was positive but the rest of tested benzodiazepines were negative.

Previous reports[2] suggest that there is no cross-reactivity among benzodiazepines. Diazepam is the most similar benzodiazepine to tetrazepam, the only difference between them is the presence at position 5 on the diazepine ring of phenyl in diazepam and clohexen in tetrazepam, and this cyclohexene conformation could explain tetrazepam sensitisation.[9] Our patient also tolerated oral administration of diazepam and other benzodiazepines. Due to the biopsy result and the positive patch test, an oral challenge with tetrazepam was not performed.

We have reported a type IV hypersensitivity reaction confirmed by biopsy as an unusual chronic eczematous reaction caused by tetrazepam with probed tolerance to other benzodiazepines.

References

1. Sanchez Morillas L, Laguna-Martínez JJ, Reaño-Martos M, Rojo-Andrés E, Gómez-Tembleque Úbeda P. Systemic dermatitis due to tetrazepam. J Invest Allergol Clin Immunol. 2008;18:404–6.
2. Bellón T, Barranco P, Padial A, Tapia B, Morel E, Alves-Ferreira J, et al. Acute generalized exanthematous pustulosis due to tetrazepam. J Invest Allergol Clin Immunol. 2008;18:119–22.
3. Pirker C, Misic A, Brinkmeier T, Frosch PJ. Tetrazepam drug sensitivity – usefulness of the patch test. Contact Dermatitis. 2002;47:135–8.
4. Ortiz-Frutos FJ, Alonso J, Hergueta JP, Quintana I, Iglesias L. Tetrazepam: an allergen with several clinical expressions. Contact Dermatitis. 1995;33:63–5.
5. Garcia-Bravo B, Rodriguez-Pichardo A, Camacho F. Contact dermatitis from diazepoxides. Contact Dermatitis. 1994;30:40.
6. Del Pozo MD, Blasco A, Lobera T. Tetrazepam allergy. Allergy. 1999;November (54):1226–7.
7. Cabrerizo Ballesteros S, Méndez Alcalde JD, Sánchez Alonso A. Erythema multiforme to tetrazepam. J Invest Allergol Clin Immunol. 2007;17:205–6.
8. Sánchez I, García-Abujeta JL, Fernández L, Rodríguez F, Quiñones D, Duque S, et al. Stevens–Johnson syndrome from tetrazepam. Allergol Immunopathol. 1998;26:55–7.
9. Barbaud A, Trechot P, Reichert-Penetrat S, Granel F, Schmutz JL. The usefulness of patch testing on the previously most severely affected site in a cutaneous adverse drug reaction to tetrazepam. Contact Dermatitis. 2001;44:259–60.

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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

The authors have no conflicts of interest to declare.

References

1. Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J, et al. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. Allergy. 2003;58:854–63.
2. Kowalski ML, Makowska JS, Blanca M, Bavbek S, Bochenek G, Bousquet J, et al. Hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) – classification, diagnosis and management: review of the EAACI/ENDA(#) and GA2LEN/HANNA. Allergy. 2011;66:818–29.
3. Celik GE, Pichler WJ, Adkinson Jr NF. Drug allergy. In: Adkinson Jr NF, Bochner BS, Busse WW, Holgate ST, Lemanske RF, Simons FER, editors. Middleton's allergy: principles and practice. 7th ed. Philadelphia: Elsevier; 2009. p. 1205–26.
4. Aberer W, Kranke B. Provocation tests in drug hypersensitivity. Immunol Allergy Clin North Am. 2009;29:567–84.
5. Romano A, Torres MJ, Castells M, Sanz ML, Blanca M. Diagnosis and management of drug hypersensitivity reactions. J Allergy Clin Immunol. 2011;127 March (3 Suppl):S67–73.
6. NIAID-Sponsored Expert PanelBoyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010;126 December (6 Suppl):S1–58.
7. Khan DA, Solensky R. Drug allergy. J Allergy Clin Immunol. 2010;125 February (2 Suppl 2):S126–37.
8. Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, Bock SA, Sicherer SH, Teuber SS. Adverse reactions to Food Committee of American Academy of Allergy, Asthma & Immunology. Work Group report: oral food provocation testing. J Allergy Clin Immunol. 2009;123 June (6 Suppl):S365–83.

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