The patient was instructed to avoid sturgeon fish and Beluga caviar, which is derived from sturgeon fish. This recommendation was made because although there were 2 cases of allergic reactions to fish roe without concomitant fish meat allergy reported,[3] no reports or studies have suggested that the reverse also may be possible (ie, fish meat allergy without fish roe allergy). Avoidance to trout and its roe was recommended as well.

The various proteins bound by the patient to the sturgeon fish meat need to be further characterized. The most common fish protein allergen is parvalbumin, but the weight typically only ranges from 11 to 45 kDa,[4] which would be inconsistent with the proteins bound by this patient. Other possibilities include formation of parvalbumin polymers, which has been suggested for snapper fish allergens,[5] derivatives of vitellogenin that have been identified in Beluga caviar,[2] or unique sturgeon flesh neoallergens. Concordantly, trout (35, 55, 65 kDa) and cod (100, 150 kDa) proteins that were bound have yet to be identified. Finally, this patient's binding patterns indicate that these fish may have cross-reactive fish proteins—sturgeon and trout at 55 and 65 kDa and sturgeon and cod at 100 kDa.

To our knowledge, this is the first report of sturgeon flesh anaphylaxis. Further research is needed to clarify the specific protein allergens that have been identified.

Sandy K. Yip, MD*
Robert A. Gomez, BS*
Kevin M. White, MD*
Ronald W. England, MD†
*Department of Allergy/Immunology
Wilford Hall Ambulatory Surgical Center
San Antonio, TX
†Spokane Allergy and Asthma Clinic
Spokane, WA
sandy.yip@us.af.mil

References

[1] Untersmayr E, Focke M, Kinaciyan T, et al. Anaphylaxis to Russian beluga caviar. *J Allergy Clin Immunol*. 2002;109:1034–1035.
[2] Perez-Gordo M, Sanchez-Garcia S, Cases B, Pastor C, Vivanco F, Cuesta-Herranz J. Identification of vitellogenin as an allergen in Beluga caviar allergy. *Allergy*. 2008;63:479–480.
[3] Mäkinen-Kiljunen S, Kiistala R, Varjonen E. Severe reactions from roe without concomitant fish allergy. *Ann Allergy Asthma Immunol*. 2003;91:413–416.
[4] Hajeb P, Selamat J. A contemporary review of seafood allergy. *Clin Rev Allergy Immunol*. 2012;42:365–385.
[5] Rosmilah M, Shahnaz M, Masita A, Noormalin A, Jamaludin M. Identification of major allergens of two species of local snappers: *Lutjanus argentimaculatus* (merah/red snapper) and *Lutjanus johnii* (jenahak/golden snapper). *Trop Biomed*. 2005;22:171–177.

Successful rapid desensitization to hydrochlorothiazide

Hypersensitivity reactions to sulfonamide antibiotics and sulfonamide non-antibiotics are well described. Most of these reactions are delayed hypersensitivity reactions, which manifest as maculopapular or morbilliform eruptions, whereas type 1, or immunoglobulin E–mediated hypersensitivity reactions are comparatively infrequent.[1] In antibiotic sulfonamides, these reactions are significantly mediated by the presence of a N4 aromatic amine and a substituted ring at N1, respectively.[1] Similar reactions are reported in non-antibiotic sulfonamides, although they do not contain any of these structures.[2]

Thiazide diuretics and loop diuretics are sulfonamide non-antibiotics that are used widely in clinical practice. We follow a recent report of rapid desensitization to furosemide in this journal and present a successful rapid desensitization schedule to hydrochlorothiazide.

We reviewed a 20-year-old patient with congenital nephrogenic diabetes insipidus at our hospital clinic. Hydrochlorothiazide, a thiazide diuretic, had been prescribed from the time of diagnosis. To age 8, he was noted to have severe pruritic bullous eruptions affecting the limbs, which resolved spontaneously over weeks on withdrawal of the drug but recurred on rechallenge. A biopsy of 1 of these lesions indicated extensive necrosis of the epidermis and a dermal infiltrate of eosinophils, neutrophils, and lymphocytes. These findings suggested drug-induced lichenoid bullous dermatosis, a type of delayed hypersensitivity reaction.

On cessation of hydrochlorothiazide, he experienced no further episodes. Nonsteroidal anti-inflammatory medications were substituted but proved unsatisfactory for disease control. At age 20, worsening chronic kidney disease and clinically significant polyuria and resistant hypertension necessitated recommencement of a thiazide diuretic. Patch testing to hydrochlorothiazide was strongly positive at 48 hours with homogenous erythema and infiltration with vesicles after application at a dilution of 10% in water and at a dilution of 10% on petrolatum. Water and petrolatum were used as negative controls.

We proceeded to desensitization with the aim of commencing a daily dose of 25 mg hydrochlorothiazide. We did not proceed to oral challenge to avoid the risk of precipitating another severe bullous eruption. A literature search located no publications in relation to desensitization to thiazide diuretics, although one protocol of rapid oral desensitization to furosemide was found, published in this journal.[3] Hence, a novel rapid schedule of desensitization to hydrochlorothiazide was formulated with the aim of achieving a daily dose of 25 mg.

A liquid preparation of the drug was used, with a concentration of 1 mg/mL. We formulated a protocol in line with existing principles of rapid desensitization. The starting dose selected was 1/1,000th of the cumulative target dose, and incremental doses were administered every 15 minutes without an adverse reaction (Table 1).[4] A cumulative dose of 25.275 mg was reached over a period of 105 minutes without an adverse reaction. The patient then commenced 6 hours later on his daily dose of 25 mg.

No recurrence of his rash was seen after the introduction of his daily dose of hydrochlorothiazide. At age 24, he has now resumed thiazide diuretic medication for 4 years and continues to have no hypersensitivity reactions to the drug. On his most recent review,

Table 1
Rapid desensitization regimen to hydrochlorothiazide

Time (min)	Dose of hydrochlorothiazide (mg)	Cumulative dose of hydrochlorothiazide (mg)
0	0.025	0.025
15	0.25	0.275
30	0.5	0.775
45	1.0	1.775
60	1.625	3.4
75	3.125	6.525
90	6.25	12.775
105	12.5	25.275

Disclosures: Authors have nothing to disclose.

the patient was well, normotensive, and maintaining a satisfactory urine output. His chronic kidney disease is stable.

Jamma Li, MB, BS
Suran L. Fernando, MB, BS, PhD
Department of Clinical Immunology and Allergy
Royal North Shore Hospital
Sydney, Australia
jamma_li@hotmail.com

References

[1] Khan DA, Solensky R. Drug allergy. *J Allergy Clin Immunol*. 2010;125(2 Suppl 2): S126–S137.
[2] Strom BL, Schinnar R, Apter A, et al. Absence of cross-reactivity between sulfonamide antibiotics and sulfonamide nonantibiotics. *N Engl J Med*. 2003; 349:1628–1635.
[3] Alim N, Patel JY. Rapid oral desensitization to furosemide. *Ann Allergy Asthma Immunol*. 2009;103:538.
[4] Castells M. Oncology: chemotherapy agents and monoclonal antibodies. In: Pichler WJ, ed. *Drug hypersensitivity*. Basel: Karger; 2007:404–412.

Successful desensitization protocol for pyridostigmine hypersensitivity in a patient with myasthenia gravis

Acquired myasthenia gravis (MG) is a chronic autoimmune disorder of the neuromuscular junction, characterized by muscle weakness and fatigability on exertion. MG is caused by autoantibodies against acetylcholine receptors in the postsynaptic membrane.[1] The pathogenesis involved in acetylcholine receptor impairment includes: accelerated endocytosis and degradation of acetylcholine receptors, functional blockade of the acetylcholine binding site, and complement-mediated damage of the postsynaptic membrane.[1] The initiating event of MG is unknown, but speculations have been made about viral infections as a possible trigger.[1]

Treatment of MG usually combines symptomatic therapy and long-term disease-modifying treatments. For symptomatic treatment, acetylcholinesterase inhibitors are considered first line.[2] Acetylcholinesterase inhibitors act by slowing the degradation of acetylcholine at the neuromuscular junction, prolonging the interaction of acetylcholine with its receptor on the muscle membrane and enhancing neuromuscular transmission.[2] They provide only short-term relief and do not possess any disease-modifying properties. Pyridostigmine is the most commonly used acetylcholinesterase inhibitor. Pyridostigmine plasma concentrations correlate with decreased acetylcholine activity and improved muscle strength.[2]

One case report has been made of acute urticaria caused by pyridostigmine followed by anaphylaxis after oral challenge with this agent.[3] Our case report describes a patient with a hypersensitivity reaction to pyridostigmine who was successfully desensitized to pyridostigmine with a 2.5-hour desensitization protocol.

A nonatopic, 43-year-old man with a medical history of hypertension, obesity, and MG was started on pyridostigmine 60 mg by mouth 3 times per day and prednisone 10 mg daily and had immediate excellent symptom control. After 8 days of treatment with pyridostigmine, he developed pruritus and an urticarial rash, which started on his legs and became diffuse. As this progressed, he noted a change in his voice. He did not have associated shortness of breath, dizziness, or gastrointestinal symptoms. The patient denied any history of allergy to aeroallergens or foods and had no known prior drug allergies. Aside from the pyridostigmine and prednisone, no new medications had been started. The symptoms resolved after the discontinuation of pyridostigmine and treatment with steroids, epinephrine, and H1 and H2 blockers.

Because pyridostigmine was highly effective for the patient, his neurologist consulted our division for assistance in desensitization. To our knowledge, there have been no published desensitization protocols for pyridostigmine. We would typically recommend a starting dose of 1/10,000 of targeted dose. However, we were unable to achieve this low of a starting dose because of unknown stability of further dilution of the commercially available suspension. Doses were administered every 30 minutes under medical supervision in the intensive care unit: This included vital signs every 30 minutes, continuous pulse oximetry, and telemetry. Total pyridostigmine desensitization length was 2.5 hours, using an escalating, 6-dose protocol that we formulated (Table 1). The patient was kept under observation in the intensive care unit for 2 hours after the final dose, with no reaction noted during the entire procedure. Afterward, the patient continued treatment with pyridostigmine 60 mg by mouth 3 times per day, with no further reaction.

Table 1
Desensitization protocol for pyridostigmine

Time, minutes	Pyridostigmine dose, mg
0	1.2
30	2.4
60	4.8
90	9.6
120	19.2
150	38.4

This is the first documented case of successful desensitization to pyridostigmine in the literature. This case demonstrates a safe and effective desensitization protocol for pyridostigmine and may provide additional treatment options for patients with MG who have evidence of prior hypersensitivity to pyridostigmine.

Tania Aung, MD
Amy Yoder Dowden, MD
University of Iowa Hospitals and Clinics
Iowa City, Iowa
tania-aung@uiowa.edu

References

[1] Gilhus NE. Myasthenia and the neuromuscular junction. *Curr Opin Neurol*. 2012;25:523–529.
[2] Maggi L, Mantegazza R. Treatment of myasthenia gravis: focus on pyridostigmine. *Clin Drug Invest*. 2011;31:691–701.
[3] Castellano A, Cabrera M, Robledo T, et al. Anaphylaxis by pyridostigmine. *Allergy*. 1998;53:1108–1109.

Disclosures: Authors have nothing to disclose.