
Letters

A NOVEL MUTATION ASSOCIATED WITH AUTOIMMUNE POLYENDOCRINOPATHY-CANDIDIASIS-ECTODERMAL DYSTROPHY

We report the case of a 5-year-old boy who presented with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) and on genetic analysis was determined to be a compound heterozygote for 2 disparate *AIRE* gene mutations: R257X and A58G. He was also a carrier for the perforin 1 (*PRF1*) gene mutation C272T. This is the first case study in the literature, to our knowledge, that suggests the possibility of the A58G mutation inducing APECED. It is also the first case, to our knowledge, of APECED in a carrier of hemophagocytic lymphohistiocytosis (HLH).

A 5-year-old boy of African American descent was diagnosed as having APECED because of a number of associated clinical presentations, which included hypoparathyroidism, hypocalcemia, oral thrush, and candidal onychomycosis. He tested positive for autoimmune hepatitis at 5 years of age based on liver biopsy results. The boy's sister had died at 7 months of age from HLH as presumed from a liver biopsy. All other family members were healthy, with no clinically significant findings or symptoms associated with either immunodeficiencies or autoimmune disease. The patient is currently being followed up, and no adrenal disorders have developed to date.

Genetic analysis was performed on the patient and his parents for known causes of APECED and HLH. The genes analyzed were *Munc* and *PRF1* because of the sibling's diagnosis of presumed HLH. *Munc* gene analysis revealed no mutations in the patient or parents. On examination of the *PRF1* gene, the father was determined to be a heterozygous carrier of the 272 C->T mutation. He had normal natural killer (NK) cell function and a normal proportion of NK cells expressing perforin; however, the level of perforin was reduced by 50% that of normal standards. The patient's mother was a carrier of a polymorphism (702 G->T) in the *PRF1* gene that did not result in a change in amino acid sequence. She had normal NK function and expression of perforin; however, a decreased number of NK cells (by 20% that of normal standards) expressed perforin. The patient displayed the same 272 variant as his father. He had normal NK cell function but reduced cytotoxic T-lymphocyte function (by 50% that of normal standards).

AIRE gene analysis of the father revealed a carrier for the R257X mutation (C->T mutation in exon 6). This variation results in a nonsense mutation by replacing the arginine codon (CGA) with a mutant stop codon (TGA) at amino acid 257. He had a normal sequence for the Ala58 codon in exon 2. *AIRE* gene analysis of the mother indicated that she is a carrier in exon 2 because of the replacement of the normal

alanine codon (GCC) with a mutant glycine codon (GCC) at amino acid position 58 (A58G). The significance of this variant is unknown. She did not express the R257X mutation. The patient displayed both the R257X and A58G mutations.

The A58G mutation has never been reported as being either a benign variant of the *AIRE* gene or associated with the pathophysiology of APECED. However, the significance of the change in codons from alanine to glycine on protein function is unknown. The pathology involved with this case of APECED would suggest that the A58G mutation causes dysfunction in the *AIRE* gene product.¹ Halonen et al² suggested that patients who have the R257X allele (both homozygotes and heterozygotes) experience a greater prevalence of Addison disease and candidiasis.

In addition to being a compound heterozygote for 2 different mutations in the *AIRE* gene, this patient is notable for also being a carrier for the C272T *PRF1* mutation. The significance of the possible combination of defects in the *AIRE* gene product and *PRF1* gene product is unknown, and this patient will be followed up carefully for any signs of HLH.³

In summary, to our knowledge, this is the first case study in the literature that demonstrates the possibility of the A58G mutation being associated with APECED.

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ADULT-ONSET PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS, AND ADENITIS

In the 1980s, the chronic clinical syndrome of periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) was defined. This condition presents in patients before the age of 5 years, with regularly recurring fever, aphthous stomatitis, cervical lymphadenitis, and/or pharyngitis, normal absolute neutrophil counts (ANCs), normal growth and development, and completely asymptomatic intervals between episodes.¹ Other than leukocytosis and an elevated erythrocyte sedimentation rate, the results of blood and imaging studies are normal.¹ Although PFAPA has been widely reported in children, we are not aware of any reports in adults. We describe a 21-year-old woman of European descent who was well until the age of 19 years, when she experienced pharyngitis, fatigue, and cervical adenopathy. After that primary episode, she developed headaches, fatigue, sore throat, cervical adenopathy, nausea, and temperatures of 38.3°C to 39.4°C, lasting 5 to 7 days, every 3 to 4 weeks, preceded by oral ulcers. Examinations when the patient was symptomatic were significant for aphthous stomatitis, cervical lymphadenopathy, and enlarged tonsils.

Differential diagnosis in this patient included familial Mediterranean fever, familial Hibernian fever and tumor necrosis factor α receptor-associated periodic fever syndrome, hyper-IgD syndrome, cyclic neutropenia, and immunodeficiency. Familial Mediterranean fever, characterized by recurrent fevers, peritonitis, and pleuritis, was ruled out by mutational analysis of our patient's DNA sample. DNA analysis was also inconsistent with familial Hibernian fever and tumor necrosis factor α receptor-associated periodic fever syndrome, characterized by periodic fever, rash, myalgias, arthralgias, abdominal pain, chest pain, conjunctivitis, and periorbital edema. Hyper-IgD syndrome, defined by recurrent fever, gastrointestinal complaints, and rash, was ruled out with normal serum IgD. Cyclic neutropenia, described as periodic fevers, pharyngitis, aphthous stomatitis, and rarely bacterial systemic infections, was unlikely because the patient had normal serial ANCs greater than 2,200 cells/mL, performed for more than 6 consecutive weeks. Human immunodeficiency virus serologic test results were negative. There was no history of severe or unusual infections, and laboratory studies revealed normal levels of immunoglobulins, complement, and T cells. Throat cultures for *Streptococcus pyogenes* group A were repeatedly negative. Serologic test results demonstrated past Epstein-Barr virus infection, past herpes simplex virus (HSV) 1 infection, but no recent HSV-1 or HSV-2 infection. The erythrocyte sedimentation rate was mildly elevated. Results of tests for antinuclear antibody, double-stranded DNA, extractable nuclear antigen-ribonuclear protein, Smith antibody, celiac antibodies, urinalysis, and antineutrophil cytoplasmic antibodies were negative.

Although the patient's age is atypical, the clinical picture is consistent with PFAPA. Although the cause of this entity is unknown, speculation exists as to whether it is caused by an unidentified infectious microbe or the result of immune dysregulation.² Several treatments have shown some success in alleviating symptoms. Daily cimetidine³ has reported immune-modulating properties, such as inhibiting chemotaxis and T-cell activation.⁴ There are reports of tonsillectomy also being therapeutic,^{5,6} because an abnormal host immune response to yet unidentified commensal microorganisms in the tonsil or oral mucosae may account for the symptoms.⁷ In addition, it has been proposed that the periodicity of the PFAPA syndrome derives from intermittent expression or suppression of antigens or epitopes of infectious agents or an alteration in the nature or kinetics of an immunologic response.² Glucocorticoids may be given briefly at the onset of an episode to abort attacks,⁸ suggesting that symptoms may be caused by inflammatory cytokines.⁷ Our patient was treated with famotidine daily and prednisone at the start of each episode, which eliminated fevers but no other symptoms. She proceeded to undergo a tonsillectomy. The results of pathologic testing of the tonsils were negative for infection, including Epstein-Barr virus, HSV, and pathogenic bacteria, and showed only enlarged hyperplastic tissue. In the 21 months after tonsillectomy, she has maintained complete resolution of symptoms without medication. This marked response to tonsillectomy further supports the suspected diagnosis of adult-onset PFAPA syndrome.

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EXERCISE-INDUCED HYPERVENTILATION

Exercise-induced respiratory symptoms are present in up to 80% of patients with asthma.^{1,2} Herein, we explore the differential diagnosis of a patient with exercise-induced dyspnea referred for an asthma evaluation.

A 42-year-old man was evaluated for dyspnea with activity. He predominantly had trouble “catching his breath” during exertive activity for several years, and he also had episodes of dyspnea at night, awaking him on occasion. Treatment with a short-acting β -agonist and a trial of an inhaled corticosteroid with a long-acting β -agonist had incompletely improved his symptoms.

On physical examination his vital signs were as follows: blood pressure, 132/83 mm Hg; heart rate, 68 beats/min; respiratory rate, 16/min; and oxygen saturation by pulse oximeter, 99% while breathing room air. His body mass index (calculated as weight in kilograms divided by height in meters squared) was 23.5. His physical examination on presentation was notable for edematous nasal mucosa and posterior pharyngeal cobblestoning. His lungs were clear, without evidence of wheezing. His examination was otherwise unremarkable. Spirometry and lung volumes revealed the following values: forced vital capacity (FVC), 4.26 L (81%); forced expiratory volume in 1 second (FEV₁), 3.32 L (80%); FEV₁/FVC ratio, 0.78; total lung capacity, 5.69 L (80%); residual volume, 1.81 L (88%); and diffusion capacity of carbon monoxide, 32.98 mL/min/mm Hg (110%). There was no response to bronchodilator therapy. Results of routine laboratory testing, including a complete metabolic panel, thyroid-stimulating hormone level, and a complete blood cell count, were within the respective reference ranges. Results of methacholine challenge testing were negative (tested to 8 mg/mL of methacholine), with a decline in FEV₁ of 2.1%.

The patient then underwent outpatient Holter monitoring, echocardiography, and treadmill stress testing, all of which revealed no cardiac etiology for his symptoms. Findings from high-resolution chest computed tomography were normal. Exercise testing was then performed and provoked symptoms; however, his FEV₁ did not change substantially after exercise. Rhinoscopy was performed while the patient was symptomatic, revealing normal vocal cord abduction and adduction and normal phonation. It was observed that he seemed to hyperventilate during exercise when his symptoms were present.

To perform testing for exercise-induced hyperventilation, a portable carbon dioxide (CO₂) monitor was used (Ohmeda 5250 CO₂ Monitor; Datex-Ohmeda, Madison, Wisconsin) to monitor the patient's end tidal CO₂ level during an exercise challenge. A control patient with stable mild asthma was also tested using the same equipment. The results are shown in Figure 1. The patient reported his index symptoms when his

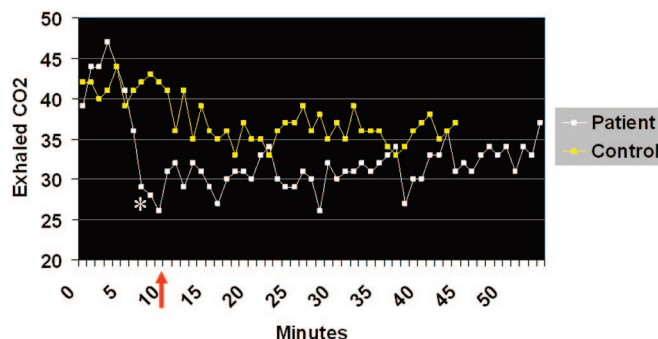


Figure 1. Carbon dioxide (CO₂) monitoring during exercise challenge and recovery (after the arrow) in the patient and the control. Asterisk indicates the patient's onset of symptoms during the challenge test.

CO₂ level dropped to less than 30 mm Hg within 6 to 8 minutes of exercise. He was monitored after the challenge for 1 hour, and his CO₂ level gradually returned to normal.

After testing, the patient was educated about the coincidence of his symptoms with his CO₂ level during exercise. He was instructed on techniques to slow his breathing and to pay attention to his symptoms and respiratory rate during exercise. He was also directed to cease using asthma medication, which he did successfully. He reports improvement in his quality of life after his workup and diagnosis and currently has minimal respiratory symptoms with exercise. On revisiting his history of nighttime episodes of dyspnea, he reported that his spouse noted snoring, gagging, and choking in the patient during sleep. A sleep study demonstrated moderate obstructive sleep apnea (apnea to hypopnea index of 18), and the patient was referred to the pulmonary department for titration of continuous positive airway pressure, which ameliorated his nighttime symptoms.

The hyperventilation syndrome is characterized by ventilation in excess of metabolic needs.³ There is no gold standard for the diagnosis of hyperventilation syndrome. Methods of diagnosis have included the hyperventilation provocation test,⁴ cardiopulmonary exercise testing,⁵ CO₂ monitoring,⁶ and a symptom questionnaire.⁷ Monitoring of CO₂ levels, whether end tidal or transcutaneous, during activities that provoke symptoms can help make the connection between symptoms and CO₂ levels. In 32 patients with atypical symptoms of exercise-induced asthma, symptomatic patients were found to have a decrease in CO₂ levels on average of 23.2% compared with 9.8% in controls.⁶ The present patient had a decrease of 34% (from 39 to 26 mm Hg), which accompanied his symptoms. He also had delayed recovery of his CO₂ level compared with the control (Fig 1). Hyperventilation syndrome should be considered during the workup of a patient with unexplained respiratory symptoms, particularly during exercise. In this patient, persistence in pursuing the differential diagnosis for his symptoms led to correct identification of the cause, avoidance of unnecessary pharmacotherapy, and improvement of symptoms. Additional research is needed to further define and standardize the diagnosis of hyperventilation syndrome.

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EPISODIC ANGIOEDEMA WITH EOSINOPHILIA: SUCCESSFUL TREATMENT WITH IMATINIB

Episodic angioedema with eosinophilia (EAE), consists of recurrent episodes of idiopathic angioedema and hypereosinophilia. Associated features seen in some but not all patients include weight gain, oliguria, fever, and elevated IgM and/or IgE levels.¹ Rapid resolution with corticosteroids is typical, although flare-ups generally resolve in 7 to 10 days without therapy. EAE is differentiated from the hypereosinophilic syndrome (HES) by its lack of end-organ damage and generally benign course. Imatinib mesylate, indicated for treatment of select patients with chronic myeloid leukemia, acute lymphoblastic leukemia, systemic mastocytosis, and gastrointestinal stromal cell tumors, was first reported to be useful in patients with HES in 2002²; its use in EAE has not been reported.

A 62-year-old Asian American woman with a history of well-controlled moderate persistent asthma, chronic rhinitis, osteopenia, and ductal carcinoma in situ (treated 3 years

earlier) presented with episodes of head and neck angioedema associated with total eosinophil count (TEC) elevations as high as $24.9 \times 10^9/L$ ($24,900/mm^3$). Flare-ups occurred every 3 to 6 weeks. Other than angioedema, a review of systems was negative for contributing factors. She denied use of new medications, recent travel, known drug allergy, and family history of atopy. Medications included montelukast, fluticasone-salmeterol (250/50 μg), as needed albuterol, calcium, vitamin D, tamoxifen, loratadine, and nasal fluticasone. Discontinuation of tamoxifen therapy was without effect. Flares of angioedema and eosinophilia were treated successfully with oral corticosteroids, because first- and second-generation antihistamines did not provide adequate control.

A comprehensive evaluation for potential infectious, connective tissue, oncologic, and immunologic causes failed to identify a definitive cause (Table 1). There was no evidence of end-organ involvement. Serum tryptase values, measured during and between flare-ups, remained less than 1.0 ng/mL. Bone marrow analysis, performed while the patient was not taking corticosteroids and during an acute flare-up of eosinophilia, revealed absence of the imatinib-sensitive gene fusion of FIP1-like-1 (FIP1L1) and platelet-derived growth factor receptor α (PDGFRA). EAE was diagnosed. A 3-month prednisone taper suppressed angioedema recurrence for 12 months; however, TEC elevations to $3,100/mm^3$ were noted while the patient was not receiving therapy. When cyclical angioedema recurred, steroid-sparing agents were investigated. Once-daily imatinib mesylate (100 mg orally) has resulted in sustained suppression of angioedema and hypereosinophilia for the past 2 years; TECs average less than $500/mm^3$.

Most experts agree with first-line imatinib use in FIP1L1/PDGFR α -positive hypereosinophilic patients.³ Imatinib use in patients without demonstrable gene fusion remains controversial; such patients are unlikely to respond to low doses (100 mg/d).^{3,4} Currently recognized imatinib-sensitive mutant kinase targets include BCR/ABL, FIP1L1/PDGFR α , fusion kinases involving PDGFR β , KIT mutations other than KIT^{D816V}, and kinesin family-5B/PDGFR α .^{5,6} Although FIP1L1/PDGFR α fusion gene negative, the patient's sustained response to imatinib is at a dosage consistent with patients with PDGFR α -associated disease. This suggests the possible existence of another tyrosine kinase–based mutation in our patient.

Although none of the individual episodes of angioedema in this patient were life-threatening, we strongly believed that continued treatment and suppression were necessary, because the frequent flare-ups caused the patient great distress. Additionally, regardless of cause, prolonged TECs of more than $2,000/mm^3$ increase risk of cardiac and other end-organ damage⁷; therefore, treatment was also aimed at improving or preventing this potential outcome. This thin, Asian, osteopenic patient would likely continue to require treatment with oral steroids. She was concerned about the possible adverse effects of steroids and elected treatment with imatinib after a full discussion of the risks and benefits.

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Table 1. Results of Studies of the Patient

Feature	Patient result (reference range)
Serum chemistry and liver function tests, urinalysis	Within the reference range
Erythrocyte sedimentation rate, mm/h	20 (0–30)
C-reactive protein, mg/dL	0.46 (0–0.75)
Stool ova and parasites	Negative ×2
Coccidioides, strongyloides titers	Within the reference range
Rapid plasma reagin	Nonreactive
Tuberculin testing	Normal
JO-1, PCNA, RNP, SCL-70 antibody titers	Within the reference range
Smith, SSA, SSB antibody titers	Within the reference range
Antinuclear antibody	<1:80 (≥1:160 significant)
Rheumatoid factor, U	187.9 (0–20) ^a
ImmunoCAP specific IgE	
20-Antigen aeroallergen panel	All negative (<0.35 kU/L)
Soy, shellfish panel	All negative (<0.35 kU/L)
Latex	Negative (<0.35 kU/L)
IgA, IgM, and IgG	Within the reference range
IgE, IU/mL	746 (1.31–183) ^a
Serum tryptase, ng/mL	<1.0 (0–11.4)
Complement C3, C4, CH ₅₀	Within the reference range
C1q, C1 esterase inhibitor function	Within the reference range
Mammogram, pelvic examination with cytologic testing, colonoscopy	Normal
Serum protein electrophoresis	Normal, without monoclonal spike
Bone marrow aspirate smear	Increased numbers of predominantly mature eosinophils; otherwise unremarkable
Bone marrow immunophenotypic analysis	Absence of monoclonal B-cell, aberrant T-cell, or increased blast populations
FISH for CHIC2 deletion	Deletion absent
High-resolution computed tomography of the chest	Normal
Echocardiogram	Normal 8/04, 10/05
Magnetic resonance imaging of head and neck	Angioedema, otherwise normal
FEV ₁	1.66, 81% predicted
FVC	2.35, 92% predicted
FEV ₁ /FVC	0.71
FEF _{25%–75%}	0.99, 45% predicted

Abbreviations: CHIC2, cysteine-rich hydrophobic domain 2; FEV₁, forced expiratory volume in 1 second; FEF_{25%–75%}, forced midexpiratory flow rate; FISH, fluorescent in situ hybridization; FVC, forced vital capacity; PCNA, proliferating cell nuclear antigen; RNP, ribonucleoprotein; SCL-70, topoisomerase I; SSA, Sjögren syndrome A; SSB, Sjögren syndrome B.

^a The value is higher than the reference range.

Although adverse effects of imatinib rarely lead to discontinuation of therapy,³ rare serious adverse effects have been reported, including pleural effusions, ascites, hematologic and hepatic toxic effects, Stevens-Johnson syndrome, bleeding, and cardiotoxicity (including severe congestive heart failure and left ventricular dysfunction). Most patients with reported cardiac reactions have had other comorbidities and risk factors or suspected eosinophilic cardiac involvement.³ Careful patient selection is suggested, as is close follow-up to monitor for potential adverse effects. Long-term toxic effects seen in animal studies include liver, kidney, and cardiac toxicity and immunosuppression. Lastly, imatinib has high potential for interactions with cytochrome P450–metabolized drugs and is rated pregnancy category D.

In conclusion, we describe the first reported case, to our knowledge, of EAE successfully treated with imatinib mesy-

late. The response to treatment suggests that the underlying origin of hypereosinophilia in our patient may be due to an imatinib-sensitive mutant kinase similar to those seen in HES or chronic myeloid leukemia; however, this warrants further study. A trial of imatinib could be considered for patients with EAE who require prolonged or recurrent treatment with systemic corticosteroids, possibly even without a demonstrable fusion gene; however, careful patient selection, consideration of adverse effects, and close follow-up by a physician with experience using imatinib are warranted.

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HYPOTENSION FROM EPINEPHRINE IN A FOOD-ALLERGIC PATIENT WITH LONG QT SYNDROME

Anaphylaxis is a potentially fatal multisystem syndrome resulting from the massive release of inflammatory mediators from mast cells and basophils.¹ Epinephrine is universally recommended as the drug of choice in the treatment of acute anaphylaxis. It is a potent catecholamine with both α - and β -adrenergic properties that can quickly reverse the pathophysiologic features of anaphylaxis. Unfortunately, epinephrine is relatively contraindicated in patients with long QT syndrome because of these same adrenergic effects.

A 12-year-old girl with a history of peanut and tree nut allergy presented with generalized urticaria, abdominal pain, and difficulty breathing immediately after ingesting aspirin and consuming peanut candy a few hours earlier. While en route to the nearest emergency department, epinephrine, 0.3 mg, was given intramuscularly, with a subsequent decrease in blood pressure from 136/64 to 71/42 mm Hg within 5 minutes. This was associated with tachycardia, with heart rates greater than 200 beats/min. A physical examination revealed a thin girl in moderate respiratory distress with generalized urticaria and abdom-

inal tenderness on palpation. She received 60 mL/kg of isotonic sodium chloride solution, and a dopamine drip was started for refractory hypotension. The dopamine drip was titrated to 15 μ g/kg per hour for mean arterial pressures of 30 to 40 mm Hg, and the girl was rapidly weaned off by hospital day 2. While receiving dopamine, her hypotension and tachycardia immediately resolved, with mean arterial pressures of greater than 60 mm Hg.

On hospital day 3, episodes of moderate bradycardia associated with junctional escape rhythms were noted. Serial electrocardiograms revealed a prolonged QTc (490–530 milliseconds). The girl was diagnosed as having long QT syndrome. A cardiology consultation initially recommended β -blocker therapy. Because of reported risks for more serious anaphylaxis in patients receiving β -blockers, this therapy was deferred, with a long-term plan of implantable defibrillator placement.

The patient had 3 prior hospitalizations for anaphylaxis. Each occurred after eating peanuts and/or tree nuts and consisted of generalized urticaria and respiratory distress. Epinephrine and diphenhydramine were given in the past, with no known problems. The patient does not have a history of asthma or atopic dermatitis. She had never ingested aspirin before this episode. In addition, she had 3 previous syncopal episodes. Her maternal grandmother died suddenly at the age of 31 years from a presumed heart attack, and her mother has a history of multiple syncopal episodes.

High levels of allergen-specific IgE to peanut, all tree nuts tested, and sesame seed were detected by an assay (ImmunoCap; Phadia AB, Portage, Michigan). A total tryptase level obtained 6 hours after onset of anaphylaxis was 5.2 ng/mL (reference range, 1–15 ng/mL).

The patient was discharged home with cetirizine for treatment of urticaria. Levalbuterol was prescribed for respiratory symptoms. Strict peanut, tree nut, and aspirin avoidance measures were reviewed with the family. A home automatic external defibrillator was prescribed, and placement of an implantable defibrillator is planned. Because epinephrine has the potential to cause lethal ventricular arrhythmia, it is relatively contraindicated in patients with a known long QT and anaphylaxis.

To our knowledge, this case represents the first reported episode of anaphylaxis in a patient with long QT syndrome. The extent of QT prolongation in this patient indicates an increased risk of having cardiac arrhythmias. The concomitant diagnosis of anaphylaxis makes the benefit of β -blockade uncertain because β -blocker therapy is thought to increase the severity of anaphylaxis in susceptible individuals and its refractoriness to therapy with epinephrine.² Theoretically, epinephrine therapy may also be provocative of arrhythmias in patients with long QT syndrome (namely, those with torsades de pointes or ventricular fibrillation).^{3,4}

Ordinarily, β -blocker therapy would be the initial treatment of choice for long QT syndrome. However, in a high-risk patient, such as this one, with a history of syncopal

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episodes and a family history of sudden cardiac death, implantable defibrillator placement would be a reasonable alternative.⁵

Glucagon activates the same intracellular enzymatic machinery as epinephrine through different receptor sites. Although no controlled human studies of glucagon's use in allergic reactions have been reported, to our knowledge, there are a number of case reports whereby the use of glucagon has been shown to be effective in reversing anaphylactic shock.⁶ The patient was trained on the use of a glucagon, 1 mg, autoinjector to be administered at the first signs of anaphylaxis. Once an implantable defibrillator is placed, the patient will be given self-injectable epinephrine to carry.

Some second-generation antihistamines, notably terfenadine and astemizole, have been associated with prolongation of the QT interval and the development of torsades de pointes. Previous studies, however, have demonstrated the absence of electrocardiographic effects of cetirizine, fexofenadine, loratadine, and azelastine in human subjects when administered at several times the recommended dose or with biological agents that inhibit their metabolism.⁷ Given these data, we decided to administer cetirizine to this patient.

Levalbuterol was prescribed for respiratory symptoms because it may produce less direct effects on β_1 -adrenergic receptors in the heart in patients with a history of arrhythmias. However, several past studies indicate that even selective β -agonists may cause QTc prolongation in some patients, thereby posing a possible risk.

Notably, the patient developed anaphylaxis immediately after ingesting aspirin. People who are allergic to foods may have a more severe reaction if they have recently taken aspirin.⁸ Aspirin allows food allergens to penetrate the intestinal walls more readily, producing more severe symptoms, as

in the case of this patient. The patient was advised to strictly avoid aspirin.

This case report of a patient with long QT syndrome highlights a rare instance when epinephrine for the management of anaphylaxis is relatively contraindicated.

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