JCRMHS

Case report

Journal of Clinical Case Reports, Medical Images and Health Sciences

Volume 5 Issue 4, 2023

Article Information

Received date: 29/07/2023

Published date: 31/08/2023

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*Key Words:

Sublingual allergen immunotherapy, children, Pollens.

Sublingual Allergen Immunotherapy in a Child Sensitized to Pollens Responder and nonresponder in one – Case Report

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Introduction

Allergen immunotherapy is a well-established way of treatment in children with allergic rhinitis (AR). The therapy is the only method of changing the natural course of the disease and may prevent new sensitizations (1) (2). Unfortunately, it is not possible to achieve this effect in all allergic patients. To implement the treatment, the following conditions have to occur: no contraindications, good cooperation with patient/parents, correct diagnosis of AR, and access to a specific allergen for immunotherapy (3). Finding the specific allergen which causes allergic symptoms is not easy in some patients, moreover, typical allergy tests, like specific IgE serum measurements or skin prick tests, are not always sufficient (4). Another problem is the similarity of some allergens of different origins, e.g. plant families, with high homology in the primary structure of the proteins or carbohydrates leading to IgE cross-reactivity (5), therefore, molecular diagnostics is often necessary and currently available. Finally, a positive result of a specific IgE measurement or skin prick test does not always mean that a patient is allergic to the tested substance (6) (7). For verification purposes, we sometimes have to perform allergen provocation challenges on our patients (8).

To highlight the problem of the proper allergen selection for allergy immunotherapy we present the history of long-term diagnostics and immunotherapy in a child with AR and asthma.

We report a 14-year-old boy, one of the monozygotic twins of healthy parents. He was healthy up to the 4th year of his life. Then, in the spring of 2013, he developed mild ocular allergy symptoms which did not require medical treatment. In July 2013 skin prick tests with common allergens showed positive results for grain and dog. Because of mild symptoms, the young age of the boy, and incompatibility between the symptoms and the test results (he had no contact with pets), we decided to refrain from pharmacological treatment.

In 2014 symptoms occurred in April, with moderate ocular problems, sneezing, and stuffy and runny nose. He received desloratadine and nasal mometasone. In June, the effect was unsatisfactory, and we decided to add montelukast to achieve a good effect.

After the pollen season, we performed diagnostic tests again. We found serum sIgE (kU/l): birch 3.60, hazel 0.73, alder 0.58, grass 62.00, rye 6.20, and positive skin prick tests to trees, grass, and weeds (Table. 1)

In the Polish climate, April is the peak time of birch pollen season and June is the peak time of grass pollen season. Due to the obtained results, we decided to initiate allergen immunotherapy to grass before the next season, i.e. in February 2015. Grass pollen seemed to be a better choice as the first

DOI: 10.55920/JCRMHS.2023.05.001224

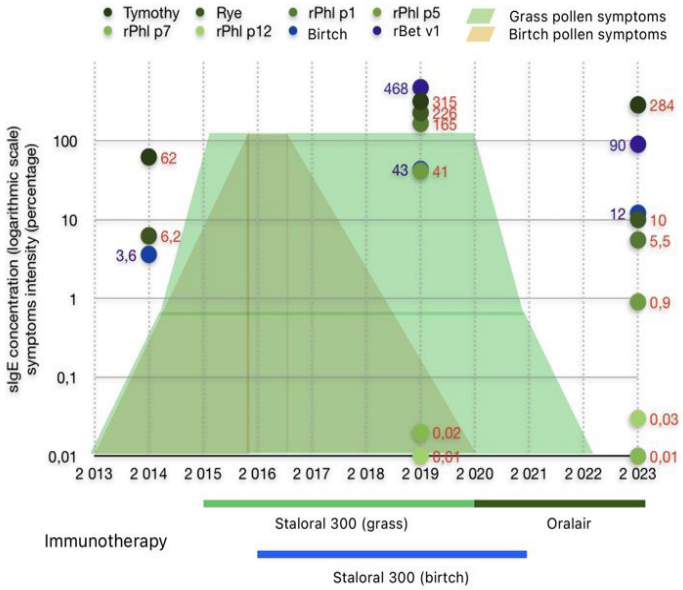

Figure 1: *The dynamics of changes in the severity of the symptoms and the need for pharmacological and immunological treatment during the last eight years.*

Table 1: *Results of the analysis performed in October 2014.*

Specific IgE serum concentrations (inhalant allergen panel, Polycheck®, Germany) kU/l	
Birch pollen	**3.60**
Hazel pollen	**0.73**
Alder pollen	**0.58**
Oak pollen	<0.15
Grass pollen	**62.00**
Rye pollen	**6.20**
Plantain pollen	<0.15
Artemisia pollen	<0.15
Dermatophagoides pteronyssinus	<0.15
Dermatophagoides farinae	<0.15
Dog dander	0.24
Cat dander	<0.15
Aspergillus fumigatus	<0.15
Alternaria tenuis	<0.15
Penicillium notatum	<0.15
Cladosporium herbarum	<0.15
Skin prick tests (Allergopharma reagents) wheel diameter in mm	
Positive control	**3**
Negative control	0
Dermatophagoides pteronyssinus	0
Dermatophagoides farinae	0
Tree I (Alder, Hazel, Populus, Elm, Willow)	**4**
Tree II (Birch, Oak, Beech, Plane)	**4**
Grass-rye	**6**
Grass	**4**
Weeds	**3**
Aspergillus fumigatus	0
Other analysis	
Total IgE serum concentration	**200** IU/l
Blood eosinophilia	3%

Table 2: *Results of the analysis performed in October 2019.*

Specific IgE serum concentrations kU/l (inhalant allergen panel, Polycheck®, Germany)	
Birch pollen	**43.00**
Hazel pollen	**3.30**
Alder pollen	**5.90**
Oak pollen	**4.60**
Grass pollen	**315.00**
Rye pollen	**226.00**
Plantain pollen	**2.20**
Artemisia pollen	**2.90**
Dermatophagoides pteronyssinus	0.10
Dermatophagoides farinae	0.16
Dog dander	0.28
Cat dander	0.16
Aspergillus fumigatus	0.02
Alternaria tenuis	0.00
Penicillium notatum	0.00
Cladosporium herbarum	0.01
Molecular diagnostics - Specific IgE serum concentrations kU/l (rec-pollen panel, Polycheck®, Germany)	
Birch	**65.00**
Bet v1	**468.00**
Bet v2	0.07
Tymothy-grass	**428.00**
rPhl p1	**165.00**
rPhl p5	**41.00**
rPhl p7	0.02
rPhl p12	0.00
Skin prick tests (Allergopharma reagents) wheel diameter in mm	
Positive control	**5**
Negative control	0
Dermatophagoides pteronyssinus	0
Alternaria tenuis	3
Aspergillus fumigatus	0
Dog dander	3
Cat dander	0
Tree I (Alder, Hazel, Populus, Elm, Willow)	**10**
Birch	**10**
Grass pollen	**7**
Plantain pollen	**5**
Other analysis	
Total IgE serum concentration	**1273 UI/l**
Blood eosinophilia	**6%**
Vitamin D serum concentration	33 ng/ml
Forced Oscylations Technique (Resmon pro)	no ventilation disturbances
Nitric oxide in exhaled air (Medisoft)	13 ppb

allergen since the clinical symptoms were more intensive in June than in April.

The boy received Staloral 300® 762 5 grass/rye (Stallergenes) sublingual drops. At the end of February and at the beginning of March, the boy required budesonide nebulization (Pulmicort 0.25mg/ml twice a day) because of dry cough and breathing difficulties, with a good effect. We had to introduce the same, as a year before, intensive treatment during June. The clinical picture and treatment were similar in 2016 - with asthma symptoms in March and

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Table 3: *Results of the nasal fluid analysis performed in October 2019.*

Molecular diagnostics - Specific IgE nasal fluid concentrations kU/l (rec-pollen panel, Polycheck®, Germany)	
Birch	**0.50**
Bet v1	**1.70**
Bet v2	0.01
Tymothy-grass	**1.40**
rPhl p1	**0.93**
rPhl p5	0.01
rPhl p7	0.00
rPhl p12	0.01

allergic rhinitis symptoms in June.

Following the pollen season, we decided to add birch pollen immunotherapy - Staloral 300® 615 birch 100% (Stallergenes) sublingual drops and applied it from December 2016 to May 2017 with no complications. We decided to change the allergen composition because of the poor effect of the implemented immunotherapy during the grass pollen season. The boy got Staloral 300® 688 5 grass 100% (Stallergenes) sublingual drops along with birch immunotherapy.

The clinical picture of the boy in spring 2017 and 2018 was better. We observed only mild ocular symptoms in April. Spring 2019 was free of symptoms, however, during all these three seasons we had to introduce the same intensive treatment during June.

Because of the poor effect of the grass pollen immunotherapy, the boy had to undergo diagnostic sensitization tests once again in October 2019. Molecular diagnostics was then available. We found serum sIgE to grass pollen and its chosen proteins (Table. 2)

We performed nasal lavage sIgE measurement and we found nasal sIgE concentrations corresponding to the observed in serum (Table. 3)

The results confirmed the properness of the allergens chosen for immunotherapy. The results of the birch pollen allergy treatment were excellent, so we decided to continue the same treatment in the two following seasons. The effects of the treatment of grass pollen allergy were disappointing, so we decided to change the allergen vaccine again. The boy was administered Oralair® 688 5 grass 100% (Stallergens) sublingual tablets from March 5 to the end of August 2020. The spring of 2020 was without any symptoms. There were only mild ocular symptoms treated with olopatadine eye drops in June. Because of better results achieved during the grass pollen season this year, we decided to continue therapy with Oralair for the next three years. Since 2022

Table 4: *Results of the analysis performed on March 2023.*

Specific IgE serum concentrations kU/l (inhalant allergen panel, Polycheck®, Germany)	
Birch pollen	**15**
Hazel pollen	**0.38**
Alder pollen	**0.96**
Oak pollen	**0.39**
Grass pollen	**>100.00**
Rye pollen	**10**
Plantain pollen	<0.15
Artemisia pollen	**0.44**
Dermatophagoides pteronyssinus	<0.15
Dermatophagoides farinae	**0.83**
Dog dander	**3.8**
Cat dander	**0.42**
Aspergillus fumigatus	<0.15
Alternaria tenuis	<0.15
Penicillium notatum	<0.15
Cladosporium herbarum	<0.15
Molecular diagnostics - Specific IgE serum concentrations kU/l (rec-pollen panel, Polycheck®, Germany)	
Birch	**12**
Bet v1	**90**
Bet v2	0.05
Tymothy-grass	**284**
rPhl p1	**5.5**
rPhl p5	**0.9**
rPhl p7	0.01
rPhl p12	0.03
Skin prick tests (Allergopharma reagents) wheel diameter in mm	
Positive control	**5**
Negative control	0
Dermatophagoides pteronyssinus	**3**
Aspergillus fumigatus	0
Dog dander	**4**
Cat dander	0
Tree I (Alder, Hazel, Populus, Elm, Willow)	**5**
Birch	**10**
Grass pollen	**7**
Plantain pollen	**3**
Other analysis	
Total IgE serum concentration	**186.2 UI/l**
Blood eosinophilia	**6%**
Vitamin D serum concentration	12.8 ng/ml
Forced Oscylations Technique (Resmon pro)	no ventilation disturbances
Molecular diagnostics - Specific IgE nasal fluid concentrations kU/l (rec-pollen panel, Polycheck®, Germany)	
Birch	0.19
Bet v1	**0.13**
Bet v2	0.12
Tymothy-grass	0.13
rPhl p1	0.02
rPhl p5	0.01
rPhl p7	0.03
rPhl p12	0.03

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the boy is free of symptoms. The allergy diagnostics were performed once again in March 2023 (Table. 4)

It is difficult to explain the low efficacy of grass pollen treatment, however, most probably, it resulted from the unstandardized allergen extract composition. The number and composition of proteins in the available allergen vaccines are not known, which leads to the random effectiveness of allergens chosen for immunotherapy. Therefore, it is difficult to match adequate allergen proteins to an individual patient's sensitizations, moreover, proper allergic protein compositions can be insufficient if the patient's immune system cannot recognize different epitopes on the proper allergen (9). Over time, there has been incremental improvement in AR symptoms observed in the boy as a result of the grass pollen immunotherapy, which proves that each of the consecutive allergen vaccines matched the boy's allergy better, giving more satisfactory results.

Conclusion

This case shows the need for improvement in allergen extract composition for immunotherapy to offer a much wider panel of commercial vaccines.

Statement of contribution by each author

Marek Mikolajczyk - substantial contributions to the conception of the work, the acquisition, analysis, and interpretation of data for the work, and drafting the work and revising it critically for important intellectual content, and final approval of the version to be published, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Zbigniew Baj - substantial contributions to the conception and design of the work, and drafting the work and revising it critically for important intellectual content, and final approval of the version to be published, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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