

A Bad Reaction: A Case Study in Immunology

by

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Part I

You have been awarded a grant in the amount of \$1200. Your research team is to use this grant to cover the costs of examining the case histories of three patients. Your goal is to make a diagnosis from these records and design a testable experiment that can be used to obtain future funding. You will not be given much time to examine the three patient histories, so be prepared to take notes and record as much information as you can in the time allowed.

Diagnosis

Your team must deliver:

- A diagnosis for Patient #1 and the major pieces of evidence that you used.
- A diagnosis for Patient #2 and the major pieces of evidence that you used.
- An explanation for why Patient #3 appears normal. What are the major pieces of evidence that you used to account for this?

Each patient record contains a reference number. When recording a piece of evidence to back up your diagnosis of a patient, you must reference the record number that you used to obtain that piece of evidence.

Experiment Proposal

Your team must also produce:

- A testable hypothesis to back up your diagnosis of the three patients.
- A description of an experiment that can be performed to test your hypothesis.

Contents and Costs of Records

Individual records cost \$200.00. This is what is available for each patient:

- Medical History—information on lifestyle, surgeries, allergies, and past medical problems.
- Interview transcripts—transcripts taken from interviews with the patients after being admitted to the hospital.
- Vitals and tests—Blood pressure, heart rate, blood counts (CBC), blood gases and results from any tests that were run.
- Organ assesment—assesments of kidney, liver, and pancreatic function.

You have been provided with a sheet that describes the contents of each of the records. Your grant provides you with enough money to purchase six of the 12 records that are available for these three patients.

Evaluation Criteria

The performance of your group will be evaluated on the following criteria:

- Your diagnosis for the three patients and the value of the evidence that you have used.
- Your proposal for your experiment.
- Residual grant funds (spending less money gives you a higher score).

Time Limitations

- All information should be recorded on the data sheets provided.
 - Your applications are due at [TIME].
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Part II

Transfer of symptomatic peanut allergy to the recipient of a combined liver and kidney transplant

(Instructor's name), Director of Grants and Research at (Hospital name), would like to acknowledge Dr. Christophe Legendre and his team of doctors for their work on identifying the causative agent of a symptomatic peanut allergy acquired by a 35-year-old male recipient of a combined liver-and-kidney transplant. The following report summarizes their work on this case.



A. Introduction

Peanuts are one of the most common causes of food allergy in the United States and Europe. They are also a leading cause of food-induced anaphylaxis and death, which usually follow inadvertent exposures. Allergy to peanuts is an IgE-mediated, mast-cell-dependent, immediate-hypersensitivity reaction. There are numerous reports of the transfer of allergen-specific IgE-mediated hypersensitivity by bone marrow transplantation. We report a case of peanut allergy transmitted through combined liver-and-kidney transplantation.

Questions

- A1. What is the difference between an “allergen” and an “antigen”?
- A2. What is meant by “anaphylaxis”?
- A3. What are the different classes of antibodies that our bodies produce? Which class is associated with the peanut allergy?
- A4. What is a mast cell? What role do mast cells play in the immune response?
- A5. Hypersensitivities can be described as immediate, subacute, or delayed. How do these sensitivities differ? What evidence did the doctors use to determine that the peanut allergy was an immediate hypersensitivity?

B. Case Presentations

A 22-year-old man with a history of allergic reactions to peanuts was admitted to our hospital in a coma. After inadvertently ingesting satay sauce, which contains peanuts, during a Chinese meal, he had become unwell and had had a cardiorespiratory arrest that resulted in cerebral anoxia, coma, and brain death. A high level of peanut-specific IgE was detected in his serum ... multiple organs were subsequently procured. The donor's HLA phenotype was A1,24;B8,44;DRB1*03,13.

...the donor's liver and right kidney were given in transplantation to a 35-year-old man, and the left kidney and pancreas were given to a 27-year-old woman. The man (HLA phenotype, A2,19;B12,-;DRB1*07,13) had end-stage renal failure.... The woman (HLA phenotype, A1,24;B8,44;DRB1*03,04) had chronic renal failure....

Both transplant recipients received immunosuppressive induction therapy with muromonab-CD3 (OKT3) and corticosteroids, azathioprine, and cyclosporine. Neither had ever had any allergy to peanuts.

Three months after transplantation, the recipient of the liver-kidney transplant reported a skin rash and laryngeal dyspnea after eating peanuts. Allergy to peanuts was diagnosed on the basis of the clinical findings; the absence of specific IgE antibodies before transplantation, their presence at the time the symptoms appeared, and their decline thereafter; and a positive basophil degranulation test.

Questions

- B1. What does HLA stand for? What is an HLA phenotype?

- B2. How does HLA relate to MHC in immune physiology?
- B3. Why is it important to understand the “HLA phenotypes” of the individuals in this case?
- B4. From what you know about the structure of an antibody, explain how an IgE can be “peanut-specific.”
- B5. One way to test for an allergy is to mix a specific allergen with basophils and mast cells from a patient and look for “degranulation.” What is occurring when these cells degranulate? How does this become a positive test for a specific allergy?
- B6. Why were the patients put on an immunosuppressive therapy after their transplantations?

C. Discussion

The transfer of allergen-specific donor lymphocytes is a likely possibility.... The production of IgE by B cells depends on the presentation of allergens by antigen-presenting cells and on cooperation between B cells and regulatory T-helper lymphocytes of the Th2 type. In our patient there may have been transfer of peanut-specific IgE-producing B cells or of peanut-specific Th2 lymphocytes that induced the recipient’s B cells to produce peanut-specific IgE.

Questions

- C1. Briefly describe the role of B cells and T-helper lymphocytes in immune physiology.
- C2. What is an “antigen-presenting cell” and what role does this type of cell play in an immune response?
- C3. Explain the interaction that occurs between a T-helper lymphocyte and a B cell when the B cell is being induced to produce peanut-specific IgE. In your explanation, explain the role that the peanut allergen plays in this interaction.
- C4. In immediate hypersensitivity, the initial exposure to an allergen usually does not produce any symptoms. The symptoms, such as those involved in anaphylaxis, usually appear in the second exposure. What events are occurring during this initial exposure that sensitizes a person to an allergen. In your description include the role of B cells, T cells, IgE, mast cells, basophils and the allergen.

Passive transfer of donor IgE is unlikely, because the half-life of IgE is only a few days, whereas the allergic reaction occurred three months after transplantation. However, we cannot rule out the possibility that donor IgE bound to the recipient’s mast cells and basophils could have persisted for more than a few days.

Questions

- C5. Describe how IgE binds and reacts with basophils and mast cells.
- C6. As described in question C4, the initial exposure to an allergen usually does not produce any symptoms. The symptoms usually appear in the second exposure. What events are occurring during this second exposure? In your description include the role of IgE, basophils, mast cells, and the allergen.

It is relevant that the allergy was transferred from the liver-kidney transplant, but not from the pancreas-kidney transplant. Pluripotent hematopoietic stem cells and dendritic cells are known to be normally resident in the liver. These passenger cells can migrate from the graft to the recipient’s lymphoid organs, and multilineage hematopoiesis derived from donor cells can persist for several months after liver grafting.

Questions

- C7. Describe the normal physiological role of a “pluripotent hematopoietic stem cell” in human physiology.
- C8. What is happening when the cells you described in C7 undergo “hematopoiesis?”
- C9. Why is it important to note the presence of these cells in the liver when trying to understand the mechanism for how the peanut allergy was transferred to the patient?
- C10. In the introduction, the doctors noted well-documented transfers of allergies when bone marrow was being transplanted. Why is this a common occurrence with this type of transplant?

D. Revisiting Patient Records

You have been supplied with the records of all three patients involved in this case. In order to confirm the conclusions of Dr. Christophe Legendre and his group, we will revisit the medical records of these patients to explore evidence in support of their claims.

Questions

Alexander Kolineski, 22-year-old male organ donor.

- D1. Review the records for Mr. Kolineski and summarize the evidence to suggest that death was caused by anaphylaxis.
- D2. Without reviewing the records from the other patients, can you positively identify the causative agent for this patient's anaphylaxis? Why or why not?

Jonathan Forken, 35-year-old male recipient of a liver and right kidney from Mr. Kolineski.

- D3. Review the records for Mr. Forken and summarize the evidence to suggest that Mr. Forken was having a peanut-specific hypersensitivity reaction.

Melissa Jachowiz, 27-year-old female recipient of a pancreas and left kidney from Mr. Kolineski.

- D4. Review the records of Mrs. Jachowiz and summarize the evidence to support the fact that she did not obtain a peanut-specific hypersensitivity from her transplant.

Internet Resources

eAllergy.net—A division of Allergy Services Inc. [An extensive collection of allergy resources (best viewed with Internet Explorer).] <http://www.eallergy.net/>

AtAllergy.com [A resource for understanding allergies; contains a searchable database of articles.] <http://www.atallergy.com/allergy/>

Food Allergy, Mayo Clinic

<http://www.mayoclinic.com/health/food-allergy/DS00082>

AAAAI Patient/Public Resource Center-Tips to Remember: Food Allergy

<http://www.aaaai.org/patients/publicedmat/tips/foodallergy.stm>

Anaphylaxis

<http://health.yahoo.net/channel/anaphylaxis.html>

Anaphylaxis: MedlinePlus, National Library of Medicine

<http://www.nlm.nih.gov/medlineplus/ency/article/000844.htm>

Understanding the Immune System, National Institute of Allergy and Infectious Disease

<http://www.niaid.nih.gov/topics/immunesystem/pages/default.aspx>

Clinical Diagnostic for the Determination of Allergen Induced Basophil Degranulation

http://www.glycotope-bt.com/en/products/diagnostics/basotest_description.php



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