



Letter to the Editor

Severe biphasic anaphylaxis: Study of a patient[☆]*Anafilaxia bifásica grave: estudio de un paciente*

Dear Editor,

Anaphylaxis is a serious systemic disease produced mainly by IgE-mediated allergic reactions.^{1,2} Its prevalence is underestimated,^{1,3} approximately 0.5%–5.1%, with exponential³ growth. Mortality is undetermined, but it is known that cofactors such as asthma are key to its management, reducing morbidity and mortality.^{1,3} We report a case of severe biphasic anaphylaxis, unusual in clinical practice⁴ which showing the need for continuous updating of the complex clinical behaviour of the condition, in order to diagnose^{2,5} and treat it early^{1–3} so as to avoid serious consequences.^{1,2,4}

A 15-year-old patient with an allergy to cow's milk proteins who, in the month of June, a month of high pollen concentration in Granada, minutes after eating biscuits with milk, began to suffer from pruritus, abdominal pain, generalised rash, and wheezing. The patient went to the emergency department of the local hospital where, after intravenous corticosteroids and subcutaneous adrenaline were prescribed, the symptoms subsided, but returned within two hours, prompting a referral to our hospital. On arrival, the patient presented with dyspnoea, hypotension, and mild exanthema. Inhaled ipratropium, intramuscular epinephrine (1.5 mg cumulative), and intravenous methylprednisolone were administered. In a first laboratory test,² acidosis and hyperglycaemia were observed, with normal results for the rest of blood parameters, lacking tryptase determination (mast cell protease, biomarker of anaphylaxis).² Insulin treatment was readjusted, and strict blood gas controls were carried out until the clinical and laboratory signs improved, leading to discharge. Six hours later, at home, wheezing and chest indrawing returned, and the patient

was prescribed methylprednisolone and subcutaneous adrenaline. Complementary tests were normal, but due to desaturation of 85% and persistent tachypnoea, admission to the Intensive Care Unit (ICU) was decided, with a diagnosis of bronchospasm due to olive pollen allergy. After 48 h, the patient was discharged with inhaled corticosteroids. After a month, the allergy study was carried out: *Prick test* and allergen-specific immunoglobulin E test (sIgE)² to pneumoallergens and food (Table 1).

Allergy diagnosis: severe biphasic anaphylaxis to cow's milk protein, confirmed by positive *prick test* and sIgE to milk and fractions and instability of seasonal asthma due to olive pollen allergy, as the main severity cofactor.^{2,3} We began the process of desensitisation to milk with omalizumab (Anti-IgE), in order to protect the patient from new anaphylactic episodes with traces of milk; successfully carried out after achieving good control of asthma, through bronchodilator treatment and omalizumab.² A lifelong LTP (Lipid Transfer Protein) allergen avoidance strategy was initiated to prevent the development of future clinical manifestations derived from the ingestion of plant foods.² In this case we found that the lack of recognition of the condition and inadequate administration of adrenaline (subcutaneous instead of intramuscular) led to a torpid evolution and recurrence within hours in a biphasic reaction.⁴ This shows the need for early and appropriate treatment with adrenaline, which has been underused until now^{1,3} and the importance of addressing associated co-factors that increase severity and complications.²

Anaphylaxis is increasingly prevalent and complex, parallel to the new allergens, with systemic manifestations other than the “classical” cutaneous ones; as has been demonstrated in many severe cases of asthma.⁵ Isolated symptoms such as hypotension^{1,2} or bronchospasm⁵ are difficult to recognise, which prevents a correct approach in the acute and critical moment.^{1,2,5} We stress the importance of airway stability^{1,2} in determining the severity of the anaphylactic presentation,^{1,2,4} as well as the relevance of tryptase

Table 1

Allergy study carried out.

	α-Lactalbumin	β-Lactoglobulin	Casein	Milk	Olive	Alternaria	(LTP) [*]
PT (mm ³)	12 × 12	10 × 10	12 × 12	10 × 10	12 × 14	5 × 4	7 × 7
IgE (KU/L)	65,5	30,7	78,6	>100	>100	9,28	3,91
Tryptase (μg/L)	3.5 (Normal <11.4)	Total IgE (IU/mL)	520,5				

PT: *prick test* performed with a positive control with histamine 10 mg/mL and a negative control with physiological saline, with >3 mm of the negative control being positive.²

tIgE: Total immunoglobulin E and sIgE (specific) determined by Thermo Fisher (*ImmunoCAP*, Uppsala, Sweden) and Siemens (*Immulite*, Los Angeles, CA) considering high tIgE > 100 kU/L, and sIgE > 0.34 kU/L.²

^{*} LTP: (Lipid transfer Protein) (Pollen-plant cross-reactive panallergen).

It has been shown that, although it is present in any plant product, it is found in greater quantities in the skin, particularly in the skin of: nuts, pink fruits (peach), tomato and lettuce.

[☆] Please cite this article as: Castro Jiménez A, García García R, Florido López F. Anafilaxia bifásica grave: estudio de un paciente. Med Clin (Barc). 2021;157:e269–e270.

determination.² Furthermore, the importance of the allergy study, which in our case stabilised the patient's olive asthma, prevented new allergens such as LTP² from producing new similar episodes in the future and, thanks to allergen desensitisation to milk, prevented new anaphylaxis due to traces of milk.²

Therefore, we corroborate that severe biphasic anaphylaxis can be the consequence of the torpid development of an allergic reaction⁴ and that the rapid and effective response using adrenaline can treat and slow down the disease, in the face of updated therapeutic guidelines in which corticoids and antihistamines are relegated to the background.^{1,3} We also demonstrate to medical specialists the need for continuous diagnostic updating of anaphylaxis, which is becoming more and more clinically atypical.^{3,5} The allergy study is essential and must be concomitant to identify new and complex triggering allergens, as well as to treat allergic comorbidities, which may influence its incidence and severity.

Funding

This article has not received any type of funding.

Conflict of interests

The authors declare no conflict of interest.

Acknowledgements

We wish to thank the Virgen de las Nieves University Hospital.

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