
Case report

Recurrence of allergic rhinitis, previously alleviated with allergen immunotherapy, after autologous bone marrow transplant

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Background: Several associations between immunoglobulin E and bone marrow transplantation (BMT) have been reported.

Objective: A patient whose allergic rhinitis (AR) resolved after allergen immunotherapy (AIT) but recurred after the patient received an autologous BMT is reported.

Methods: Allergy skin tests were performed before AIT began and after 4 years of therapy. Skin tests were repeated after a recurrence of symptoms 6 years later after an autologous BMT for breast cancer.

Results: Six years of AIT led to a near complete resolution of AR symptoms. Skin tests showed a marked reduction in reactivity to allergens in the AIT. After an additional 6-year symptom-free interval off AIT, symptoms returned after the BMT. Repeat skin tests showed a marked increase in reactivity.

Conclusions: Patients reconstituting their immune systems after autologous BMT may have a recurrence of AR previously suppressed with AIT.

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INTRODUCTION

Several associations between immunoglobulin E (IgE) and bone marrow transplantation (BMT) have been reported. Most BMT recipients have a transient increase in total serum IgE.^{1–5} In addition, specific allergies have been transferred from donor to recipient,^{6–11} and other specific allergies have resolved after receiving a BMT.¹² Reported here is a patient whose allergic rhinitis resolved after allergen immunotherapy (AIT), but recurred after she received an autologous BMT.

CASE REPORT

A 38-year-old woman reported that she had allergic rhinitis symptoms consisting of rhinorrhea, nasal congestion, watery eyes, and itching of nose, eyes, ears, and palate since childhood. Allergy skin testing in late 1986 (age 26) revealed large positive reactions to numerous pollens and to cat and dust mites (Table 1). She was treated with AIT for 6 years, from early 1987 to 1992 (age 26 to 31). These allergy shots contained extracts of several grasses (Bahia, Bermuda, John-

son, orchard, rye, and timothy), trees (birch, elm, hickory, maple, oak, pecan, and poplar), weeds (English plantain and ragweed), *Alternaria* and house dust mites. She had so thorough a resolution of her symptoms that she no longer required any medication. Subsequent skin testing in 1991, after 4 years and 4 months of AIT, revealed marked decreases in skin test reactivity, with most of the specific extracts in the allergy shots now giving negative skin test results (Table 1). She remained symptom free from 1992 to 1998 (age 32 to 38). In 1998, she was diagnosed with breast cancer and, after pre-treatment conditioning with chemotherapy and radiation, underwent an autologous BMT. Several months later, her allergic rhinitis symptoms returned to a level that she described as comparable with that before receiving allergy shots. Repeat skin test results (in 1999) showed markedly positive reactions to pollens and cat and dust mite (Table 1).

DISCUSSION

As many as 95% of BMT recipients have a sharp but transient increase in total serum IgE levels.^{1–5} The rise typically begins approximately 2 weeks after transplant, peaks at approximately 30 days, and returns to normal by approximately 60 days.^{1–5} The phenomenon is seen with both allogeneic^{1–4} and autologous⁵ BMT. The IgE peak can be temporally associated with acute graft-versus-host disease, but it also occurs in the absence of this complication.^{1–4} Some authors have suggested that the IgE peak is the result of the conditioning treatment of chemotherapy and irradiation that most BMT recipients receive before transplant.⁴ However, it can also be seen in patients with severe combined immune deficiency who re-

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Table 1. Skin test results before allergen immunotherapy (12/17/86), after allergen immunotherapy (4/15/91), and after bone marrow transplant (4/26/99)

	12/17/86	4/15/91	4/26/99
GRASSES			
<i>Bahia</i>	4+	0	3/25
<i>Bermuda</i>	4+	0	5/40
Bluegrass, Kentucky			0
<i>Johnson</i>	4+	0	4/25
<i>Orchard</i>	4+		
<i>Rye, perennial</i>	4+	0	5/15
<i>Timothy</i>	4+	0	12/30
TREES			
Ash		2+	5/35
Bayberry		0	
Beech		0	3/10
<i>Birch</i>	4+		0
Box elder		0	
Cedar		0	0
Cottonwood		0	9/40
Cypress		0	
<i>Elm</i>	4+	0	0
Eucalyptus			7/30
Hackberry		1+	
<i>Hickory</i>	4+	0	
<i>Maple</i>	4+	0	5/10
Mesquite			4/10
Mulberry			6/15
<i>Oak</i>	4+	0	11/50
Olive tree			10/42
<i>Pecan tree</i>	4+	0	3/31
<i>Poplar</i>	4+		
Sycamore		3+	11/45
Walnut tree			9/11
WEEDS			
Cocklebur	0	0	
Dock		0	5/11
Kochia		0	6/38
Lambs quarter		0	7/45
Marshelder			0
Pigweed		0	9/50
<i>Plantain, English</i>	4+	0	4/32
<i>Ragweed</i>	4+	0	3/20
Russian thistle		0	11/35
Sage			4/35
Wingscale			6/41
MOLDS			
<i>Alternaria</i>	0	0	0
<i>Aspergillus</i>	0	0	0
<i>Chaetomium</i>	0		
<i>Cladosporium</i>			0
<i>Curvularia</i>	0	0	0
<i>Epicoccum</i>	0		0
<i>Fusarium</i>	0	0	
<i>Helminthosporium</i>	0	0	0
<i>Hormodendrum</i>	0	0	
<i>Mucor</i>		0	0
<i>Penicillium</i>	0	0	0
<i>Phoma</i>	0	0	
<i>Pullularia</i>	0	0	
<i>Rhizopus</i>		0	
HOUSEHOLD			
Cat	4+	4+	5/16
Cockroach	0	1+	3/4
Dog	0	4+	0
<i>Dust mite (Der f)</i>	4+	3+	4/30
<i>Dust mite (Der p)</i>	4+	4+	12/60
CONTROLS			
+	4+	4+	4/50
-	0	0	0

Allergen extracts shown in bold italics were included in allergen immunotherapy from 1987 to 1992. Skin test results from 1986 and 1991 were recorded on a scale of 0 to 4+ without further details. Skin tests from 1999 were recorded in mm wheal/mm erythema.

ceived BMT without pretransplant conditioning.³ The IgE peak may be related to a temporary imbalance in regulatory T cells in the period after BMT¹⁻⁵ and is probably of recipient origin.^{3,4}

Several reports have also detailed the apparent transfer of IgE-mediated allergy from bone marrow donor to recipient.⁶⁻¹¹ These cases involve recipients developing immediate-type skin test or IgE-antibody patterns that are similar to those of their donors.⁶⁻¹¹ Many of the recipients developed not only a similar pattern of sensitization to that of their donors, but the recipients also developed similar clinical allergic disease, including allergic rhinitis,^{9,10} asthma,¹⁰ atopic dermatitis,^{7,11} and food⁷ and drug allergies.^{7,9} This transferred sensitization is seen as early as 30 days after BMT but, unlike the transient peak in total IgE, it persists.¹⁰

Another intriguing phenomenon after BMT is the cure of allergy in the recipient.^{10,12} Some aeroallergen skin tests that were positive in recipients became negative after BMT from skin test-negative donors.¹⁰ Similarly, in a child with an anaphylactic sensitivity to latex, a class 6 positive CAP-radioallergosorbent test (Pharmacia, Peapack, NJ) to latex became negative after BMT.¹²

The patient presented here seems to demonstrate yet another association between BMT and allergy. She had classic allergic rhinitis symptoms and markedly positive skin tests before undergoing AIT. With AIT, she had a marked reduction in her symptoms and skin test reactivity. As is often the case,¹³ she remained symptom-free for several years after stopping AIT. However, she had a dramatic recurrence of her allergic rhinitis symptoms within months of an autologous BMT. Although it is certainly possible that she had a spontaneous recurrence of her allergic rhinitis, the timing of the recurrence suggests a relationship to the BMT. Her skin test reactions had again become positive in a pattern remarkably similar to her pre-AIT testing. She thus appears to have redeveloped the same allergies she had previously, as a result of the BMT. Whatever immunologic changes resulted in the decrease in allergic rhinitis symptoms and skin test reactivity with AIT seem to have been undone by the BMT. Atopy is felt to be related to a T helper cell 1 (TH1) to T helper cell 2 (TH2) ratio of cytokines favoring TH2.¹⁴ AIT seems to work in part by shifting this cytokine ratio toward TH1.¹⁵ There is evidence that early in life, the default pattern is TH2, and that normal development of the immune system in most people then shifts toward a TH1 pattern.¹⁶ There is also evidence that the reconstitution of the immune system after BMT may also favor a TH2 pattern.¹⁷ This patient may have reconstituted her immune system in a TH2 pattern that has allowed her atopic tendency, previously altered by AIT, to again result in positive skin test reactions and clinical allergy.

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