

## Serum tryptase, Immunoglobuline E assay and circumstantial data are fundamental tools for the post-mortem diagnosis of food anaphylaxis: a case report and literature review

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**Abstract: Introduction.** The most recent literature suggests that postmortem diagnosis of anaphylaxis remains a significant challenge for pathologists. Even with autopsy examination, the diagnosis of anaphylactic shock is difficult due to the complexity of the pathogenetic factors and the lack of pathognomonic data.

**Case presentation.** The authors present a case of death for anaphylactic shock after food ingestion. Laboratory examinations carried out on blood taken from femoral arteries, approximately 5 hours after death, showed a value of 120 ng/ L of tryptase (n.v. <11.4 ng/ L). Examination aimed at detecting IgE confirmed the existence of milk proteins allergy. Autopsy findings were suggestive of sudden death of cardiovascular origin, characterized by multi-organ congestion, petechiae and tracheal and bronchial foam.

**Conclusions.** The combination of autopsy findings with serum tryptase and immunoglobuline E assay, histological preparations and anamnestic-circumstantial data provided the necessary elements for the postmortem diagnosis of anaphylactic shock caused by milk proteins ingestion.

**Key Words:** Anaphylaxis, anaphylactic shock, postmortem diagnosis, tryptase, IgE.

### INTRODUCTION

Anaphylactic shock is the most severe manifestation of anaphylaxis and can lead to death in a few minutes for cardiovascular collapse. Even after autopsy examination, the diagnosis of anaphylactic shock is difficult due to the complexity of the pathogenetic factors and the lack of pathognomonic data.

The most recent literature suggests that postmortem diagnosis of anaphylaxis remains a significant challenge for pathologists. Postmortem serum tryptase and immunoglobuline E assay is commonly used in the investigation of suspected anaphylactic deaths. However neither tryptase dosage nor IgE concentration are pathognomonic. Moreover the tryptase, protease produced by the mast cells, has been found to be elevated

also in non anaphylactic deaths. In addition, the effect of the postmortem interval on serum tryptase is not fully understood.

In many cases, lacking specific autopsy findings, the cause of death is often identified on the basis of circumstantial data [1, 2]. In this context, pathologists must suspect anaphylaxis exclusively on the basis of circumstantial data, as well as on autopsy findings, and arrange laboratory tests that can contribute to determine the cause of death [3].

### CASE PRESENTATION

The authors present a case of death caused by anaphylactic shock after food ingestion. A 17 years old male went to a friend's house to have dinner at about

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20 pm. By the time he ingested the meal, he felt sick with respiratory distress. The first rescuers who arrived on the scene about half an hour later, found the patient cyanotic on the floor, with midriasis and no central pulse. They administered 4 adrenaline vials and resuscitatory maneuvers were performed for 30 minutes. At 21:30 the subject was declared dead. Circumstantial data were indicative of a sudden death occurred soon after the meal. The coroner who performed the body inspection on the scene immediately asked for the medical records related to the boy's clinical history. The boy suffered from allergy to cow's milk protein and had several episodes of bronchospasm and cyanosis since 3 months, after ingestion of products containing milk and its derivatives.

Laboratory examinations carried out on blood taken from femoral arteries, approximately 5 hours after death, showed a value of 120 ng/L of tryptase (n.v. <11.4 ng/L) [4, 5]. Examination aimed at detecting IgE confirmed the existence of milk allergy and its derivatives (Allergen-specific IgE concentrations above 0.1 kUA/L indicate the presence of sensitization):

total IgE 403 kU/L;  
nBosd4 maltalbumin milk 4.39 kUA/L;  
nBosd betalattoglobulin milk 4.84 kUA/L;  
nBosd 8 casein: 95.1 kUA/L;  
milk: 79.2 kUA/L.

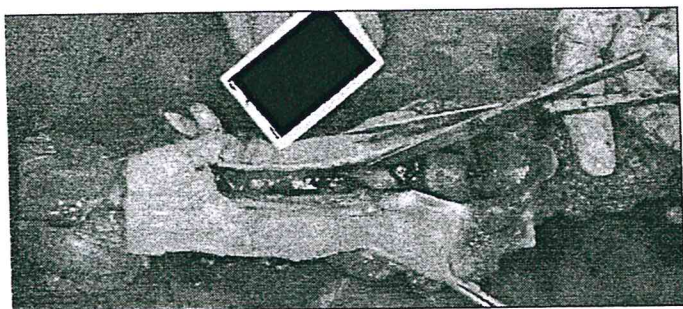
### Autopsy results

External examination, performed 13 hours after death, revealed, valid cadaveric stiffness in all muscular

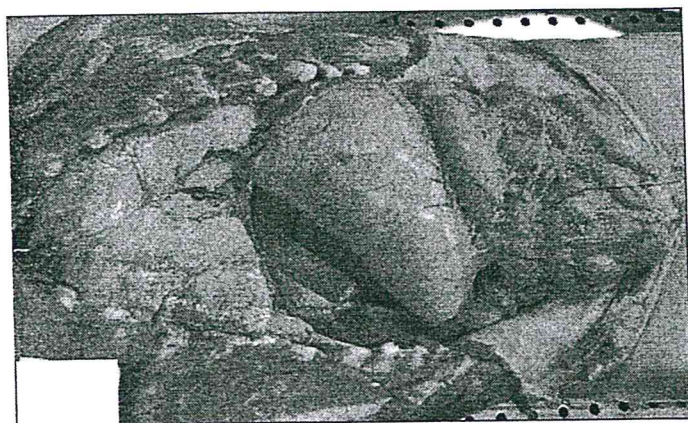
districts; rectal temperature of 27 ° C (room temperature of 22 ° C); hypostasis was on face, upper chest and limbs, slightly disappearing to the digital pressure; eyes petechiae and blood from the mouth and right nasal nostril were detected. The autopsy showed edema of laryngeal and tracheal mucosae with reddish mucus and whitish foam (Fig. 1). At the chest opening, the lungs completely covered the pericardium (Fig. 2). The pleural spaces were empty. The right lung had regular shape and consistency, increased volume, reddish color, measured 24.5 x 20 x 8 cm and weighed g. 570. The left lung had regular shape and consistency, increased volume, reddish color, measuring 24 x 18.5 x 7.5 cm and weighed g. 540. Large and medium bronchi were intact, containing abundant whitish foam; the arterial and venous vessels had intact walls. The visualization of the histological preparations showed the presence of inflammatory cells at the glottides submucosal site (Fig. 3), in the spleen and pulmonary acute emphysema. Autopsy findings were indicative of a sudden death of cardiovascular origin, characterized by multi-organ congestion, petechiae and tracheal and bronchial foam.

### DISCUSSION

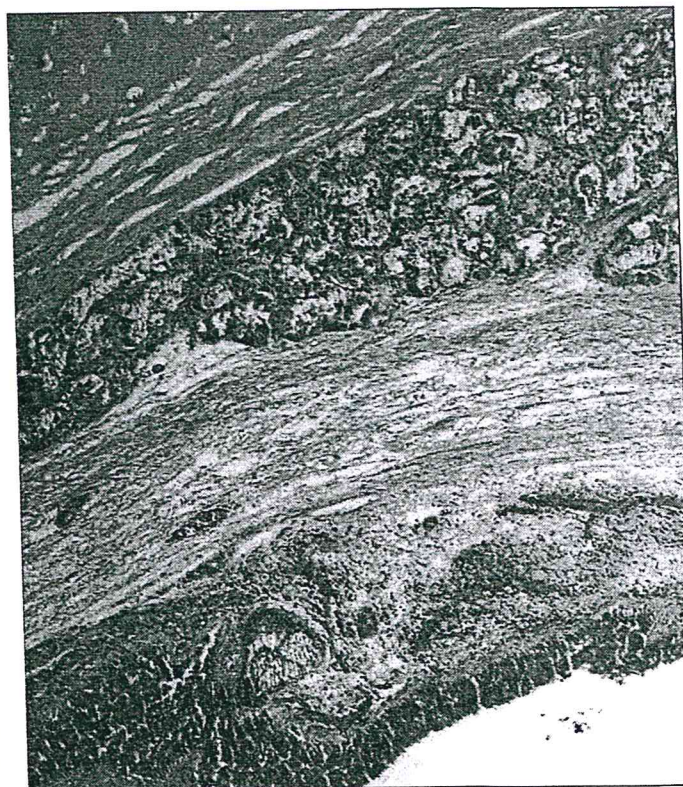
In this case, the cause of death was identified in anaphylactic shock resulting from the ingestion of food containing proteins to which the subject was allergic (a very scarce amount of cheese on pasta). The combination of autopsy findings with laboratory analysis,



**Figure 1.** The autopsy showed edema of laryngeal and tracheal mucosae that contained reddish mucus and whitish foam.

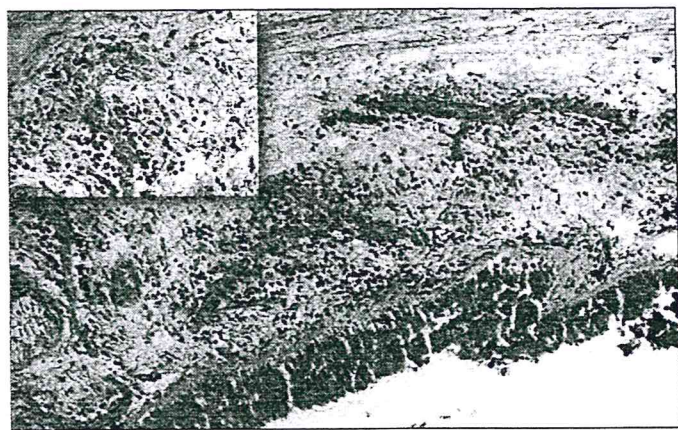


**Figure 2.** At the chest opening, the lungs completely covered the pericardium.



**Figure 3.** Severe edema and vascular congestion of the mucosa and submucosa, mononuclear inflammatory infiltrate, mostly perivascular. (H&E 50x)





**Figure 4.** Mononuclear inflammatory cells, small and medium size, possibly lymphocytes, plasma cells and mast cells; (H&E 100x, 400x).

histological preparations and anamnestic-circumstantial data provided the necessary elements for postmortem diagnosis of anaphylactic shock caused by food ingestion.

The diagnosis of anaphylaxis as a cause of sudden death in legal medicine is complex [6]. Tryptase is a protease secreted in blood and interstitial space after degranulation of mast cells [7]. According to the literature, very high post-mortem values of tryptase are interpreted as a significant finding in deaths resulting from anaphylactic shock [8-10]. In fact,  $\beta$ -tryptase secreted after one anaphylactic stimulus, is identifiable in blood after 30 minutes, with a peak after 1-2 hours. The baseline level of  $\beta$ -tryptase in serum is 1 ng/ mL, while the total value of tryptase ( $\alpha$  protryptase and  $\beta$ -protryptase) is 1-15 ng/mL [11-13].

It has been shown that a value of 10  $\mu$ g/L or greater has a sensitivity of 86% and a specificity of 88% for post-mortem diagnosis of anaphylaxis. The ideal sample for blood tryptase measure should be taken 1-2 hours after the allergic reaction [14].

Nevertheless, many studies attest to its usefulness even when done 3-6 days after death, but with a substantial decline [15, 16]. Therefore, it is appropriate to take the

blood sample as soon as possible in cases of suspected anaphylaxis [14]. It is preferable to take the blood sample from the femoral vessels to avoid the increase of mast cell-induced tryptase due to prolonged cardiac massage or defibrillation [17].

Tryptase concentration alone, however, does not allow to diagnose death for anaphylactic shock.

It should be noted that high levels of tryptase can also be detected in case of trauma, heroin abuse, myocardial infarction, sudden infant death syndrome [18-20].

In a recent study of 57 non-anaphylactic deaths conducted by Horn *et al.*, gradual increase in serum tryptase concentrations was observed at post-mortem intervals of at least 50 hours. [21].

Stravan *et al.*, reported a case of death from anaphylaxis in which 2 separate serum tryptase measurements taken 24 hours apart from the same femoral vein showed a decline from 130.0  $\mu$ g/L at day 2 after death to 84.4  $\mu$ g/L at day 3, hypothesizing a decline due to degradation of the degranulated mast cell tryptase in anaphylactic deaths [14].

Additional evidence for diagnosing death by anaphylactic shock is seen by IgE dosage, which remains stable in plasma for a few weeks and provides important indications about the subject's allergies [22]. These data, in addition to the spleen-related hypereosinophilia, help in the diagnosis of anaphylactic shock.

## CONCLUSIONS

The combination of autopsy findings with serum tryptase and immunoglobulin E assay, histological preparations and anamnestic-circumstantial data provide the necessary elements for postmortem diagnosis of anaphylactic shock caused by food ingestion.

**Conflict of interest.** The authors declare that there is no conflict of interest.

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