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Bovine Serum Albumin: a double allergy risk

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SUMMARY

We analyse two cases of Bovine Serum Albumin (BSA) allergy. The first regards a female laboratory technician with a history of bronchial asthma due to cat allergy, who developed an exacerbation of bronchial symptoms as a consequence of BSA powder inhalation at work. To date, sensitization to BSA as a cause of occupational asthma has rarely been reported in the scientific literature. The second case concerns a woman with a similar cat sensitivity, who presented an oral allergy syndrome-type clinical reaction, gastric pain and diarrhoea immediately after eating cooked pork meat. Subsequently, she developed the same reaction after eating goat meat and goat cheese, and then also after eating beef. Both patients resulted specifically sensitized to BSA and to other mammalian serum albumins which play a role as panallergens in animals. The two cases show that BSA, a well known cause of food allergy in childhood, may also provoke symptoms of food allergy in adulthood, though in case of powder inhalation, it may provoke respiratory symptoms. Prior animal sensitization appears to represent a risk factor.

Introduction

Serum albumin is the main protein in mammalian tissues. Bovine Serum Albumin (BSA) is found as a major allergen (Bos d 6) in beef, while it is a minor allergen in cows' dander and milk (1). Serum albumins from many mammalian species have been reported to be both food allergens and aeroallergens, causing anaphylaxis and IgE-mediated respiratory symptoms (2,3). Some cases of anaphylaxis due to BSA during artificial insemination (4) or BSA contained in foetal calf serum during bone marrow transplantation have been published (5).

BSA is a 66 kDa heat-labile protein obtained from bovine plasma that is highly purified and widely used in immunochemistry, haematology and microbiology. The use

of this substance is on the rise in several fields, including the manufacture of cosmetics, biologic reactants and media for in-vitro fertilization techniques and cryopreservation of bone marrow cells. Thus, as a consequence, occupational exposure to BSA in laboratory workers is also on the rise. The first report of occupational sensitization to inhaled BSA powder dates back to 1991 (6), and was recently confirmed by a similar case (7). Bovine albumin is considered a minor allergen as compared to the major allergen (Bos d2), a lipocalin from cows' dander and urine which is responsible for occupational asthma and urticaria in breeders (8). More recently, some cases of occupational asthma due to exposure to airborne particles during raw meat cutting have been reported as likely being caused by serum albumins (9,10).

Meat allergy is a rare allergic disorder which is observed more frequently as a food allergy during the first years of life, but that is unusual in adults. Interestingly, milk allergy is not usually associated to meat allergy in adults, while in children it is frequent (11,12). A “pork-cat syndrome”, described in the nineties (13,14), was probably caused by cross-reactivity between serum albumins. This reactivity among various mammalian albumins has recently been confirmed (15,16).

We report two cases involving female adult patients who are examples of the possibility of developing various clinical symptoms over time due to this cross-reactivity. Both of them had a pre-existing allergy to cat. In one patient, this evolved into a situation of occupational-exacerbated asthma due to BSA exposure, while the second patient developed a food allergy from the ingestion of various meats.

Case one

A 45 year old female laboratory technician, exposed to purified crystalline BSA for 6 years, was referred to our department because of exacerbation of respiratory symptoms at work. Over the last three years she complained of wheezing and shortness of breath while diluting BSA powder in 1% aqueous solution. The reaction was immediate and recently sometimes so severe as to require medical therapy. The patient's medical history was negative for food allergy, but positive for allergic rhinitis dating back to childhood. She had also complained of intermittent asthma since the age of 28, which was treated with inhalant therapy when necessary. She had a dog during childhood, while over the last eight years she has had a cat.

Skin prick testing (SPT) was performed using commercial extracts of all the common inhalant allergens, milk proteins, cow dander and meat (Lofarma Lab, Milan, Italy). Low grade positivity (4mm wheal) was observed for dog, cat, cow dander and lactalbumin. Purified lyophilized crystalline BSA was prick tested at the same concentration that the patient used at work (1%) and resulted in a strong positive reaction (15 mm wheal). Five control subjects had negative SPT at the same concentration of BSA.

Total IgE was 451 kU/l and specific IgE was detected using the CAP System (Thermo Fisher Scientific) with these results: BSA (4.43 kU/l), cat dander (74.1 kU/l) and dog dander (24.5 kU/l).

Lung function tests showed a mild degree of basal obstruction (FEV1 82%, FVC 102%, FEF 25-75 46% of

predicted) and severe bronchial hypersensitivity with a 40% positive response to Metacholine inhalation (Pd20 FEV1: 0.021 micrograms). The patient's pulmonary function, which was tested during BSA powder dilution in the laboratory, showed a 25% reduction in FEV1 from baseline and she experienced an immediate reaction of wheezing and shortness of breath.

Case two

A 54 year old woman presented with allergic rhinitis and asthma with cat sensitivity which was being treated with antihistamines and nasal and bronchial steroids.

Despite her symptoms, the cat is still living with her. A few years after the onset of respiratory allergic disease, she presented an oral allergy syndrome-type clinical reaction, gastric pain and diarrhoea immediately after eating cooked pork meat. SPT was performed by commercial extracts and fresh meat and resulted positive for pork meat. Subsequently, she presented the same symptoms after eating goat cheese and goat meat. A prick by prick for the culprit foods confirmed the sensitization. Recently, she reported the same symptoms after eating not fully cooked beef.

Specific IgE detection (microarray IMMUNOCAP ISAC system) was positive for: bovine, cat, dog and horse serum albumin (Bos d6, Fel d2, Can f3, Equ c3). Moreover, we confirmed the cat and dog allergy through the cat and dog lipocalin positivity (Fel d4, Can f1). No other foods or respiratory allergen specific IgEs were detected.

Discussion

The clinical importance of BSA as an allergen in cows' milk and in beef has been well known for a long time. The relationship between this protein and the other animal allergens is very complex (16), but the use of recombinant allergens has been very helpful in understanding it (17-18).

In the past, it was demonstrated that patients with respiratory allergy to animal dander frequently produce IgE directed to serum albumin of that specific animal (19), and these allergens were then well characterized (20). A more recent finding shows that patients with persistent milk allergy and specific IgE to BSA have a greater risk of developing respiratory symptoms caused by animal dander (21). This relationship has not been confirmed in atopic adults (22). BSA-hypersensitivity with urticaria-angioedema caused by meat ingestion has been suggested

as a possible consequence of a subclinical sensitivity to dog and cat epithelium (23). Immunoblotting studies on various species of animals have demonstrated that albumins play a role as a panallergen in mammals and, being major allergens, they are responsible for sensitization to epithelia that developed without any direct contact with animals (24).

The occupational risk of respiratory allergy among laboratory workers is well known. The most common causes are animal dander and urinary proteins. Atopic subjects, particularly those sensitive to pets, are considered at greater risk (25). In our first case, the patient was not directly exposed to laboratory animals but to a protein of bovine origin, BSA, in the form of a powder, which is particularly harmful because it may trigger severe respiratory reactions. Inhalation of crystalline BSA, most likely with a high allergen concentration, led her to an evident asthmatic exacerbation, as demonstrated by the worsening of her parameters during the occupational monitoring of respiratory function. Considering her history of pre-existing allergic asthma, we can hypothesize a case of Work Exacerbated Asthma (WEA) due to specific sensitization to BSA (26).

At home, both patients had been constantly exposed to a cat, becoming allergic and showing mild respiratory symptoms for years. Interestingly, the first patient had never shown any symptoms of food allergy to cow's milk or to beef in her life, while the second one developed allergy to different types of meat some years after the beginning of respiratory symptoms. It was quite unusual to observe that the reactions to pork and goat meat appeared before the appearance of symptoms from beef ingestion. The hypothesis is that the primary sensitizing allergen in both patients was cat serum albumin, and the component-resolved diagnosis that was made in the second patient would seem to confirm this sensitization. The results of the allergological evaluation by SPT and by serological tests also confirmed the sensitization towards other mammal serum albumins, even though the clinical symptoms differed.

In conclusion, the first case shows that inhalation of BSA powder can provoke respiratory symptoms in professionally exposed subjects and must be considered a risk factor in medical surveillance. Atopic subjects, particularly those with a history of food allergy and sensitization to serum albumins, as well as those with respiratory allergy to domestic animals should be considered at greater risk. The second case shows that sensitization to BSA is important not only as a cause of respiratory symptoms, but

because it can lead to food allergy even in adulthood. The use of recombinant allergens for diagnosis can be a useful tool in identifying these cases, in particular among subjects with a history of respiratory or food allergy and long term exposure to animal dander. The importance of serum albumin as a panallergen needs to be evaluated and confirmed in clinical practice.

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