Paracetamol: a rare culprit in anaphylaxis

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Aims: Anaphylaxis to paracetamol is rare and the underlying mechanisms are poorly understood. We aimed to review the cases of anaphylaxis to paracetamol in our Drug Allergy Unit (DAU) in the last five years.

Methods: The authors did a retrospective analysis of all cases of anaphylaxis to paracetamol studied in our DAU between January 2011 and December 2015. The data were analysed using SPSS, version 21.

Results: Twelve adult patients with anaphylactic reaction to paracetamol were studied (67% males, aged 18-72y), 25% had allergic respiratory disease. All patients were medicated with oral paracetamol for pain relief. Six patients also had anaphylaxis to nonsteroidal anti-inflammatory drugs (NSAID’s): acetylsalicylic acid (n=4), ibuprofen (n=3), naproxen (n=1), nimesulide (n=1) and diclofenac (n=1). Nine patients had immediate reactions (75%), and 3 (25%) late reactions (onset 3-12h). Eleven patients (92%) had mucocutaneous involvement, 11 respiratory manifestations, 3 (25%) cardiovascular and 1 (8%) gastrointestinal. None had anaphylactic shock. Only 8 (67%) patients were admitted to the emergency department (ED), none was treated with adrenaline nor had tryptase determined. Because the in vivo work up of these patients is very limited, they all underwent an oral challenge (OC) with an alternative drug (etoricoxib) and tolerance was confirmed.

Discussion: In the 6 cases of multiple-reactors, the authors postulate an underlying COX-1 inhibition mechanism since paracetamol is a weak inhibitor of COX-1. In the cases of single-reactors (SR) IgE-mediated mechanisms may be involved. A possible explanation for the late anaphylaxis (12h) in a SR is COX-1 inhibition; alternatively, IgE involvement may be considered if this “late anaphylaxis” is in fact the late manifestation of a bifasic response. The in vitro study of this patient is in progress.

Conclusion: Paracetamol is a widely used drug, available over-the-counter in most countries, but not entirely without risks. The allergy diagnosis work-up in cases of anaphylaxis to paracetamol is difficult and mostly based on a detailed clinical history. Skin tests are not standardized and positive results are doubtful. In vitro assays such as specific IgE and Basophil Activation Test have poor specificity and sensitivity. Moreover OC with the culprit drug are contraindicated in anaphylaxis.