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Atrial fibrillation in anaphylaxis

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Title page:**Atrial fibrillation in anaphylaxis*****Three cases of atrial fibrillation during anaphylaxis.***

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All the authors take responsibility for all aspects of the reliability and freedom from bias of data presented and their discussed interpretation.

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The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received

sufficient information and have given their informed consent in writing to participate in that study.

The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

All authors mentioned above have been participated in different forms of the total result of this manuscript.

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ABSTRACT:

Background: The relationship between anaphylaxis and cardiovascular events has been reported in the past. While skin and respiratory symptoms are usually the most common and the first to appear, cardiovascular complications play a key role and represent the leading cause of death in anaphylaxis.

Methods: We report 3 episodes of atrial fibrillation triggered by anaphylaxis. Allergy and cardiology studies were performed. In both patients, the etiological agent was identified: *Anisakis simplex* hypersensitivity and food allergy.

Results and Conclusions: Heart is the source and target of chemical mediators released during an allergic reaction. In the heart, there are plenty of mast cells, and are predominantly located around the coronary adventitia and in close contact with small vessels in the muscle wall. The release of mediators can influence ventricular function, heart rate and coronary artery tone. Anaphylaxis can trigger any kind of arrhythmia. In these cases, the very interesting point of discussion was: which should be first, treating anaphylaxis or cardiac events?

The other controversial point was the use of epinephrine, the first line of treatment for anaphylaxis. Recommendations about epinephrine in cardiac patients during an anaphylactic event, is still a mayor dilemma. We emphasize the importance of the priority of establishing protocols between cardiologist and allergist in treatment of cardiac complications during anaphylaxis and we warn about the correct diagnosis of arrhythmias in anaphylaxis, in order to treat them as soon as possible, to prevent other consequences and complications.

Manuscript:

The relationship between anaphylaxis and cardiovascular events has been reported in the past (1). While skin and respiratory symptoms are usually the most common and the first to appear, heart and cardiovascular complications play a key role and represent the leading cause of death in anaphylaxis. Such complications include: arrhythmias, angina/ischemia, hypotension, syncope, or even cardiac arrest.

Atrial fibrillation is the most common cardiac arrhythmia (4-5% in patients older than 40 years) (2) and is associated with increased morbidity and mortality, being a risk factor for embolic events and heart failure.

We report three atrial fibrillation episodes associated with anaphylaxis in two different patients.

First case: A 42-year-old man with personal history of dyslipidaemia, but with no other remarkable medical records, was attended at the Emergency Department (ED) of our Hospital, complaining of general discomfort, itching, facial angioedema and tachycardia, 45 minutes after eating fresh grilled fish (hake). Blood pressure (BP) was 155/90 and electrocardiogram (EKG) showed atrial fibrillation with a ventricular rate of 160 bpm.

Initially he was treated with 5 mg of subcutaneous (SC) dexchlorpheniramine and 100 mg of intravenous (IV) dexamethasone. Chest X-ray, blood count and biochemical tests were all normal. No data available on tryptase levels at the moment of the anaphylaxis were registered.

Cutaneous symptoms disappeared in less than 30 minutes, but atrial fibrillation persisted after all, so he was treated with 5 mg of IV atenolol and 200 mg of oral flecainide. After a 24-hour observation period at the ED, the patient was asymptomatic with a heart sinus rhythm so he was discharged.

Allergy workout showed a positive skin prick test with *Anisakis Simplex*, negative specific IgE (0.15 kU/L) and challenge test with hake. Total IgE: 6820 KU/L, specific IgE to AS >100 KU/L. Biochemical tests were normal, including parameters of thyroid function. The transthoracic echocardiography showed no structural heart disease and no arrhythmias were recorded in a 24-hour EKG-Holter.

Diet recommendations for *Anisakis simplex* allergy were applied and no new allergic events were observed or atrial fibrillation after one year-follow-up.

Second case: An 84-year-old patient with a history of allergy to beta-lactams and hypertensive cardiomyopathy, was attended at the ED because he developed generalized

urticaria, palpebral angioedema, syncope, vomiting and atrial fibrillation after the intake of a piece of kiwi. At this time BP was 130/70, oxygen saturation 92%, heart rate 160 bpm and EKG showed atrial fibrillation rhythm. He was treated with 80 mg of IV 6-methylprednisolone, 5 mg of SC dexchlorpheniramine, IV metoclopramide and 5 mg of IV atenolol. After an observation period of 24 hours, he was discharged asymptomatic in sinus heart rhythm.

Three months later he developed another similar acute episode of generalized pruritus and hives, dizziness and vomiting after the intake of peanuts and again atrial fibrillation was registered. He was treated with 80 mg of IV methylprednisolone, 5 mg of IV dexchlorpheniramine and 5 mg of IV atenolol and symptoms resolved in two hours, with a normal sinus rhythm in EKG upon discharge.

Allergy workup confirmed hypersensitivity to food allergy: skin tests were positive to peanuts and kiwi. Total IgE: 444 KU/L, specific IgE to peanut 1.16 KU/L. Basal tryptase: 7.8 mcg/L. No data of tryptase levels was recorded during anaphylaxis. The transthoracic echocardiography showed normal left ventricular function and moderate left ventricular hypertrophy. Culprit food were forbidden and no new allergic reactions were observed during more than two years of follow-up.

We report 3 episodes of atrial fibrillation triggered by anaphylaxis. In both patients, the aetiological agent was identified: hypersensitivity to *Anisakis simplex* and food allergy.

The heart is the source and target of chemical mediators released during an allergic reaction. In the heart, there are plenty of mast cells, and are predominantly located around the coronary adventitia and in close contact with small vessels in the muscle wall. The release of mediators can influence ventricular function, heart rate and coronary artery tone. Anaphylaxis can trigger any kind of arrhythmia: atrial fibrillation in the course of an allergic reaction has been reported specially after insect sting (3).

In these cases, the very interesting point of discussion was: which should be first, the treatment of anaphylaxis or cardiac event?

Treatment with H1-antagonists is controversial; in fact, these drugs prevent slow atrioventricular conduction and inhibit ventricular fibrillation (4) but they are considered safe. Corticosteroids are potent anti-inflammatory and immunosuppressant agents. However, a meta-analysis has ruled out incidental to its use in cases of ischemia (5) and no contraindications have been reported in the literature in case of arrhythmias.

Our patients were treated with antihistamines and corticosteroids with good response in both cases, and no adverse effects were observed.

Another important point was treatment with beta-blockers *versus* other antiarrhythmic drugs, like calcium channel blockers.

Beta-blockers could be considered an absolute contraindication in anaphylaxis, but there are no really treatment guidelines of arrhythmias during the acute episode. Cardiologists considered that beta-blockers were the first election instead of calcium channel blockers in these cases, for a better control of the rhythm and low risk of inotropic negative effect than calcium channel blockers. In some interesting works reported in the literature (6,7) about the effect of antihypertensive medication associated with anaphylaxis, is not clear that beta-blockers *per se* could be a risk factor, taking into account that patients treated with this drugs have cardiac diseases as well as other facts such as advanced age (8). In these 3 cases, the treatment of atrial fibrillation was prior than the anaphylaxis and atenolol was administered. Assessing risks and benefits cardiologists considered the best option to treat atrial fibrillation. Although in our experience beta-blockers were safe and no complications appeared, we think that the fact that atenolol is a selective inhibitor of B1-adrenoceptor, could explain its better tolerance regarding to other B2-adrenoceptor inhibitor beta-blockers in these situations (9).

The other controversial point was the use of epinephrine, the first line treatment for anaphylaxis, which was not administered in any of these cases. Recommendations about epinephrine in cardiac patients during an anaphylaxis continue to be a dilemma (10). We assume that epinephrine was not administered because of the risk of worsening atrial fibrillation.

We only report 3 cases, so we emphasize the importance of registering more cases, the priority of establishing protocols between cardiologist and allergist for the treatment of cardiovascular complications during anaphylaxis. We also warn about the correct diagnosis of arrhythmias in these patients, in order to treat them as soon as possible to prevent other consequences or a worst prognosis of anaphylaxis.

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Clinical Significance points:

The heart is the source and target of chemical mediators released during an allergic reaction.
Anaphylaxis can trigger any kind of arrhythmia.
Recommendations about epinephrine in cardiac patients during an anaphylactic event continued to be a dilemma.
We emphasize the needed of established protocols between cardiologist and allergist in treatment of cardiovascular complications during anaphylaxis