A case of anaphylaxis caused by the inhalation of sheep's milk vapors in a child with severe multi-food allergy.

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TITLE PAGE

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I. CONFLICT OF INTEREST

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III. KEYWORDS

Milk; Allergy; Inhalation; Case Report.

IV. MAIN TEXT

To the Editor,

Nowadays food allergy represents an important public health problem both in children and in adults, with an increasing prevalence in the last years [1, 2]. The worldwide epidemiology depends on diagnostic methods, dietary habits and cultural practices[2]. The most common foods involved in children are cow's milk, egg, peanut, tree nut and wheat flour [1, 2]. It is well known that adverse reactions commonly occur after ingestion

of food, with a wide range of clinical manifestations, such as respiratory, cardiovascular, cutaneous and gastrointestinal symptoms, and anaphylaxis [3]. In literature adverse reactions after inhalation of food particles are also described in highly sensitive patients [3], so it is important to identify and to follow-up them.

Here we describe the case of S., a 4-year-old female child followed up by the Pediatric Allergology Unit of Messina University Hospital for severe atopic dermatitis, allergic rhinitis, severe IgE-mediated multi-food allergy (milk, egg, peanut, nut, legumes, kiwi) and suspected transient hypogammaglobulinemia of infancy. Family history of allergic rhinitis asthma and food allergy. Her parents are dairy owners. S. didn't take milk since she was five months old because of a failure to thrive, vomiting, bloody diarrhoea and skin rashes after cow's milk consumption. At the beginning of our follow-up at the age of 2 years old, Skin Prick Tests (SPT), Prick by Prick (PbP), Component Resolved Diagnosis (CRD) and cow's milk Challenge were performed. SPT were positive for alpha-lactalbumin, beta-lactoglobulin and casein, with PbP positivity for milk. CRD showed high specific IgE levels for Bos d_milk, Bos d 4, Bos d 5, Bos d 8, Cap h_milk and Ovi a_milk (*Table 1*). During the cow's milk Challenge the baby developed a severe anaphylaxis, characterized by urticaria, wheezing and loss of consciousness, after the ingestion of 0,2 ml of milk. Intramuscular injection of adrenaline and intravenous infusion of methylprednisolone were administered, with the complete resolution of the symptoms in three hours. Self-injectable adrenaline and strict avoidance of exposure to cow's milk proteins were prescripted. After some months, S. developed an adverse reaction following the administration of nasal drops containing lactoferrin, characterized by mild angioedema of the face and sneezing attacks. At the age of 3 years old a new adverse reaction occurred in a very unusual circumstance: the mother reported that the baby was playing with her sister inside the parents' dairy farm where she inhaled the milk vapors released by the sheep milk making process. She immediately developed anaphylaxis characterized by hives, angioedema of the face and wheezing; the symptoms regressed after the oral administration of antihistamines and oral corticosteroids.

The real epidemiology of allergic reactions induced by the inhalation of food vapors and/or particles in children is still unknown[3, 4]. There are few data about its frequency in current scientific literature. Roberts et al. reported that 5% of children followed up for food allergy and asthma have respiratory symptoms after inhaling food particles [5]. The inhalation of food allergens depends on its presence in the air: farms or food industries, restaurants, school or home have been described as the places where the reaction can most frequently occur[4]. In particular, processing of food, such as boiling, may release a significant quantity of particles in the air. All of the foods may induce clinical symptoms when inhaled, but the most commonly reported in children are wheat flour, seafood, soy, legumes, peanut, tree nut and cow's milk [4]. According to the clinical case reported in this manuscript, Leonardi et al. wrote that allergic reactions to airborne milk proteins have been described in literature, in particular in children and adolescents with cow's milk allergy during the administration of inhaled drugs containing milk proteins[3]. Barbi et al. described the case of an 8-year-old girl with asthma and cow's milk allergy who developed a fatal anaphylaxis while she was in a dairy shop [6]. Nowak-Wegrzyn et al. reported a case of anaphylaxis in an eight-year-old boy with cow's milk allergy and persistent asthma occurred after the administration of Fluticasone/Salmeterol contaminated by lactose[7]. The diagnostic workup in these subjects is complex and it is based on the history and the clinical evaluation of the patient [3]. The most frequent clinical manifestations include respiratory symptoms (asthma, wheezing, coughing, sneezing attacks and rhinitis), skin reactions (rashes or urticaria), ocular symptoms (conjunctival hyperemia and lacrimation) and rarely anaphylaxis[3, 4]. It is important to establish the relationship between the inhalation of the foods and the onset of the symptoms. Skin testing (SPT and PbP) or serum-specific IgE for the foods suspected are also important for the diagnosis [3], but nowadays CRD, also known as Precision Allergy Molecular Diagnostic Applications (PAMD@), have an increasing role in improving the management of allergic diseases, in particular food allergy, because it may stratify the risk of anaphylaxis during the Challenge [3, 8]. However the gold standard actually used to confirm the diagnosis of food allergy is the Oral Challenge, with the ingestion of the suspected food by the patient [3]. There is no evidence in literature about the use of specific inhalation Challenge in the field of food allergy, although it is considered the reference for the diagnosis of Occupational Rhinitis and Occupational Asthma; however its use is limited in specialized centers [9]. Being asthmatic is the main risk factor in these patients.

When an allergic patient has experienced an adverse reaction after inhalation of food particles, the dietary and environmental avoidance of the offending food has an essential role [9, 10], as well as the educational interventions on children and their families and the use of emergency treatment in case of exposure to the allergen, represented by intramuscular administration of Adrenaline, Short-Acting Beta Agonists (SABAs), oral corticosteroids and antihistamines.

Our case report highlights the risk of anaphylaxis caused by inhalation of milk vapors in children with severe food allergy. It is an event rarely described and only adverse reactions related to cow's milk vapors are reported in current literature, hence to date our case represents the first report describing an adverse reaction caused by the inhalation of sheep's milk vapors. According to the severe clinical course and the possible airways involvement it is essential to identify the subjects at risk, to limit the exposure to aerosolized food with environmental measures and to practice the allergen avoidance diet and the emergency treatment when anaphylaxis occurs.

V. ACKNOWLEDGMENTS

We thank our patient's mother for her precious collaboration.

VI. INFORMED CONSENT

Informed consent was obtained.

VII. IMPACT STATEMENT

Adverse reactions after the inhalation of food particles are an emerging problem among children with food allergy, with an important impact on their daily life. It's essential to identify and to follow-up these patients, in order to implement educational and environmental measures, with the essential role of the avoidance diet and the emergency treatment in case of anaphylaxis.

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IX. TABLE

Total IgE	340 IU/ml	0,00-48,00
Bos d_milk	31,38 kU_A/L	$< 0,3$
Bos d 4	9,07 kU_A/L	$< 0,3$
Bos d 5	21,88 kU_A/L	$< 0,3$
Bos d 8	29,41 kU_A/L	$< 0,3$
Cap h_milk	18,22 kU_A/L	$< 0,3$
Ovi a_milk	25,18 kU_A/L	$< 0,3$
Gal d_white	13,44 kU_A/L	$< 0,3$
Gal d 2	10,56 kU_A/L	$< 0,3$
Gal d 3	1,75 kU_A/L	$< 0,3$
Ara h 1	10,43 kU_A/L	$< 0,3$
Cic a	10,87 kU_A/L	$< 0,3$
Gly m 6	3,88 kU_A/L	$< 0,3$
Len c	3,79 kU_A/L	$< 0,3$
Pis s	3,48 kU_A/L	$< 0,3$
Ave s	4,69 kU_A/L	$< 0,3$
Act d 1	18,66 kU_A/L	$< 0,3$
Ana o	10,56 kU_A/L	$< 0,3$
Ber e	8,42 kU_A/L	$< 0,3$
Car i	2,35 kU_A/L	$< 0,3$
Cor a 9	17,67 kU_A/L	$< 0,3$
Cor a 11	5,84 kU_A/L	$< 0,3$
Jug r 1	1,27 kU_A/L	$< 0,3$
Jug r 4	11,24 kU_A/L	$< 0,3$
Pru du	15,77 kU_A/L	$< 0,3$
Cuc p	2,01 kU_A/L	$< 0,3$
Hel a	2,95 kU_A/L	$< 0,3$
Pap s	8,86 kU_A/L	$< 0,3$
Ses i	2,37 kU_A/L	$< 0,3$
Cor a_pollen	4,79 kU_A/L	$< 0,3$
Der f 1	4,13 kU_A/L	$< 0,3$
Der p 1	10,98 kU_A/L	$< 0,3$
Cap h-epithelia	7,12 kU_A/L	$< 0,3$

Table 1. Component Resolved Diagnosis results.