AT THE FOREFRONT
UChicago Medicine

A Case of Recurrent Anaphylaxis

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Case

A 35-year-old female with a history of post-partum depression was referred for recurrent anaphylaxis

Initial Visit

- Awoke suddenly in the middle of the night with the urge to defecate
- While in the restroom, developed swelling and itchy rash throughout her body including legs, arms, face, neck, and earlobes. A few minutes later, started to wheeze, felt dizzy, and was taken to the ED
- In the ED, she was given diphenhydramine and methylprednisolone. After observation, was discharged with an epinephrine autoinjector, albuterol, and prednisone 60 mg/day x 4 days

Initial Visit

- Four days later, awoke from sleep with similar symptoms except for emesis x1, which relieved her GI symptoms without medication
- Within 20-30 minutes, the itching, swelling, and wheezing had resolved
- Continued to have episodes (2x per week) of hives and itching on her neck and face that resolve within ~30 minutes after taking diphenhydramine. No pain, burning, or residual bruising

History

- PMH: Post-partum depression, ectopic pregnancy (2016), Enteroaggregative E. coli (EAEC, 2022) and abnormal thyroid studies at recent visit to PCP
- PSHx: Pelvic laparoscopy for ectopic pregnancy
- Family history:
  - Father: HTN, brain tumor
  - MGM: Diabetes, depression
  - Paternal aunts: Gastric cancer, pancreatic cancer, breast cancer
- Social history: Never-smoker. Lives with husband and 2yo daughter. Former medical assistant, now stay-at-home mom
- Medications: None taken regularly. No new medications prior to presentation

Physical Exam

- Vital signs stable
- Only pertinent positive was active itching of skin and redness present on the anterior neck and lower half of the face

Labs Drawn by PCP

- ***TSH: 5.54 (Ref 0.30-4.00 mcU/mL)***
- Hemoglobin A1c: 5.1 (<5.7%)
- C4 Complement: 29 (18-45 mg/dL)
- C1 Esterase Inhibitor: 35 (19-37 mg/dL)
- Tryptase: 2.2 (<11.5 ng/mL)

Repeat labs:

- TSH: 3.20 (0.30-4.00 mcU/mL)
- FT4: 1.04 (0.9-1.7 ng/dL)
- ***TPO Antibody: 415.9 (<9.0 iU/mL)***

What other testing would you consider?

Initial Visit Plan

- Labs:
  - TSH: 3.73 (0.30-4.0 mcU/mL)
  - ***FT4: 0.85 (0.9-1.7 ng/dL)***
  - CBC w/ absolute eosinophils: 190 (0-600 10*3/uL)
  - IgE Receptor Antibody: 5.3 (0-12%)
- Started cetirizine 10 mg daily and prescribed epinephrine autoinjector
- Diary of possible triggers

Three Month Follow Up Visit

- Had one episode of itching accompanied by dyspnea and dizziness
  - » Used epinephrine autoinjector
- Went to the ED and was treated with steroids and diphenhydramine
- Discharged with diphenhydramine and prednisone, but did not take them as her father was ill and died the following day
- Patient stopped cetirizine just prior to next follow up visit

Three Month Follow Up Visit

- SPT to common foods was negative
- SPT to aeroallergens was positive to cat and mold (alternaria)
- Recommended restarting cetirizine 10 mg/day
- Upon onset of itching/hives start cetirizine 20 mg twice daily and prednisone 40 mg/day for 2 days
- Recommended follow up with PCP or endocrinology for abnormal thyroid labs (had not yet done so)
- Gave allergy action plan

Six Months Later

- Had three episodes despite taking cetirizine 10 mg/day
  - » All episodes included abdominal cramps with generalized itching +/- tongue swelling, diarrhea, vomiting, and dyspnea
  - » Symptoms resolved after 20-60 minutes using action plan
  - » Recommended increasing cetirizine 20 mg twice daily
  - » Still didn’t follow-up with PCP or endocrinology regarding abnormal thyroid labs
  - » Scheduled GI evaluation in the setting of strong family history of abdominal cancer

Three Month Follow Up

- Over three months, episodes became more frequent (~3x per week), but “less intense” overall
- Had occasional “severe” episodes of flushing, itching, and intense abdominal cramping with diarrhea and vomiting
- Continued cetirizine 20 mg twice daily
- Used action plan (~1-2x per month for severe episodes)
- Patient was still concerned about foods. Indicated symptoms temporally associated with eating out at McDonalds and having chicken and beef outside the home. Symptoms then started occurring when eating at home

Differential?

- Food allergy
- Exercise-induced anaphylaxis
- Food-dependent, exercise-induced anaphylaxis
- Alpha-gal syndrome
- Angioedema (Autoimmune vs. HAE vs. histaminergic)
- Chronic spontaneous urticaria (CSU)
- Mast cell activation syndrome (MCAS)
- Systemic mastocytosis
- Hereditary alpha-tryptasemia (HαT)
- Carcinoid syndrome
- Pheochromocytoma
- Celiac disease
- Progesterone hypersensitivity
- Postural orthostatic tachycardia syndrome (POTS)
- Vocal cord dysfunction (VCD)
- Somatoform disorder
- Panic disorder

Three Month Follow Up

- Scheduled for EGD/colonoscopy, abdominal/pelvic CT with contrast
  - » GI labs: 24-hour urine for carcinoid/pheochromocytoma workup, and blood work for celiac disease screening
- Patient requested hematology/oncology referral
- Other labs: Alpha-gal panel, tryptase, and 24-hour urine for metabolites of mast cell mediators
- Switched to fexofenadine 360 mg twice daily and started famotidine 20 mg twice daily

Labs

- CBC: WNL
- CMP: WNL

Alpha-Gal panel:

- Galactose-alpha-1,3-galastose IgE: <0.10 (<0.70 kU/L)
- Beef IgE: <0.10 (<0.70 kU/L)
- Pork IgE: <0.10 (<0.70 kU/L)
- Lamb IgE: <0.10 (<0.70 kU/L)
- Milk IgE: <0.10 (<0.70 kU/L)

- Total IgE: 83.8 (<214 kU/L)
- Tissue transglutaminase IgA Ab: 1 (<4.0 U/mL)
- ***CRP: 7 (<5 mg/L)***

Quantitative Immunoglobulins:

- ***IgA: 93 (100-490 mg/dL)***
- IgG: 908 (800-1700 mg/dL)
- IgM: 116 (50-320 mg/dL)

Labs/Procedures

- Tryptase: 2.1 (<11.5 ng/mL)
- ***Thyroid peroxidase antibodies: 16.3 (<0.4 kU/mL)****
- TSH: 2.32 (0.3-4.0 mcU/mL)
- FT4: 1.09 (0.9-1.7 ng/dL)

- CT abdomen/pelvis and EGD/colonoscopy were unremarkable

Labs

24-Hour Urine:

- N-methylhistamine: 154 (30-200 mcg/g)
- ***Leukotriene E4: 125 (<104 pg/mg Cr)****
- 2,3-Dinor 11B-Prostaglandin F2a: 811 (<1802 pg/mg Cr)

- Metanephrines: 180 (30-180 mcg/24 hr, normotensive)
- Normetanephrine: 388 (111-419 mcg/24 hr, normotensive)
- Total Metanephrines: 568 (149-535 mcg/24 hr, normotensive)

- 5-Hydroxyindolacetic acid: 4.4 (<6.9 mg/24 hr)

Next Steps?

Curr Treat Options Allergy (2017) 4:312–319
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Anaphylaxis (M Sánchez-Borges, Section Editor)

Idiopathic Anaphylaxis

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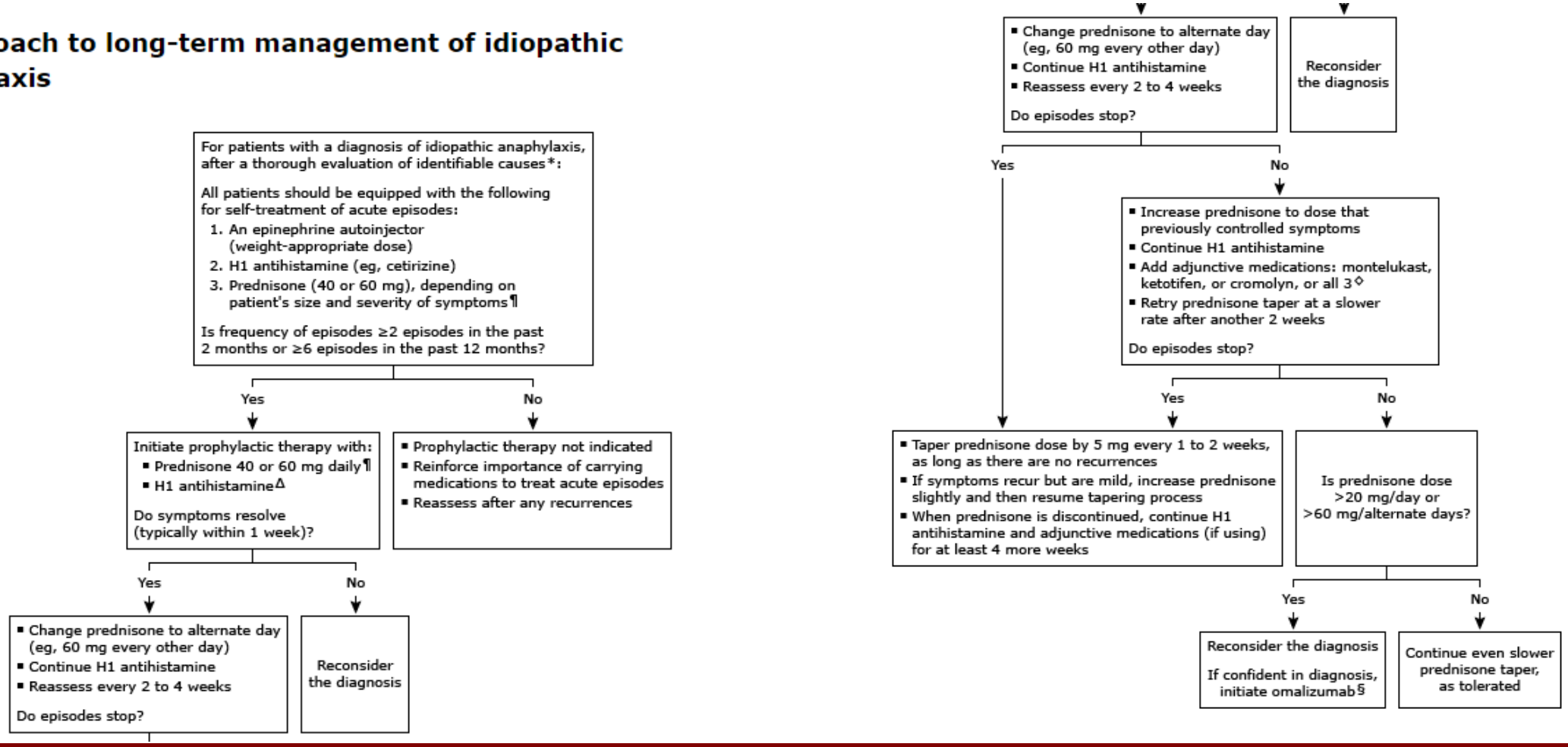
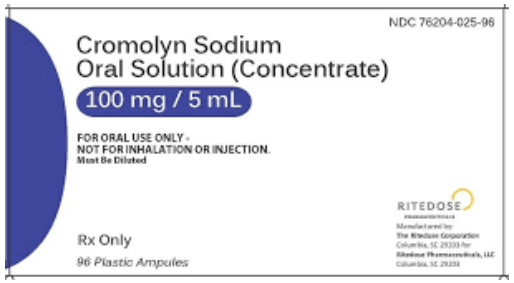
Next Steps?

UpToDate®

An approach to long-term management of idiopathic anaphylaxis



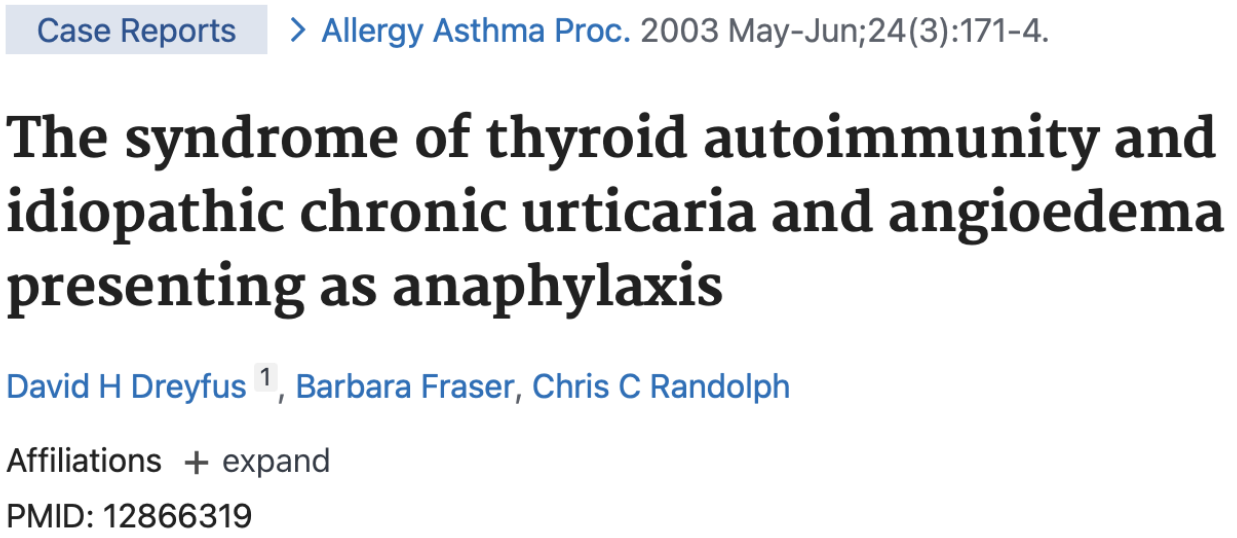
Next Steps/Discussion



- Our plan:
  - » Start omalizumab 300 mg qMonth (First injection 1/23/24)
    - » Hematology awaiting Xolair prior to considering bone marrow biopsy
  - » Continue fexofenadine 360 mg twice daily and famotidine 20 mg twice daily
  - » Upon onset of severe symptoms, take an additional fexofenadine 180 mg and prednisone 40 mg
  - » Stopped montelukast due to intolerance
  - » Start cromolyn sodium 200 mg before meals and bedtime

Next Steps/Discussion

- Send genetic testing for hereditary alpha-tryptasemia?
- Endocrinology referral?



Case Reports > Allergy Asthma Proc. 2003 May-Jun;24(3):171-4.

The syndrome of thyroid autoimmunity and idiopathic chronic urticaria and angioedema presenting as anaphylaxis

David H Dreyfus [1], Barbara Fraser, Chris C Randolph

Affiliations + expand

PMID: 12866319

» Autoimmune subclinical hypothyroidism → levothyroxine?

Next Steps/Discussion

CASE REPORTS | MAY 04 2012

Recurrent Anaphylactic Reactions: An Uncommon Debut of Lymphocytic Hypophysitis

Subject Area: Immunology and Allergy

Irina Bobolea; Daiana Guillén; Pilar Barranco; Cristina Alvarez-Escola; Santiago Quirce

Int Arch Allergy Immunol (2012) 159 (1): 103–106.
https://doi.org/10.1159/000335231 Article history

- Cases of lymphocytic hypophysitis → a rare chronic autoimmune disease in which adenopituitary dysfunction can lead to functional adrenal insufficiency, and in severe cases, adrenal crisis

References

- Bobolea I, Guillén D, Barranco P, Alvarez-Escola C, Quirce S. Recurrent anaphylactic reactions: an uncommon debut of lymphocytic hypophysitis. Int Arch Allergy Immunol. 2012;159(1):103-6. doi: 10.1159/000335231. Epub 2012 May 4. PMID: 22573101.
- Dreyfus DH, Fraser B, Randolph CC. The syndrome of thyroid autoimmunity and idiopathic chronic urticaria and angioedema presenting as anaphylaxis. Allergy Asthma Proc. 2003 May-Jun;24(3):171-4. PMID: 12866319.
- Nwaru BI, Dhami S, Sheikh A. Idiopathic Anaphylaxis. Curr Treat Options Allergy. 2017;4(3):312-319. doi: 10.1007/s40521-017-0136-2. Epub 2017 Jun 3. PMID: 28890861; PMCID: PMC5569651.

Thank You

Dr. Sharmilee Nyenhuis

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