

Detection of specific IgE antibodies to cefotiam-HSA conjugate by ELISA in a nurse with occupational anaphylaxis

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Cefotiam is a widely prescribed second generation of cephalosporin, and has been exposed to nurses and hospital workers via inhalation or skin contact. There have been several case reports of contact urticaria or anaphylaxis induced by cefotiam in hospital workers (1–3), among which one case report detected serum-specific IgE antibody to cefotiam-human serum albumin (HSA) conjugate using paper disc and radioallergosorbent test (RAST) (1). However, this technique cannot be used any more due to isotope regulation. In this study, we developed enzyme-linked immunosorbent assay (ELISA) technique to detect serum-specific antibodies, which will be useful for screening a large number of exposed workers.

This report presents a serious anaphylaxis following skin contact to cefotiam in a nurse working in a university hospital. Her symptoms included dizziness, sweating, chest tightness, angio-oedema, and generalized urticaria. As she had suffered from allergic rhinitis and conjunctivitis

for 5 years, the results of skin prick tests (SPTs) showed strong positive reactions to house dust mites and weed pollens, but negative responses to cefaclor or other penicillin derivative antibiotics extracts. However, we did not perform SPT with cefotiam because it may induce anaphylaxis during SPT procedure. Serum total IgE measured by immunoCAP system (Phadia, Uppsala, Sweden) was 276 kU/L. To detect serum-specific IgE, we prepared two conjugates of cefotiam- and cefaclor-HSA in our laboratory as described previously (4, 5). When the positive cut off value was determined as mean + 3 standard deviation of the absorbance values in 10 unexposed nonatopic controls, ELISA result showed high serum-specific IgE level to cefotiam-HSA conjugate in serum of the patient, while minimal bindings were noted in sera of controls (Fig. 1A). ELISA inhibition tests showed significant inhibitions with additions of both free cefotiam and cefotiam-HSA conjugate in dose-dependent manners, while no inhibitions were noted with additions of free cefaclor and cefaclor-HSA conjugate (Fig. 1B). Her symptoms developed after 1.5 year of latent period. The patient repeatedly presented an immediate onset of urticaria and systemic anaphylaxis after skin

contact exposure to cefotiam. High serum-specific IgE antibody to cefotiam-HSA conjugate was found in her serum by ELISA. Based on these findings, we confirmed that she had occupational urticaria and anaphylaxis induced by skin contact to cefotiam, by IgE-mediated mechanism. After complete removal from exposure, she is working free of symptoms.

Several commonly prescribed cephalosporins or cephalosporin derivatives including cefaclor, cefotaxime, 7-ACA and 7-ADCA could induce occupational asthma and rhinitis which were sensitized via inhalation route in nurses or pharmaceutical industry workers (5, 6), while the most common clinical symptoms with cefotiam induced occupational allergy were contact urticaria or anaphylaxis, not respiratory allergies (1–3). This study is the first to succeed to detect serum-specific IgE to cefotiam-HSA conjugate by ELISA, which binding specificity was confirmed by ELISA inhibition test. As significant inhibitions were noted by both free cefotiam and cefotiam-HSA conjugate, we can speculate that the pathogenic mechanism is derived from IgE response to hapten part of cefotiam. We also detected serum-specific IgG4 antibody

Skin contact to cefotiam in working place could induce occupational urticaria and anaphylaxis, which are mediated by IgE antibody to hapten of cefotiam.

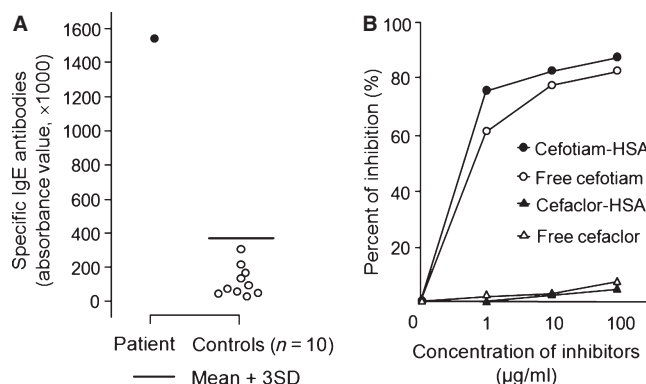


Figure 1 (A) Serum-specific IgE levels to cefotiam-human serum albumin (HSA) conjugate in sera of the patient (●) and 10 unexposed nonatopic controls (○). The molar ratio of cefotiam to HSA was 1:50. SD, standard deviation. (B) Results of IgE ELISA inhibition tests with additions of free cefotiam (○), cefaclor (△) and two conjugates of cefotiam-HSA (●) and cefaclor-HSA (▲).

to cefotiam-HSA conjugate in serum of the patient with minimal bindings in controls' sera (data not shown). Further studies will be needed to understand the role of serum-specific IgG4 antibody in cefotiam induced occupational allergy. Considering that IgE sensitization can be possible through skin contact to low concentration of cefotiam exposure, this ELISA system will be useful for screening the asymptomatic sensitized subjects or early detection of occupational allergy subjects.

In conclusion, we report a case of severe occupational urticaria and anaphylaxis caused by skin contact to cefotiam in a nurse, which was mediated by specific IgE mechanism to the hapten part.

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