



Allergologia et immunopathologia

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LETTER TO THE EDITOR

Based on a patient: Dermographism should be routinely investigated before every provocation test

To the Editor,

Drug provocation tests (DPTs) are widely considered to be the gold standard to establish or exclude the diagnosis of drug allergy or intolerance.¹ However, some causes such as self infliction, psychological or dermatological problems may lead to false-positive results when performing DPTs.¹ Hereby, we report a child who admitted to our clinic with suspicion of drug allergy and was consequently diagnosed as symptomatic dermographism.

A 12-year-old boy was admitted to our outpatient department because of suspected drug allergy. He suffered from itching, hives, swelling of eyelids, nausea, malaise, dizziness and dyspnoea within 30 min after taking 100 mg acetylsalicylic acid (aspirin®) perorally, 2 years ago. He had similar complaints, within half an hour after 500 mg of metamizole sodium, and 15 min after 500 mg acetaminophen 1 year and 4 months ago, respectively. He was admitted to the emergency room and diagnosed as anaphylaxis in all three incidents. There was no family or personal history of drug allergy or atopy. Open drug provocation tests in order to obtain an alternative analgesic drug were performed on different days. His physical examination and pulmonary function tests were within normal limits before each DPT.

The drug doses in provocation tests were initially adjusted as 1/8 of the patient's ordinary doses and doubled after every 30 min. The procedure was suspended for at least 1 week between two DPTs. Initially, a DPT with ibuprofen was performed. However, the test was terminated when a few urticarial plaques on his trunk occurred within 20 min after the first dose. Additionally, he suffered from itching, nausea and malaise. His blood pressure and oxygen saturation remained within normal range and he had no angio-oedema. One and 2 weeks later, DPTs were performed with meloxicam and nimesulide, respectively. In both DPT, a few linear urticarial plaques were seen on his trunk following the first dose. Thereafter, symptomatic dermographism was established with a blunt object pressed along his forearm which caused hyperaemia, oedema and itching within 10 min. Finally a DPT with placebo was performed and once again urticaria plaques occurred on his

trunk following scratching and itching. Consequently, a DPT with benzydamine was performed as preventing physical stimuli that may trigger the symptomatic dermographism and no reaction was seen.

Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to be the second most common cause of drug hypersensitivity reactions in childhood.² There were signs of anaphylaxis due to NSAIDs such as acetylsalicylic acid, acetaminophen and metamizole sodium in the history of our patient. We established positive DPTs with NSAIDs such as ibuprofen, meloxicam and nimesulide (urticaria). Many NSAIDs exhibit cross reactivity suggesting common functional property of cyclooxygenase inhibition is somehow involved in the pathogenesis.³

Drug provocation tests are considered to be the gold standard tests whether used with other in vitro tests such as skin prick tests. However, in clinical practice, they are usually performed to find an alternative drug or in patients with suspicious medical history.¹ Therefore, we performed DPTs to provide an alternative analgesic because of his consistent history of analgesic intolerance. We have encountered positive provocation reactions after four distinct provocation including placebo. Although the DPT is the gold standard diagnostic method for drug allergy or intolerance, false positive or false negative results may occur during test procedure.⁴ Some reasons such as psychological problems or any underlying diseases such as urticaria can lead to false-positive results.¹ As in our patient symptomatic dermographism which is characterised by itching, hyperaemia, oedema followed by physical stimuli such as scratches or compression of the skin may be potential reason of false-positive provocation results.¹ Our patient had no history suggestive of symptomatic dermographism. Before the DPT, the patient was informed about the possible symptoms that may evoke during the process. Therefore, he may be psychogenically affected and the itching sensation that developed during the DPT may be attributed to this phenomenon.

Drug provocation test, performed by preventing physical stimuli that may trigger the symptomatic dermographism, was negative with benzydamine in our patient. His medical history and clinical findings suggested anaphylaxis with acetylsalicylic acid, metamizole sodium and acetaminophen. However, positive DPT results with meloxicam, nimesulide and ibuprofen might have been triggered by scratching. Actually, these provocation tests must be repeated by eliminating physical stimuli that may trigger

symptomatic dermographism to make differential diagnosis of symptomatic dermographism or drug allergy. However, as we provided an alternative analgesic drug (benzydamine), DPTs with meloxicam, nimesulide and ibuprofen were not repeated.

In conclusion, even though DPTs are considered to be the gold standard to establish or exclude the diagnosis of drug allergy or intolerance, as we observed in our patient some causes such as symptomatic dermographism may cause false-positive test results. Careful investigation of symptomatic dermographism before performing DPTs may be helpful for the correct evaluation of test results. To our knowledge there is no clear information in the guidelines regarding this issue although investigating pre-existing symptoms such as urticaria has been suggested.^{1,2,5-8} Based on this patient we suggest that symptomatic dermographism should be routinely investigated as first step before all provocation tests such as food or drug even without suggestive history of symptomatic dermographism and in the presence of symptomatic dermographism it should be performed by eliminating physical stimuli.

Conflict of interest

All authors declare that there is no conflict of interest and no funding involved.

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