Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
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RESPONSE TO THE LETTER TO THE EDITOR

OPEN ACCESS

Drug-induced enterocolitis, a new condition under consideration

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Received 23 January 2025; Accepted 24 January 2025
Available online 1 March 2025

Dear Editor,

We thank Professor Özdemir for his critical reading of our case report. Here, we have provided answers to his questions to help readers clarify some aspects of the clinical cases, which for reasons of brevity we could not include in the text.[1]

First, it should be noted that the diagnosis of Drug-induced enterocolitis (DIES) is eminently clinical.[2] Strictly speaking, both patients met the diagnostic criteria indicated in Table 1.[1,3] As indicated in our report, the second case raised diagnostic doubts, as he presented exclusively with digestive symptoms (recurrent vomiting, abdominal pain, dysphagia, sialorrhea) and lethargy after controlled provocation tests with acetylsalicylic acid and ibuprofen, and previously at home after taking ibuprofen and metamizole. As we have already indicated, hypersensitivity to nonsteroidal anti-inflammatory drugs (HS-NSAIDs) should also be included in his differential diagnosis.

Given that the patient presented with digestive symptoms after the three NSAIDs, it could be a nonallergic cross-hypersensitivity reaction, mediated by a nonimmunological mechanism associated with cyclooxygenase-1 (COX-1) inhibition or, less likely, a selective (multiple) reaction to each of those NSAIDs. However, it should be recalled that he did not present with urticaria or angioedema, nor respiratory symptoms, which makes it difficult to classify him into any of the phenotypes of NSAIDs hypersensitivity reactions listed in the guidelines[3] or in the mixed forms proposed by Doña et al.[4]

In the observation room, the patient's peripheral oxygen saturation ($SatO_2$) was 100%, heart rate 76 bpm, and BP 109/66 mmHg. The hemogram and blood biochemistry of both patients were normal, and blood gases were not performed.

We cannot state that this is (or not) an allergic reaction, nor that there could be an underlying mixed mechanisms (immunoglobulin E [IgE] and non-IgE) responsible for the symptoms. Drug challenge tests with the suspected NSAID and/or other NSAIDs remain the main diagnostic tool. In vitro tests are not routinely performed because they are of limited value and their clinical validity is not well established for either HS-NSAIDs or DIES. The basophil activation test (BAT) may have some role in immediate reactions and the lymphocyte transformation test (LTT) in severe nonimmediate reactions. Skin tests have low diagnostic yield and are limited to cases of immediate (IgE-mediated) selective HS reactions to metamizole and paracetamol.

Drug provocation test with COX-2 inhibitors in children has controversial aspects—most drugs are not indicated for use in children. Meloxicam (Food and Drug Administration [FDA] off-label approved in children ≥ 2 years with juvenile idiopathic arthritis) and etoricoxib (≥16 years) are not free of side effects and their usefulness as antipyretic, analgesic, and anti-inflammatory drugs is limited. Given these circumstances, and that the patient also has alternatives for treating pain, fever, and inflammation (he tolerates paracetamol and corticosteroids without reaction), challenge test with COX-2 inhibitors has not yet been performed.

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https://doi.org/10.15586/aei.v53i2.1314
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With regard to the acronym PEOC, it was our mistake to keep the Spanish acronym which corresponds to COCT (controlled oral challenge test).

COCT with paracetamol was not performed because the patient had recently consumed it at home.

We hope we have been able to clarify the issues raised.

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