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Drug-Induced Enterocolitis Syndrome (DIES) by Amoxicilin.

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Capsule Summary

Non Ig-E-mediated gastrointestinal allergic disorder, such as Enterocolitis Syndrome, is usually due to food's proteins. There is only one case reported of Enterocolitis Syndrome Induced by Drugs until now.

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Key Words

Drug-induced enterocolitis syndrome, Food protein-induced enterocolitis syndrome, Non-IgE-mediated allergy.

To the Editor:

Enterocolitis syndrome is a non-IgE-mediated allergy usually due to foods (Food Protein-Induced Enterocolitis Syndrome (FPIES)). The symptoms consist on recurrent delayed vomiting, diarrhoea, hypotension, and may progress to a state of dehydration and hypovolaemic shock. It remembers a septic shock and that is the prime differential diagnosis. The clinical feature repeated every single time the child eats the responsible protein, and is totally resolved once this protein is removed from the diet (1).

The mechanism underlying FPIES remains poorly characterized. FPIES is presumed to be a cell-mediated disorder with negative skin prick test and lack of specific IgE to the offending food. Few studies have investigated T cells in patients with FPIES. There is some evidence of T-cell proliferation on stimulation with food antigens; however, the stimulation index is not always different from that in nonallergic control subjects. In patients with FPIES, imbalance between intestinal TNF- α levels and decreased expression of TGF- β has been found (2).

Until now there is only one report about FPIES-like diseases caused by drugs or Drug-Induced Enterocolitis Syndrome (DIES) (3).

A 3-year old boy was referred to our Paediatric Allergy Unit for suspected drug allergy. When he was 2-years old he developed an acute episode of urticaria while he was receiving amoxicillin for acute otitis media (AOM). He was admitted into the emergency room (ER) and received treatment with dexchlorfeniramine with resolution of the cutaneous rash in 48 hours. Few months before, he had tolerated amoxicillin without any problem.

Suspecting an infectious urticaria we performed an oral challenge with 250 mg of amoxicillin (50 mg/kg/day). The parents signed the informed consent. Two hours after the dose intake, the patient developed abdominal pain, vomiting and mild malaise. The symptoms remitted, in two hours, with dexchlorfeniramine and metilprednisolone.

We performed an allergy study with skin prick test and intradermal test with Penicilin G, PPL, MDM and amoxicillin. The cutaneous test resulted negative in immediate and delayed lecture.

According to parents, the negative results of the cutaneous test, and the fact that the only clinical manifestations were gastrointestinal symptoms in a toddler we performed another oral challenge with amoxicillin. Four hours after the dose intake he was admitted into the ER because he developed vomiting, moderate abdominal pain and diarrhoea. He required treatment with antiemetics, hidrocortisone and saline solution infusion. Vomiting lasted 2 hours with progressive improvement to a complete recovery.

The blood test showed an increased of the white blood cell count (17.800 mm³) with neutrophilia (13.100/ μ L) with normal triptase levels (4.82 μ g/L).

The laboratory findings in combination with delayed onset of gastrointestinal symptoms, that occurred twice, and the negativity of the cutaneous test suggested the diagnosis of DIES due to Amoxicilin.

Drug-Induced Enterocolitis Syndrome is an uncommon disease. In 2014, Novembre et al (3) reported the first case of DIES provoked by amoxicillin. It was a 6-year-old girl who developed prolonged vomiting 1-2 hours, after the ingestion of amoxicillin syrup. Previously, when she was one-yr-old, she had developed urticaria after the ingestions of cefixime. The allergologic study (cutaneous test and specific IgE to cefaclor, penicillin, ampicillin and amoxicillin) was negative so she underwent an open challenge to amoxicillin. Two hours after the last dose intake she developed vomiting, diarrhoea, pallor and lethargy. The blood test showed a raise white blood cell count with neutrophilia. The clinical manifestations and the laboratory findings are similar in both cases.

As in our case, the onset was an urticaria, probably an infectious urticaria, so perhaps an infection is need to developed DIES.

Although gastrointestinal symptoms are sometimes related to amoxicillin in this child a case of amoxicillin-induced enterocolitis syndrome was hypothesized based on Sicherer's (4) criteria for FPIES, that are: (1) Repeated exposure to the incriminated food elicited diarrhoea and/or repetitive vomiting within 24 hours without any other plausible cause of the symptoms, (2) there where no symptoms other than gastrointestinal symptoms elicited by the incriminated food and (3) removal of the offending protein from the diet resulted in resolution of the symptoms, and/or an oral food challenge elicited vomiting and/or diarrhoea within 24 hours after administration of the food. This was supported by the laboratory findings (increased neutrophils count in the peripheral blood) (5).

Afterwards tolerance to phenoxymethylpenicillin has been confirmed which demonstrated that the side chain is the responsible of the reaction in our case.

In conclusion, we reported a DIES induced by amoxicillin, with tolerance to other betalactamic drugs, confirmed by an oral challenge. This is an exceptional syndrome with only one case reported until now.

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