HOUSE DUST MITE ALLERGY AND SHRIMP ALLERGY: A COMPLEX INTERACTION

Giorgio Celi MD (1), Ignazio Brusca MD (2), Enrico Scala MD (3), Danilo Villalta MD (4), Elide Pastorello MD (5), Laura Farioli BSc (6), Gabriele Cortellini MD (7), Gaia Deleonardi MD (8), Pietro Galati MD (8), Laura Losappio MD (5), Giuseppina Manzotti MD (9), Barbara Pirovano MD (10) Lionello Muratore MD (11), Francesco Murzilli MD (12), Francesco Cucinelli MD (12), Antonino Musarra MD (13), Marcello Cilia MD (13), Eleonora Nucera MD (14), Arianna Aruanno MD (14), Francesco Ria MD (15), Maria Francesca Patria MD (16), Elena Varin MD (17), Battista Roberto Polillo MD (18), Vittorio Sargentini (19), Oliviero Quercia MD (20), Carina Gabriela Uasuf MD (21), Stefania Zampogna MD (22), Michela Carollo MD (23), Stefania Graci MD (24), Riccardo Asero MD (1).

1. Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano, Italy
2. U.O.C. di Patologia Clinica Ospedale Buccheri La Ferla F.B.F. Palermo, Italy.
3. Allergy Unit – Istituto dermopatico dell'Immacolata – IDI-IRCCS, Rome, Italy
4. SSD di Immunologia e allergologia; Ospedale S. Maria degli Angeli, Pordenone, Italy
5. Struttura Complessa di Allergologia e Immunologia – ASST GOM Niguarda, Milano, Italy
6. Dipartimento di medicina di Laboratorio, ASST GOM Niguarda, Milano, Italy.
7. Unità Operativa di Medicina Interna Rimini, Ambulatorio di Allergologia, Azienda Sanitaria Romagna, Rimini, Italy
8. LUM AUSL Bologna, Italy
9. Sevizio di Allergologia, Casa di Cura Beato Palazzolo, Bergamo, Italy
10. Servizio Medicina di Laboratorio - ASST Bergamo Ovest, Bergamo, Italy
11. UOC Allergologia ed Immnologia Clinica ASL Lecce "P.O. V. Fazzi" Lecce, Italy
12. U.O.S.D di Allergologia, Ospedale S.S. Filippo e Nicola di Avezzano (AQ)
13. Servizio di Allergologia, Casa della Salute di Scilla, Italy
14. Servizio di Allergologia, Fondazione Policlinico Universitario A. Gemelli, Roma, Italy
15. Istituto di Patologia Generale, Fondazione Policlinico Universitario A. Gemelli, Roma, Italy
16. Pediatric Intermediate Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
17. Pediatric Highly Intensive Care Unit, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy
18. Servizio di Allergologia, UOC Medicina Interna, Polo Ospedaliero S. Spirito e Nuovo Regina Margherita, Roma, Italy.
19. Servizio di Allergologia di Laboratorio, UOC Patologia Clinica, Ospedale S Filippo Neri, Roma, Italy.
20. Unità di Allergologia, Medicina interna Ospedale di Faenza (RA), Italy
21. Centro Malattie Allergiche Bonsignori, Istituto di Biomedicina e Immunologia Molecolare, CNR, Palermo, Italy.
22. Pronto Soccorso Pediatrico, Azienda Ospedaliera Pugliese Ciaccio, Catanzaro, Italy
23. Patologia e Biochimica Clinica Universita' Magna Graecia, Catanzaro, Italy

24. Istituto Zooprofilattico Sperimentale della Sicilia "A. Mirri", via G. Marinuzzi, Palermo

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Corresponding Author:
Dr Riccardo Asero
Ambulatorio di Allergologia, Clinica San Carlo
Via Ospedale 21, 20037 Paderno Dugnano (MI), Italy
r.asero@libero.it

ABSTRACT

BACKGROUND AND OBJECTIVE: Sensitization and allergy to shrimp among Italian house dust mite allergic patients are not well defined and were investigated in a large multicenter study.

METHODS: Shrimp sensitization and allergy were assessed in 526 house dust mite (HDM)-allergic patients submitted to the detection of IgE to Der p 10 and 100 atopic control not sensitized to HDM.

RESULTS: Shrimp allergy occurred in 9% of patients (vs 0% of 100 atopic controls not sensitized to HDM; $p < 0.001$). Shrimp-allergic patients were less frequently hypersensitive to airborne allergens other than HDM than crustacean-tolerant subjects (35% vs 58.8%; $p < 0.005$). Only 51% of tropomyosin-sensitized patients had shrimp allergy, and these showed significantly higher Der p 10 IgE levels than shrimp-tolerant ones (mean 22.2 KU/l vs 6.2 KU/l; $p < 0.05$). Altogether 53% of shrimp-allergic patients did not react against tropomyosin.

CONCLUSIONS: Shrimp allergy seems to occur uniquely in association with hypersensitivity to HDM allergens and tropomyosin is the main shrimp allergen but not a major one, at least in Italy. Along with tropomyosin-specific IgE levels, monosensitization to HDM seems to represent a risk factor for the development of shrimp allergy among HDM allergic patients.

INTRODUCTION

House dust mites are one of the main causes of respiratory allergy worldwide, and shrimp represents the second cause of primary food allergy in Italy (1). These two allergies are strictly interconnected as both mites and shrimps are invertebrates and share cross-reacting allergens, the best known being tropomyosin (table 1). Shrimp allergens identified so far belong to diverse protein families characterized by conserved three-dimensional structures leading to potential IgE cross-reactivity among different members of crustaceans and mollusks (2). It is presently still unclear whether, in patients allergic to both house dust mite and crustaceans, sensitization occurs via the respiratory or the gastrointestinal tract. Prevalence studies of shrimp allergy in house dust mite allergic patients are missing. In the present work we investigated a large population of house dust mite-allergic patients, the vast majority selected within a national multicenter study (3) with the aim to detect the prevalence and features of shrimp allergy.

MATERIALS AND METHODS

PATIENTS

Five hundred twenty six house dust mite-allergic patients (M/F: 261/265; mean age 28.2 years, range 4-79 years) were studied. This population was virtually the same recently investigated to study the clinical significance of Der p 23, a major HDM allergen (3). Methods employed to diagnose HDM allergy included a positive SPT with a commercial extract of either *Dermatophagoides pteronyssinus* (D1) or *Dermatophagoides farinae* (D2), and the measurement of IgE specific for the HDM whole extracts D1, and D2, by ImmunoCAP (Thermo- Fisher Scientific, Uppsala, Sweden). IgE specific for Der p 10, the house dust mite tropomyosin, were measured as well in all study patients. Levels exceeding 0.35 kU/L were considered positive; this cut-off level was chosen with the aim to improve the specificity of in-vitro tests. Further, all patients underwent SPT with a large series of commercial extracts of seasonal (grass, mugwort, ragweed, pellitory, plantain, birch, olive, and cypress) and perennial (Alternaria, cat and dog dander) allergens. Patients were thoroughly interviewed about their tolerance to crustaceans. Those reporting suspect allergic reactions associated with the ingestion of shrimp or other invertebrates (i.e., oral allergy syndrome, contact urticaria, generalized urticaria, asthma, or anaphylaxis) underwent SPT with either commercial extract of shrimp (1:20 w/v; ALK-Abello', Madrid Spain) or fresh shrimp and/or shrimp-specific IgE measurement to confirm sensitization status. Skin tests with fresh material were carried out using the most common seawater shrimp species eaten in Italy, all belonging to the Penaeideae family (*Aristeus antennatus*, *Parapenaeus longirostris*, *Parapeneopsis cornuta* and *Melicertus kerathurum*). Patients scoring positive on SPT and/or on ImmunoCAP were considered as clinically allergic to shrimp.

One hundred randomly selected atopic patients sensitized to different airborne allergens except house dust mites were assessed for crustacean allergy in the same way and were used as controls.

STATISTICS

Statistical methods as well as ethical issues have been detailed elsewhere (3). Probability levels < 5% were considered statistically significant.

ETHICAL ISSUES

The clinical part of the study as well as specific IgE measurement were carried out as part of the clinical routine of every participating center. Patients gave an informed consent to the use of their clinical data in an anonymous form. The study was approved by the internal review board of the leading center. In view of the essentially observational nature of the study a formal approval by an external ethical committee was not requested.

RESULTS

The main findings are summarized in table 2. The prevalence of shrimp allergy in the general house dust mite allergic population was 45/526 (9%) vs 0/100 (0%) in the control population ($p < 0.001$). No differences in the prevalence of shrimp allergy between female (7.5%) and male (9.6%) patients was detected. Similarly, patients allergic and not allergic to crustaceans showed the same mean age (30 [16.2] years vs 28.2 [16.2] years, respectively), and no difference in the prevalence of asthma was observed between patients allergic or tolerant to shrimp (40% vs 40%, respectively). In contrast, patients with crustacean allergy were much less frequently hypersensitive to airborne allergens other than house dust mites than tolerant patients (35% vs 58.8%; $p < 0.005$).

The prevalence of hypersensitivity to tropomyosin in the study population was 7.8% (41/526). Of tropomyosin reactors, only 21 (51%) were clinically allergic to crustaceans, whereas 20 (49%) reported good tolerance to shrimp and other invertebrates. Interestingly, those with shrimp allergy showed a significantly higher mean level of IgE to Der p 10 than patients reporting good tolerance to crustaceans (22.2 [SD 28.0] KU/l vs 6.2 [9.6] KU/l; $p < 0.05$). Altogether, Der p 10 reactors were more frequently allergic to crustaceans than patients that did not show IgE specific for Der p 10 (21/41 [51%] vs 24/485 [4.9%]; $p < 0.001$). Nonetheless, notably 24/45 (53%) patients allergic to crustaceans did not react against tropomyosin. Finally, no difference in the prevalence of shrimp allergy was detected between patient monosensitized to Der p 10 (7/14 [50%]) and Der p 10 reactors who were sensitized to other mite allergens also (13/27 [48%]; p: NS).

DISCUSSION

The present study, which was carried out on a large population of patients with clinically defined house dust mite allergy, shows once more to which extent hypersensitivity to house dust mites and to shrimp are strictly linked. In effect, none among the atopic controls reported symptoms suggestive of shrimp allergy whereas the prevalence of shrimp allergy in the study population was nearly 10%. Such prevalence suggests that the cross-reactivity between HDM and other invertebrates involves minor mite allergens. Tropomyosin was the first shrimp allergen to be identified more than 25 years ago (4). Although it has been considered the major shrimp allergen ever since, recent multicenter studies carried out in the Mediterranean area were able to detect tropomyosin hypersensitivity in less than 50% of shrimp allergic patients (5). This observation was fully confirmed by the present study that was carried out on a completely different population, where 53% of shrimp-allergic patients were not tropomyosin reactors. Further, interestingly, among tropomyosin-hypersensitive patients the occurrence of shrimp allergy was strongly related to specific IgE levels, suggesting the clinical relevance of sensitization degree. Nonetheless, the present study confirmed the association between tropomyosin sensitization and shrimp allergy.

A number of shrimp allergens other than tropomyosin have been detected during the last years (2); most of these seem phylogenetically conserved throughout the invertebrates' kingdom and hence able to cross react with homologous house dust mite allergens (5, 6). Although in-vitro cross-inhibition experiments were not carried out in the present study it has to be considered that the whole study population was represented by patients with house dust mite-induced respiratory allergy, and no atopic control reported a history of food allergy to shrimps. In one shrimp allergic patients that did not react to recombinant Der p 10 the relevant shrimp allergen, that showed a molecular weight at about 100 kDa on immunoblot analysis was characterized by mass spectrometry (3) as paramyosin, a potentially cross-reacting muscular allergen of invertebrates.

Another interesting finding was the significantly higher prevalence of shrimp allergy among subjects monosensitized to HDM than among those who reacted to different airborne allergens. This observation is in keeping with similar findings in patients with food allergy to lipid transfer protein, that show more severe reactions if they are monosensitized and less severe allergic reactions in case of co-sensitization to airborne allergens (7). These findings might suggest that the dispersion of specific IgE reactivity over a larger number of targets is protective against severe allergic reactions or against food allergy per se.

In conclusion, shrimp allergy seems to occur uniquely in association with hypersensitivity to HDM allergens and, at least in this geographical area, tropomyosin is the main shrimp allergen but not a major one. Along with tropomyosin-specific IgE levels, monosensitization to HDM seems to represent a risk factor for the development of shrimp allergy among HDM allergic patients.

OBITUARY: This paper is in memory of our colleague Elena Varin

DISCLOSURE: No author has conflicts of interest to disclose.

AUTHOR CONTRIBUTION STATEMENT: Every author listed participated in the recruitment of patients and in the clinical workup at their own allergy centers. RA conceived and managed the multicenter study, and wrote the manuscript. ES and DV revised the manuscript. GC performed the statistical analyses.

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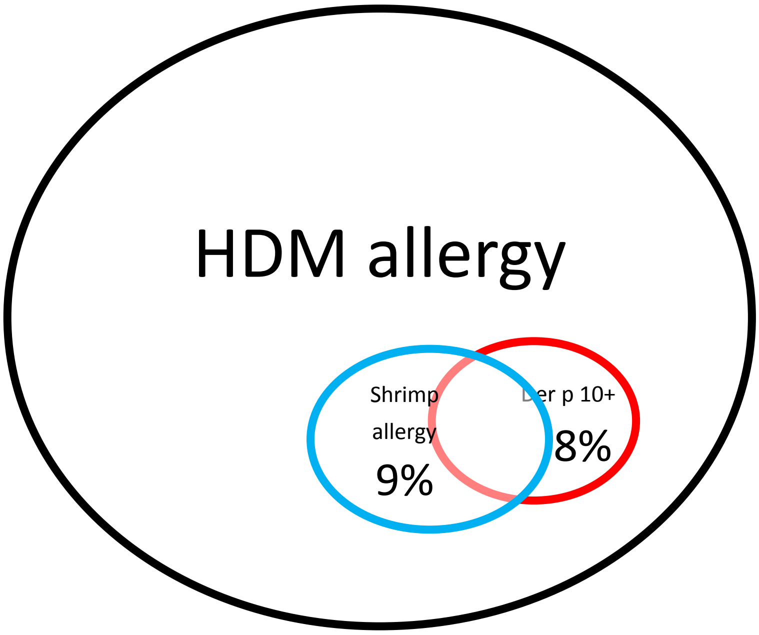
Legend to Table 1: House dust mite allergens. Shared allergens between house dust mite and Official shrimp are highlighted.

Legend to Figure 1: Venn diagram showing the prevalence and serological features of shrimp allergy among 526 HDM-allergic patients

Allergen	Biochemical name	MW	Allergen
Dermatophagoides farinae			*Dermatophagoides pteronyssinus*
Der f 1	Cysteine protease	27	Der p 1
Der f 2	NPC2 family	15	Der p 2
Der f 3	Trypsin	29	Der p 3
Der f 4	alpha-amylase	58	Der p 4
			Der p 5
Der f 6	Chymotrypsin	25	Der p 6
Der f 7	Bactericidal permeability-increasing like protein	30	Der p 7
Der f 8	Glutathione S-transferase	32	Der p 8
	Collagenolytic serine protease	29	Der p 9
Der f 10	Tropomyosin	37	Der p 10
Der f 11	Paramyosin	98	Der p 11
Der f 13	Fatty acid binding protein		Der p 13
Der f 14	Apolipophorin	177	Der p 14
Der f 15	Chitinase	98	Der p 15
Der f 16	Gelsolin/villin	53	
Der f 17	Calcium binding protein	53	
Der f 18	Chitin-binding protein	60	Der p 18
Der f 20	Arginine kinase	40	Der p 20
Der f 21		14	Der p 21
Der f 22			
Der f 23	Peritrophin-like protein	19	Der p 23
Der f 24	Ubiquinol-cytochrome c reductase binding protein homologue	13	Der p 24
Der f 25	Triosephosphate isomerase	34	
Der f 26	Myosin alkali light chain	18	
Der f 27	Serpin	48	
Der f 28	Heat Shock Protein	70	
Der f 29	Peptidyl-prolyl cis-trans isomerase (cyclophilin)	16	
Der f 30	Ferritin	16	
Der f 31	Cofilin	15	
Der f 32	Secreted inorganic pyrophosphatase	35	
Der f 33	alpha-tubulin	52	
Der f 34	enamine/imine deaminase	16	
Der f 35		14	
Der f 36		23	Der p 36
	Petrotrophic like protein domain	30	Der p 37


HDM allergy
Shrimp
allergy
9%
Der p 10+
8%