

DQB1*0303-DPB1*0501 haplotype who are exposed to MDI have a higher probability of developing serum specific IgG to MDI, which could lead to a greater risk of MDI-OA.

This study is the first, to our knowledge, to examine genetic susceptibility in MDI-OA using HLA analysis. We suggest that the HLA allele DRB1*0901-DQB1*0303-DPB1*0501 may increase specific IgG sensitization, which could contribute to the development of the MDI-OA phenotype in exposed workers.

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1. Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, eds. *Asthma in the Workplace*. 3rd ed. New York, NY: Taylor & Francis; 2006.
2. Chan-Yeung M, Malo JL. Aetiological agents in occupational asthma. *Eur Respir J*. 1994;7:346–371.
3. Mapp CE, Balboni A, Baricordi R, Fabbri LM. Human leukocyte antigen associations in occupational asthma induced by isocyanates. *Am J Respir Crit Care Med*. 1997;156:S139–S143.
4. Bignon JS, Aron Y, Ju LY, et al. HLA class II alleles in isocyanate-induced asthma. *Am J Respir Crit Care Med*. 1994;149:71–75.
5. Fabbri LM, Mapp CE, Balboni A, Baricordi R. HLA class II molecules and asthma induced by toluene diisocyanate. *Int Arch Allergy Immunol*. 1995;107:400–401.
6. Kim SH, Oh HB, Lee KW, et al. HLA DRB1*15-DPB1*05 haplotype: a susceptible gene marker for isocyanate-induced occupational asthma? *Allergy*. 2006;61:891–894.
7. Balboni A, Baricordi OR, Fabbri LM, Gandini E, Ciaccia A, Mapp CE. Association between toluene diisocyanate-induced asthma and DQB1 markers: a possible role for aspartic acid at position 57. *Eur Respir J*. 1996;9:207–210.
8. Hur GY, Koh DH, Choi GS, et al. Clinical and immunologic findings of methylene diphenyl diisocyanate-induced occupational asthma in a car upholstery factory. *Clin Exp Allergy*. 2008;38:586–593.

MAST CELL DISEASES AND THE SEVERITY AND COURSE OF INTRAOPERATIVE ANAPHYLAXIS

It is well known that certain drugs may induce severe and fatal intraoperative anaphylactic reactions in patients with mast cell diseases.^{1–3} Identifying these disorders is crucial for intraoperative patient management. According to some studies, medication seems to be the second cause of biphasic reactions. Unlike other risk factors for biphasic reactions (that include more rapid onset of anaphylaxis delayed use of epinephrine, low doses of epinephrine, etc), mast cell diseases have never been studied as such.⁴ We describe 2 patients with intraoperative anaphylaxis who were diagnosed postoperatively as having mastocytosis.

A 70-year-old woman was seen for a preoperative evaluation for malignant colon cancer. The patient had a history of polypharmacologic intolerance with pruritus caused by cyclooxygenase-1 inhibitors, cutaneous rash from an unspecified local anesthetic, and an episode of severe intraoperative anaphylaxis in 1983. Because her medical records were unavailable, allergy testing was performed as per the guideline protocol^{5,6} for latex, mepivacaine, marcaine, lidocaine, suxamethonium, atracurium, cisatracurium, pancuronium, vecuronium, rocuronium, thiopentale, propofol, atropine, morphine, fentanyl, remifentanyl, chlorhexidine, polyvinylpyrrolidone, polygeline, major and minor antigenic determinants of penicillin, ampicillin, and piperacillin. All the results were negative. Two basal serum tryptase concentration measurements yielded 275 and 306 $\mu\text{g/L}$, respectively (reference range, $\leq 11.4 \mu\text{g/L}$). Objective examination of the patient showed a few skin lesions, which were fixed, red-brown, and hyperpigmented. Histopathologic examination of the skin biopsy sample confirmed the diagnosis of urticaria pigmentosa. The patient refused a bone marrow biopsy to evaluate the presence of indolent systemic mastocytosis. Although drug desensitization may occur across time or we may not have tested for the offending drug administered in 1983, the final diagnosis was “probable non-IgE-mediated intraoperative anaphylaxis in a patient with urticaria pigmentosa.” Although it is well known that mastocytosis can lead to the development of non-IgE-mediated severe intraoperative reactions, without standard guidelines for the intraoperative management of these patients, premedication consisted of antihistamines, corticosteroids, and disodium cromoglycate by means of nebulization and the oral route; stress-reducing anxiolytics were administered, and safer anesthetic drugs were used.^{7,8} No undesired intraoperative or postoperative reactions occurred.

A 57-year-old woman was seen for an allergologic evaluation after severe intraoperative biphasic anaphylaxis. The second reaction (urticaria and hypotension) was less severe than the first and occurred 14 hours after resolution of the first episode. The patient had no history of previous drug-related reactions or atopy and had never had general anesthesia. Her medical record stated that she was administered fentanyl, remifentanyl, propofol, rocuronium, ampicillin, and ketorolac. Allergy testing, following the guidelines,⁵ was performed for latex, atracurium, cisatracurium, pancuronium, vecuronium, rocuronium, suxamethonium thiopentale, propofol, atropine, fentanyl, remifentanyl, chlorhexidine, polyvinylpyrrolidone, and polygeline. All results were negative. Furthermore, CAP system results vs latex, suxamethonium, ethylene oxide, and polygeline were negative but vs penicilloyl G (1,410 U/mL), penicilloyl V (1,680 U/mL), amoxicillin (1,200 U/mL), and ampicillin (1,280 U/mL) were positive. The hypothesis was “IgE-mediated intraoperative anaphylaxis due to ampicillin.” However, basal serum tryptase concentrations in 2 determinations were 36.3 and 42.0 $\mu\text{g/L}$. Histopathologic examination of the skin biopsy sample was negative for urticaria pigmentosa, whereas a bone marrow biopsy confirmed the presence of indolent systemic mastocytosis. The final diagnosis was “IgE-mediated intraoperative biphasic anaphylaxis due to ampicillin in a patient with indolent systemic mastocytosis.”

In patients with severe intraoperative reactions, irrespective of the allergy test results, it is advisable to measure serum basal tryptase levels. In the presence of increased basal serum tryptase levels, patients should be evaluated for mast cell diseases. Such cases suggest that mast cell diseases could affect not only the severity of drug-induced anaphylaxis but also its course. Patients with mastocytosis should be informed of the risk factors involved and provided with medical alert identification describing their condition. In these

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patients, a pluridisciplinary approach to intraoperative care and management among anesthetists, surgeons, and allergists is vital. Multicenter studies should be organized to evaluate the frequency of mast cell diseases or elevated basal tryptase levels in patients with a history of severe drug-induced anaphylaxis, irrespective of the presence of specific IgE, and to confirm the hypothesis that these disorders or elevated basal serum tryptase concentrations may represent a new potential risk factor for the development of biphasic anaphylaxis.

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1. Vaughan ST, Jones GN. Systemic mastocytosis presenting as profound cardiovascular collapse during anaesthesia. *Anaesthesia*. 1998;53:804–807.
2. Damodar S, John CN, Gopalakrishnan G, et al. Mast cell disease: surgical and anesthetic implications. *J Pediatr Hematol Oncol*. 2006;28:446–449.
3. Müller UR, Haeberli G. The problem of anaphylaxis and mastocytosis. *Curr Allergy Asthma Rep*. 2009;9:64–70.
4. Tole JW, Lieberman P. Biphasic anaphylaxis: review of incidence, clinical predictors, and observation recommendations. *Immunol Allergy Clin North Am* 2007;27: 309–326.
5. Mertes PM, Laxenaire MC, Lienhart A, et al; Working Group for the SFAR; ENDA; EAACI Interest Group on Drug Hypersensitivity. Reducing the risk of anaphylaxis during anaesthesia: guidelines for clinical practice. *J Invest Allergol Clin Immunol*. 2005;15:91–101.
6. Torres MJ, Blanca M, Fernandez J, et al; ENDA; EAACI Interest Group on Drug Hypersensitivity. Diagnosis of immediate allergic reactions to β -lactam antibiotics. *Allergy*. 2003;58:961–972.
7. Borgeat A, Ruetsch YA. Anesthesia in a patient with malignant systemic mastocytosis using a total intravenous anesthetic technique. *Anesth Analg*. 1998;86: 442–444.
8. Villeneuve V, Kaufman I, Weeks S, Deschamps A. Anesthetic management of a labouring parturient with urticaria pigmentosa. *Can J Anaesth*. 2006;53:380–384.

HYPEREOSINOPHILIA: A CASE WITH AN ELUSIVE ETIOLOGY

A 48-year-old man residing in Iowa visited the emergency department with severe abdominal cramping, diarrhea, and an eosinophil count of 14,000/mm³. Results of extensive evaluation, including abdominal/pelvic computed tomography, a complete metabolic panel, urinalysis, human immunodeficiency virus testing, and hepatitis B/C screening, were negative. His total IgE level was normal at 94 IU/mL. A stool study for ova and parasites was negative. An echocardiogram did not reveal any abnormalities. A colonoscopy with biopsies revealed small scattered lymphoid aggregates with no

significant eosinophilia or parasites. Esophageal biopsy samples showed evidence of esophagitis and scattered intraepithelial lymphocytes with rare eosinophils. Duodenal biopsy samples were without evidence of organisms. A bone marrow biopsy sample had no evidence of FIP1L1-PDGFRA or JAK2 mutations but revealed hypercellular bone marrow with 13% eosinophils. Chest computed tomography revealed mediastinal lymphadenopathy, with the largest lymph node measuring 5 × 17 mm. A lymph node biopsy revealed benign sinus histiocytic hyperplasia. Treatment with prednisone, 40 mg daily for 2 months, normalized his eosinophil count, but abdominal cramping persisted. Eosinophilia (eosinophil count at this time, 2,158–4,454/mm³) rebounded after discontinuation of prednisone therapy. He was treated empirically for a parasitic infestation with mebendazole for 3 days, with partial improvement of his abdominal cramping. Hypereosinophilic syndrome was considered, and he was treated with imatinib, 100 mg daily for 5 weeks and then 400 mg daily for 8 weeks, without improvement of his eosinophilia. Eight months after his initial presentation, he was referred to us for further evaluation. A detailed history revealed that he had cut his hand while repairing a broken sewer line 1 week before the onset of his symptoms. Stool ova and parasite evaluation was repeated 3 times. All 3 samples were positive for *Strongyloides stercoralis*. He received ivermectin, 18 mg (0.2 mg/kg) daily for 5 days. A subsequent eosinophil count was normal 4 weeks after treatment. Results of repeated stool studies for ova and parasites were negative, and abdominal cramping completely resolved.

Worldwide, helminth infestations are the leading cause of eosinophilia. *Strongyloides* is found routinely in the tropics and subtropics and in certain areas of the United States, such as the southern Appalachian region, and an estimated 55 million to 100 million people are infected worldwide.¹ *Strongyloides* enters the body via the skin and then travels hematogenously to the lungs before migrating to the gastrointestinal tract.¹ The initial stool ova and parasite evaluation was performed once 2 weeks after the patient cut his hand while working on the sewer line. The rate of detection of *Strongyloides* larvae in 1 stool sample is 25% and would be a possible explanation for the initially negative stool sample result.^{1–3} In addition, parasite excretion is intermittent, and, thus, it is important to obtain a minimum of 3 stool samples at least 24 hours apart.⁴ Use of corticosteroids and other immunosuppressants can lead to life-threatening disseminated *Strongyloides* infestations.⁵ Thus, ruling out parasitic infestation is critical before initiation of treatment with corticosteroids or other immunomodulators.

This patient illustrates the importance of a detailed history in the workup of persistent eosinophilia. Evaluation for *Strongyloides* infestation should start with stool studies for ova and parasites. If clinical suspicion remains high in a setting of negative stool studies, *Strongyloides* IgG levels should be evaluated. If suspicion remains, an endoscopic evaluation with biopsy and aspirate samples of the duodenum can be considered.⁶

Treatment for strongyloidiasis is ivermectin, with several studies^{7,8} demonstrating its superiority compared with albendazole and thiabendazole. The dosing recommendation is 200 μ g/kg as 1 oral dose. If disseminated disease is a concern or the patient is immunosuppressed, it is usually necessary to prolong or repeat therapy.⁹

Klion et al¹⁰ proposed diagnostic and therapeutic algorithms for the evaluation of hypereosinophilic syndromes. Parasitic infestation can be an elusive diagnosis, and reevaluation may be necessary 4 to 6 weeks after the possible exposure. A detailed dissertation on the differential diagnosis of hypereosinophilia has recently been published.¹¹

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