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CASE REPORT

Erik Edston · Marianne van Hage-Hamsten

Death in anaphylaxis in a man with house dust mite allergy

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Abstract Up to recently the post-mortem diagnosis of anaphylaxis has been based solely on circumstantial evidence. With the development of assays for mast cell tryptase it is now possible to verify cases of suspected anaphylaxis. Here we present one such case, which initially appeared to be due to sudden death of unknown cause. A 47-year-old farmer was found dead in his bathroom around midnight. Hospital records revealed that he had previously been diagnosed with an allergy to house dust mites. He had also had infrequent episodes of airway symptoms, nausea, hypotension and diarrhoea usually after going to bed. The forensic autopsy did not give any clue to the cause of death. Serum tryptase in post-mortem blood was found to be substantially elevated in two samples (170 and >200 μg/L). Analysis of allergen-specific IgE showed high values for *Dermatophagoides pteronyssinus* and *farinae*. High mite allergen levels were found in dust obtained from the patient's mattress. The results of the immunological tests support the assumption that he died of anaphylactic shock. The circumstances and the patient's history of previous attacks after going to bed point to the fact that exposure to mite contaminated food and/or exposure to mite allergens in bed might have caused his death.

Keywords Anaphylaxis · Sudden death · Tryptase · Allergy · Mites

Introduction

Sudden deaths in previously healthy children, younger and middle-aged individuals are not uncommon [1] and a few cases will remain unexplained when cardiovascular and other less common diseases have been ruled out. Quite a few of these cases might have died from anaphylaxis [2]. By measuring mast cell tryptase in serum it is possible to diagnose cases who died in anaphylactic shock [3, 4, 5, 6, 7] but to ascertain that anaphylaxis was the cause of death, complementary measurements of total-IgE, and allergen-specific IgE should be performed [8]. However, the circumstances of death and clinical records of the deceased patient must initially be clarified. By these procedures we have previously succeeded in identifying the cause of death in a few unclear cases [9].

Here, we present an unusual case of anaphylactic death of a man with dust mite allergy. Although not previously described in the medical literature the circumstances point to the fact that death was caused by inhalation of dust mite allergens in his bed.

E. Edston (✉)
Institute of Forensic Medicine Department of Molecular and Clinical Medicine,
University of Linköping, 58185 Linköping, Sweden
Tel.: +46-13-364259, Fax: +46-13-364270,
e-mail: eried@ihm.liu.se

M. van Hage-Hamsten
Department of Medicine Unit of Clinical Immunology and Allergy, Karolinska Hospital and Institute, Stockholm, Sweden

Case history

A 47-year-old farmer was found dead during the night of Christmas Eve in the bathroom about 2 h after going to bed. Allergy to house dust and storage mites had been diagnosed with RAST and a skin prick test in 1988 when he suffered from rhinoconjunctivitis and asthma-like symptoms. Allergen-specific IgE antibodies to mite allergens were measured in 1995 as 12 kU/l (*Dermatophagoides pteronyssinus*) and 6.9 kU/l (*Dermatophagoides farinae*). At that time he had begun suffering from attacks usually after going to bed, which started with a feeling of tickling in the hands, headache, nasal obstruction, shortness of breath and a feeling of nausea, followed by tachycardia, lightheadedness, tremors, a feeling of heat all over the body, diarrhoea, and a feeling of extreme thirst. The attacks lasted for 30–45 min and afterwards he had a period of shivers followed by extreme exhaustion. The attacks came infrequently, sometimes every week, and sometimes at intervals more than 6 months apart.

Heart disease, hyperthyroidism, pheochromocytoma and carcinoid disease had been excluded by clinical and laboratory investigations. The patient had had all his amalgam fillings removed, but this did not ameliorate symptoms which were explained as attacks of panic and he was started on antidepressant medication (paroxetin). The patient had no history of alcohol or drug abuse, had normal cholesterol levels and did not smoke.

Methods

The patient was subject to a routinely performed forensic autopsy at the Department of Forensic Medicine at Linköping, Sweden. Blood from the femoral vein was collected for forensic chemistry and immunological analyses. Blood for immunological tests was also sampled from the heart ventricles. After centrifugation serum was frozen at –20°C until analysis. Tissue samples were taken from the brain, the lungs, the heart, the liver, the kidneys, the thyroid and pituitary glands, the adrenals and the pancreas, and were fixed in 4% buffered formalin for histological and immunohistochemical studies.

Mast cell tryptase was measured by a commercial method (Tryptase FEIA, Pharmacia Diagnostics, Uppsala, Sweden). The method measures both α-tryptase and β-tryptase and the normal reference value is <14 µg/l. Total IgE was measured with the Pharmacia CAP System IgE FEIA where the normal reference value for adults is <122 kU/l. Allergen-specific IgE analyses were performed against the house dust mites *Dermatophagoides pteronyssinus* and *D. farinae*, the storage mite *Lepidoglyphus destructor* and a mix of common food allergens (egg white, milk, fish, wheat, peanut, soya bean fx5) using the Pharmacia CAP system specific IgE FEIA. A value of >0.35 kU/l is regarded as positive. Mite allergens levels (*Dermatophagoides pteronyssinus*, Der p1, *Dermatophagoides farinae*, Der f1 and *Lepidoglyphus destructor*, Lep d2) were measured in a dust sample collected from the bed mattress by suctioning 1 m^2 for 2 min with a vacuum cleaner using a separate filter bag (Medeca AB, Uppsala, Sweden) and prepared and stored as described earlier [10]. Values ≥55 ng/g are regarded as positive for Der p/f1 and ≥90 ng/g for Lep d2.

Results

The findings at autopsy were as follows: a male of normal stature measuring 190 cm and weighing 104 kg, with pulmonary congestion and edema, slight cardiac hypertrophy (490 g) and moderate steatosis of the liver. Histological examination of the brain, lungs and heart revealed no ischaemic or inflammatory changes in hematoxylin-eosin and Mallory's PTAH stains. Immunohistochemical investigations using antibodies against complement factor 9 (C9) and mast cell tryptase showed no ischaemic changes in the myocardium and normal numbers of mast cells in the lungs and myocardium. Neither could apoptosis be detected in the myocardial sections using the Cardiotacs kit [11].

The forensic toxicological analyses were negative except for low concentrations of alcohol in the blood and urine.

The results of the immunological tests are presented in Tables 1, 2 and 3. Mast cell tryptase was measured in heart blood and femoral blood, and was found to be substantially elevated at >200 and 170 µg/L, respectively (Table 1). Total IgE in serum was 200 kU/l and IgE specific for all mite allergens tested was found, and especially elevated for the house dust mites *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (Table 2). Allergen-specific IgE to the mix of common food allergens was negative. Dust analysis from the patient's mattress showed a very high concentration of Der f1 (Table 3).

Table 1 Mast cell tryptase, total IgE, and IgE to a mix of food allergens

s-Tryptase (µg/l) Femoral blood	s-Tryptase (µg/l) Cardiac blood	Total s-IgE (kU/l) Femoral blood	s-IgE food-mix (kU/l) Femoral blood
>200	170	200	<0.35

Normal values for s-tryptase <14 µg/l and total s-IgE <122 kU/l.

Table 2 Mite allergen-specific ige levels

s-IgE *Dermatophagoides pteronyssinus* (kU/l)	s-IgE *Dermatophagoides farinae* (kU/l)	s-IgE *Lepidoglyphus destructor* (kU/l)
19	15	0.84

Levels below 0.35 kU/L are considered negative.

Table 3 Mite allergen levels in vacuum cleaned mattress dust

Der p1 (ng/g dust)	Der f1 (ng/g dust)	Lep d 2 (ng/g dust)
700	12,000	<90

Values ≥55 ng/g for Der p1/f1 and ≥90 ng/g Lep d2 are regarded as positive.

Discussion

Deaths from anaphylaxis in forensic autopsy populations are infrequent, but might be underestimated due to lack of methods to diagnose anaphylaxis post-mortem. The most common causes are due to bee/wasp stings, drugs and diagnostic agents, and food [12, 13, 14]. Non-fatal anaphylactic reactions to house dust and storage mites have been described after ingestion of contaminated food [15, 16, 17].

Several studies have shown that allergies to house dust and storage mites are common among farming populations [18, 19, 20]. Two large cross-sectional studies among Swedish farmers have demonstrated that mites are dominant allergens in rural surroundings [19, 21] and that sensitisation to these species is significantly associated with asthma and rhinoconjunctivitis [22]. Exposure to mite allergens has been recognised worldwide as an important risk factor for development of sensitisation and allergic disease [23]. The significant source of exposure to house dust mite allergens is mattresses [24], which is in line with the current findings and our recent report where we have shown that farmers' mattresses contain high levels of mite allergens [10]. Our patient was a part-time, small-scale farmer from a relatively humid area in southeastern Sweden. His allergy to house dust mites was diagnosed early in 1988, when he only had respiratory symptoms. The allergy appears to have been exacerbated in 1994 when systemic reactions might have been misinterpreted as being non-allergic in origin. Many of the symptoms were typical for anaphylaxis: a prickling sensation in the skin, hypotension, shortness of breath, nasal obstruction, lightheadedness, and diarrhoea [25]. Despite the negative outcome of extensive tests for alternative explanations, the symptoms were not linked to an allergy and a psychiatric diagnosis was given. Panic syndrome can give rise to similar symptoms but the prescribed medication for the panic attacks was without any apparent effect.

The findings at autopsy were in concordance with the non-specific changes that are usually seen in cases of anaphylaxis [12, 26]. Sudden cardiac death was ruled out as far as possible with the available diagnostic methods. The cardiac hypertrophy and steatosis of the liver were not of such a degree as to indicate that death was due to chronic alcohol abuse or primary heart disease.

The concentration of tryptase was extremely high in both serum samples, and high levels of mite-specific IgE and of mite allergens in the mattress were found. It is known from our previous studies that post-mortem elevation of tryptase can be found in individuals who died from non-allergic causes, e.g. trauma [27] and positional asphyxia [28]. In other cases a slight to moderate non-specific elevation of unknown cause occurs in blood samples taken from the heart chambers [29] but in these cases total IgE levels are always normal. Thus, it seems highly unlikely that such high concentrations of tryptase in both heart and femoral blood in combination with elevated IgE as in the present case would be an artefact. The symptoms came irregularly, almost always after going to bed, usually about 20.00 h. He usually had his last meal of the day, at about 18.00 h. Whether his last meal (Christmas dinner) contained any mite-contaminated food or food that cross-reacts with mites (e.g. shrimps) is not known for certain. Allergic reactions vary in severity from time to time in the same individual and to link a especially severe reaction to a specific episode of exposure is to say the least difficult for both the clinician and the pathologist [30].

With regard to all available facts in our case, and current knowledge of anaphylaxis and anaphylactic deaths, it is not unlikely that this mite allergy was the cause of the previous attacks and subsequent death either as a result of ingestion of mite-contaminated food and/or inhalation of mite allergens in bed. Either way it is to our knowledge the first case to be described in the medical literature. It is conceivable that such deaths may have passed unrecognised previously, especially as dust mite allergens are the most important allergens worldwide.

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