by cefachlor and twice by erythromycin. Thereafter 2 years later, the patient had erythromycin for maxillar sinusitis for 10 days without any skin reactions. The patient did not remember these 4 later antibiotic treatments.

Discussion

The patient had the tendency for atopy without clear atopic diseases. Serum IgE was only slightly over the reference range. Prick test positivity for birch and alder pollen were without clinical symptoms and only slight reactivity to apple and house dust mites.

The patient had very obviously an urticarial episode. At that time, antibiotics were repeatedly changed after 2 to 5 days and urticaria flared repeatedly in the same time manner. By evaluation afterwards, it is likely that urticaria flared due to constant infection and not due to used medication. Also, the time frame of less than 5 days for development of IgE antibodies is too short.

The repeated urticarial flares in a few days fit to the phenomenon where histamine-containing granules in the skin

mast cells will get filled and mast cell membrane will re-gain the reactivity capacity. This is supported by studies in patients with cold urticaria where there were found development of tolerance after repeated cold challenges¹⁻³.

In addition, the patient - after the urticarial episode - already was exposed bravely 4 times in the next 3 months to 2 years to the same antibiotics that were suspected to cause urticaria, excluding of the original estimation for cause of urticaria. It remained unclear, from where the cephalosporin allergy diagnosis appeared to the patient's medical files.

The oral challenge exposure studies in the Dermatology clinic very likely would not have been carried out if the complete accurate patient history would have been known. Thus, the easy and fluent information flow without any blocks or barriers between different Health Care Units is of importance, to avoid unnecessary examinations, to clarify the real diagnosis and to make patient care safer. In these circumstances, we did not make the oral penicillin challenge with negative IgE antibodies.

Penicillin allergy is rare⁴⁻⁶. In the Western countries, about 10% of adults declare to be allergic for penicillin, and adverse effects, like stomach symptoms, are believed to mean allergy. However, the real penicillin allergy is very rare: of patients claiming to be allergic for penicillin, up to 98% of them still tolerate penicillin⁷.

The majority of skin symptoms during penicillin use is likely due to reactivity to viruses, bacteria and possibly to bacterial toxins. The same likely applies to other antibiotics, too.

Penicillin allergy is very rare as studied in Kuopio University Hospital District area with population of about 251,000 as by a recent retrospective study and case report⁸. During close to 12 years (Jan 2010 to Aug 2021) of data collection, only 5 clinically relevant immediate penicillin allergy cases were found by IgE-antibody-RAST studies.

However, it is of interest that a patient had specific IgE antibodies for phenoxymethylpenicillin, benzylpenicillin and cefaclor, but not for amoxicillin. Another patient had IgE antibodies for phenoxymethylpenicillin, benzylpenicillin and amoxicillin, but not for cefaclor. One patient had IgE antibodies for amoxicillin but not for phenoxymethylpenicillin and benzylpenicillin⁸.

Earlier it was generally believed that members of penicillin group share the same allergic potential and oral exposure to 250 mg amoxicillin with negative challenge result excludes also allergies for benzylpenicillin and phenoxymethylpenicillin. However, this assumption shall be re-evaluated by the results of the recent study⁸. In the case penicillin would be needed for treatment in penicillin-allergic patient, desensitization therapy, first with phenoxymethylpenicillin and later with benzylpenicillin, might be possible, but the procedure requires several weeks to complete⁹.

It is likely that information recorded in any patients' Medical Risk Files are based to a major part on information obtained from patients or their parents even by over the phone and not critically evaluated by Health Care professionals. Patients and their relatives may remember wrong the names of drugs. Also, prescription-free drugs obtained over the pharmacy counter or natural products containing effective substances may not be considered as real medication by patients and not informed to

the Health Care personnel. By own personal experience, a drug suspected to cause an allergic reaction was either never obtained from the Pharmacy or never started to use or was initiated several days after the skin reactions were already started. In such cases, no further allergologic studies are needed.

As summary, it is of importance to collect all relevant and accurate data, even from different sources, for critical evaluation of the patient case and to make appropriate plans for tests to make the correct diagnosis.

Conflict of Interest

Author declares none.

Other Statements

This case is based on our previous article in 2000 in Finnish language with permission and updated review of literature since then: Harvima R, Laukkanen A, Harvima I, Mattila R and Hollmén A. Lääkkeiden käytön ja ihoreaktioiden kuvauksen ja kirjaamisen tärkeys myöhemmälle diagnostiikalle. (The importance of documentation of drug use and importance of description of skin reactions for diagnostics made afterwards). *Suom Lääkäril* 55: 2195-2196, 2000.

The patient has given her consent and the Ethics Committee of Kuopio University Hospital has given permit to publish this patient case.

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