

Incidence, clinical features and management of acute allergic reactions: the experience of a single, Italian Emergency Department

E.C. LAURITANO, A. NOVI, M.C. SANTORO, I. CASAGRANDA

Emergency Department, SS. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy

Abstract. – OBJECTIVES: Few data on the incidence, aetiology, clinical features and management of patients with acute allergic reactions presenting to the Emergency Department are currently available. The aim of the study was to report the annual experience of a single Italian adult Emergency Department about anaphylaxis.

PATIENTS AND METHODS: This is a retrospective, case-based study of adult patients attending the Emergency Department in Alessandria, Italy, during the years 2009-2010. We evaluated the medical records of patients satisfying diagnostic codes involving acute allergic reactions. Incidence, demographic data, causative agents, clinical features, management and outcome were reported.

RESULTS: 390 patients with acute allergic reactions were evaluated during the year, corresponding to 0.7% of all Emergency Department visits. Causative agents were recognized in 55.1% of patients and more commonly included drugs (26.9%), insects (14.8%) and foods (8.9%). Cutaneous features were the single most common clinical presentation although two or more clinical features were frequently reported (17.7%). Anaphylaxis was diagnosed in 4.6% of patients. After therapy and a period of monitoring, 92.8% of patients were discharged directly from the Emergency Department, 7.0% were admitted and one patient died, corresponding to a fatality rate of 0.2%.

CONCLUSIONS: Acute allergic reactions are common diseases referring to our Emergency Department. In the half of cases a precipitant agent was identified and cutaneous and/or mucosal changes were often the first feature. Most patients were definitely treated and discharged but about 7.0% of patients required hospitalisation. Observation Unit and Intermediate Care Unit were essential for clinical management of these patients.

Key Words:

Acute allergic reactions, Emergency Department.

Introduction

Acute allergic reactions are significant and increasing clinical problems in the emergency set-

ting¹. Currently, few epidemiological data on the incidence are available and they come from a very different categories of patients, including the general population², Emergency Department (ED) patients³⁻⁶, hospital admissions⁷ and specialist allergy clinics⁸. The heterogeneity of these data makes difficult to interpret the real impact of this condition. However, some studies seem to suggest that the incidence of acute anaphylaxis is increasing; the reasons are largely unknown although several factors including changes in diet and increasing use of therapeutic drugs could play a role⁷.

An other limit in the allergic reactions approach is the lack of any consistent clinical manifestation; a constellation of signs and symptoms, none of which completely specific, generally cause significant diagnostic difficulties⁸⁻⁹. Confusion also arises from the wide and mutable range of severity of the clinical features, coming from cutaneous changes alone to life-threatening airway and/or breathing and/or circulation problems¹⁰. Moreover, no universally accepted clinical definition of anaphylaxis exists and the etiologic distinction between immune-mediated anaphylactic reactions and non-immune anaphylactoid ones is extremely difficult¹¹, particularly in the emergency setting.

The therapeutic approach to these patients is not always obvious; some anaphylaxis guidelines and algorithms for drugs administration exist, but the evidence to support their use is generally weak¹²⁻¹⁵.

Finally, although the definitive management of allergic acute reactions in the Emergency Room alone is possible in most cases⁶, a significant increase in the rate of hospital admission is reported in recent studies, suggesting the need of Intermediate Care Units that are specialized in management of life-threatening conditions⁷.

The aim of the study was to report our case-load about the epidemiology, causative agents, clinical features, management and outcome of a

large group of patients presenting to our ED with signs and/or symptoms suggestive for acute allergic reaction.

Patients and Methods

We performed a retrospective, case-based study on all patients presenting to our ED during 1 year, from September 30, 2009, to September 30, 2010 and having as final diagnosis one of these Classification of Diseases–9th revision–Clinical Modification (ICD-9-CM) codes: allergy/allergic reaction (995.3); anaphylactic shock (995.0); angioedema (995.1); urticaria (708.0); allergic asthma (493.9)¹⁶. Our Hospital directly serves a local population of 150.000 persons and it recorded a total of 55.000 ED attendances during the study period. Children (age < 18 years) were not included because they are generally treated at the nearby pediatric hospital. The Department is staffed 24 hours per day by emergency physicians. The study was approved by local Ethic Committee.

Definitions

The patients presentations were divided into 4 groups: patients with acute allergic reactions confined to cutaneous symptoms, patients with only upper respiratory tract involvement, patients with gastrointestinal symptoms alone and patients affected by anaphylactic reaction.

We defined skin or mucosal changes as generalised or patchy erythema, pruritus, urticaria, and angioedema without any other systemic symptoms or signs. Upper respiratory tract involvement included rhinitis, conjunctivitis, asthma. Vomiting, diarrhea and abdominal pain were the most common gastrointestinal symptoms. Finally, anaphylaxis was defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction rapidly developing life-threatening airway and/or breathing and/or circulation problems¹⁷.

Further data included previous history of allergy, causative agent, treatment and final decision about discharge/admission. We also reported data about patients subsequently admitted to our Observation Unit and Intermediate Care Unit.

Statistical Analysis

Descriptive statistics were calculated; results are expressed either as means \pm SDs and ranges or as percentages. ANOVA was used to compare continuous variables between multiple groups.

$p < 0.05$ was considered statically significant.

Results

Demographic Data

We evaluated 390 patients with acute allergic reactions, corresponding to 0.7% of all ED visits (1 in 128); the mean age was 40.0 years (SD, 14.7; range, 18-83 years). Female/male ratio was ratio 1:1. Comorbidity was present in 25% of patients; white-race patients were the majority (77%). More than one fourth of patients (30%) had a known previous history of allergy (Table I).

Causative Agents

A causative agent was known in 215 patients (55.1%). The most common categories were drugs (26.9% of all cases), followed by insects (14.8%) and foods (8.9%). The other causative agents included chemicals, pollens, powder (Table II). Drug-related most frequent agents included antibiotics in 37.1% of patients (penicillins 56.4%, cephalosporins 12.8%, fluoroquinolones 12.8%; unknown antibiotic 12.8%; macrolides 5.2%), nonsteroidal anti-inflammatory agents in 27.6%, intravenous iodinated contrast in 14.3% and angiotensin-converting enzyme (ACE) inhibitors in 5.7% (Table III). Insect causes included wasp in 41.4% of patients, bee in 12.0% and hornet in 13.8%. In 32.8% of cases, the insect type was unknown. Food agents included fish and seafood in 40.0% of cases, nuts in 28.6%, milk, peach and vegetables in 5.7%, respectively and miscellaneous in 14.3% of causes. Finally, the majority of chemicals-related allergic reactions were due to cosmetic products and paints (41.6% and 33.3%, respectively).

Clinical Features

Skin or mucosal changes alone were present in 211 patients (54.1%). Upper respiratory features

Table I. Demographic data.

Patients (No.)	390
Sex	
Male	195 (50%)
Female	195 (50%)
Mean age (years)	40.0
Comorbidity	98 (25.1%)
Race	
Caucasian	301 (77.2%)
Black	54 (13.8%)
Asiatic	35 (9.0%)
Atopy	120 (30.7%)

Table II. Causative agents.

No. of patients (%)	
Unknown	172 (44.2)
Drugs	105 (26.9)
Insects	58 (14.8)
Foods	35 (9.0)
Chemicals	12 (3.1)
Pollens	6 (1.5)
Powder	2 (0.5)

alone were reported in 85 patients (21.8%). About 1.8% of patients referred only gastrointestinal symptoms (7 patients). Two or more clinical features were reported in 69 patients (17.7%). Finally, in 18 patients (4.6%) of patients anaphylaxis diagnosis was established. In Table IV, we reported the clinical features of these patients in details.

Treatment Before at the Hospital Arrival

One hundred seventy five patients (44.9%) received H1-antihistamine agents and/or steroids before presentation at the hospital. Only 2 patients (0.5%) received intramuscular adrenaline from an ambulance physician. No patients were self-medicated with adrenaline.

Treatment in the Hospital

In the Emergency Room, 56.4% of patients were treated with steroids, 53.1% with H1-antihistamine agents, 19.2% with H2-antihistamine agents, and 23.8% with bronchodilator therapy. Finally, 5.9% received a rapid intravenous fluid

Table III. Drugs responsible for acute allergic reactions.

No. of patients (%)	
Antibiotics	39 (37.1)
• Penicillins	22 (56.5)
• Cephalosporins	5 (12.8)
• Fluoroquinolones	5 (12.8)
• Unkown	5 (12.8)
Macrolides	2 (5.2)
NSAID	29 (27.6)
Intravenous iodinated contrast	15 (14.4)
ACE-inhibitors	8 (7.7)
Local anaesthetic	5 (4.8)
Myorelaxants	4 (3.7)
Gadolinium	3 (2.8)
Proton-pump inhibitors	2 (1.9)

NSAID: Nonsteroidal anti-inflammatory drugs; ACE: Angiotensin-converting enzyme.

challenge and intramuscular adrenaline, with mandatory vital signs and electrocardiographic monitoring (Table V).

Disposition of Patients with Anaphylaxis

After a period of monitoring, 92.8% of patients were discharged directly from our Emergency Room. Only 7.0% were admitted, of which 70.4% to our Observation Unit and Intermediate Care Unit, 22.2% to Pneumology Ward and 7.4% to Internal Medicine Ward. One 35-year-old man who collapsed after wasp stings arrived in electro-mechanical dissociation and died (0.2%).

Observation Unit and Intermediate Care Unit Admitted Patients

Nineteen patients were admitted to our Short-Stay Observation/Sub Intensive Care Unit. These patients were older (45.4 years; SD, 13.6; range, 22-80) and had more frequently comorbidity (36.8%) as compared general population, but there was not a statistically significant difference ($p > 0.05$). An atopic history was present in 31.5% of patients.

Among these patients, 84.3% had severe, potentially life-threatening anaphylaxis; 10.5% had acute, severe asthma, 5.3% had a severe non-responsive urticaria. A causative agent was known in 16 patients (89.5%) as compared 55.1% of general population ($p < 0.05$) and drugs were again more commonly responsible for allergic reactions (56.3%), followed by insects (25%) and foods (18.7%). Steroids and H1-antihistamine agents were given in 94.7% of patients, H2-antihistamine agents in 84.2%, bronchodilator therapy in 52.6% and supplementary adrenaline in 10.5% for treating severe biphasic reactions (Table V). In one patient (5.2%) affected by a systemic reaction with a severe asthmatic component, non-invasive mechanic ventilation was needed¹⁸.

Table IV. Clinical features in 18 patients with anaphylaxis.

No. of patients (%)	
Systolic blood pressure < 90 mmHg	16 (88.8)
Urticaria/angioedema	15 (83.3)
Dyspnea	10 (55.5)
Decreased conscious level or loss of consciousness	9 (50)
Respiratory rate > 25	8 (44.4)
Bronchospasm	8 (44.4)
Cyanosis	4 (22.2)
Laryngeal edema	3 (16.6)
Vomiting	3 (16.6)

Table V. Treatment data in Emergency Room and in Intermediate Care Unit.

	No. of patients (%)	
	In Emergency Room	In Intermediate Care Unit
Steroids	220 (56.4)	18 (94.7)
Histamine H1 antagonists	207 (53.1)	18 (94.7)
Histamine H2 antagonists	75 (19.2)	16 (84.2)
Adrenaline	23 (23.8)	2 (10.5)
Bronchodilators	93 (5.9)	10 (52.6)

All patients were discharged after a mean hospital stay of 3.6 days. They received follow-up care from Allergy Department.

Discussion

At our best knowledge, this is the largest cohort of patients with acute allergic reactions referring to a single Italian adult ED in one year.

Our data seem to confirm epidemiological results coming from the literature. The American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis working group, summarising the results of several epidemiological studies, concluded that anaphylaxis frequency ranges from 30 to 950 cases per 100,000 persons¹⁹. Retrospective studies of ED attendances, estimating only ED patients and relating this number to the population served, reported that annual incidence of acute allergic reactions ranged from 1:439 to 1:1000 and the annual incidence of severe anaphylaxis from 1:1000 to 1:3500^{3,6,20}. In our experience, we reported 390 acute allergic reactions in one year, corresponding to 0.7% of all ED visits (1 in 128); considering that we serve a population of 150,000 persons, we estimated an incidence of 260 cases per 100,000 persons per year for acute allergic reactions and 12 cases per 100,000 persons per year if we consider only severe anaphylaxis. Our data are likely to reflect underestimation, because some cases might be treated or resolved before ED presentation and others might have gone unrecognised. Our annual mortality was 1:390 (0.2%) that is in line with case fatality ratio of less than 1% reported in most population-based studies^{2,6,21-23}.

As concerned clinical features, skin and mucosal features were the most common, although in a significant percentage of patients a combination of signs involving different organs can be detected. However, only when an airway problem, respiratory difficulties and circulation prob-

lems were present, we diagnosed an anaphylactic reaction. Overall, 84% of all our patients with anaphylaxis had cutaneous changes; this is in contrast with other Authors reporting that all of their patients had cutaneous manifestations^{24,25}. The complete absence of cutaneous signs, their spontaneous resolution or because of treatment before ED presentation, the rapid onset of airway, breathing or circulatory problems can explain our findings.

Drugs, and particularly antibiotics, were the most common cause of acute allergic reactions and anaphylaxis, reflecting their increasing use in the clinical practice^{1,7}. Foods were not frequently associated with allergies, in contrast with some authors recognizing an increasing role of food-induced anaphylaxis^{8,26}. However, the relative importance of the triggers significantly varies with age; foods are particularly important in children, that don't refer to our ED²⁷.

Moreover, unknown agent was found in 44.9% of all acute allergic reactions, but only in 22.3% of severe anaphylaxis; this is similar to rates reported by Yocum et al (32%)² and Brown et al (27%)⁶. We were unable to clearly establish whether there had been a failure of patient record documentation, an inadequate or absent physician inquiry, or simply insufficient notice taken, reflecting the retrospective nature of data collection. However, the possibility to identify the trigger seems to be related to severity of clinical presentation.

As concerned the treatment, antihistamines were largely administered, according with the logical reasons and literature evidences supporting their use¹². The steroids administration was much as expected, as reported in previous studies^{28,29}. Moreover, although there is little evidence to support the routine use of H2 antihistamines, they were administered in a significant proportion of our patients³⁰. Adrenaline and fluids, however, continue to be the first-line therapy in severe anaphylaxis^{31,32}.

Adrenaline was given by intramuscular route in all patients, because it has a greater margin of safety, it is easy to administer and an intravenous access is not needed³³. Doses and route were conform to current guidelines in all cases. Adrenaline was given before hospital presentation only in 2 patients from an ambulance physician; we had no cases of adrenaline auto-injection.

Moreover, although most cases of acute allergic reactions can be completely managed and solved in the Emergency Room³⁴, our data confirm the increase in the rate of hospital admission reported by recent works. The most common circumstances requiring hospitalisation were severe reactions caused by idiopathic agent, possibility of continuing allergen absorption, presence of severe asthmatic component and patients coming from areas where access to ED is difficult. According to local disposition, the most patients were kept under observation in our Observation Unit and Intermediate Care Unit, that is staffed 24 hours per day by emergency physicians. Steroids and antihistamine agents were given in most patients, while supplementary adrenaline doses were needed for treating 2 severe biphasic reactions. In one case of severe asthma, non-invasive mechanic ventilation was mandatory. The presence of emergency physicians is crucial to ensure a correct and early management of these potentially life-threatening late-onset reactions³⁵. Finally, after the acute event, it is important that all severe anaphylaxis patients are referred to an allergy clinic, specially when the causative agent is unknown or unavoidable and attacks are recurrent^{36,37}.

In conclusion, although our data were collected retrospectively and than could be altered by reporting bias, they add to the literature a defined description of the epidemiology, causative agents, and clinical features of a large group of acute allergic patients presenting to our ED. Prospective, multicenter, large-cohort studies are particularly needed to clarify and establish the best treatment approach and management of these patients.

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