CASE REPORT

Catamenial anaphylaxis: a woman under monthly progesterone curse

Kyawzaw Lin,¹ Ameer Rasheed,¹ Sithu Lin,¹ Louis Gerolemou²¹Internal Medicine Department, The Brooklyn Hospital Center, Brooklyn, New York, USA²Pulmonary Department and MICU, The Brooklyn Hospital Center, Brooklyn, New York, USACorrespondence to
Dr Sithu Lin,
dr.sithulin@gmail.com

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SUMMARY

Catamenial or cyclical anaphylaxis is a complex clinical syndrome with poorly reported incidence and prevalence in the literature review. The underlying mechanism is still a myth although a few proposed hypotheses are stated. Early recognition of these symptoms will bring optimal treatment and prevent unnecessary intubation and complications. Here, we present a 48-year-old woman without significant medical and family history with recurrent angioedema in the setting of catamenial anaphylaxis or cyclical anaphylaxis in the setting of progesterone hypersensitivity.

BACKGROUND

Catamenial anaphylaxis is a rare and overlooked disorder in setting of hypersensitive to either endogenous or exogenous progestogen hormones. Most patients with catamenial anaphylaxis experience symptoms from mild dermatitis, urticaria, asthma attack to angioedema and anaphylactic shock in the luteal phase of the menstrual cycle usually on the 20–21 day of the 28-day cycle. However, the reactions may occur in any phase of menstrual cycle. Primary endogenous catamenial anaphylaxis usually occurs during menstruation and gestational period, but secondary exogenous reaction is precipitated with progesterone supplementation.

CASE PRESENTATION

A 48-year-old non-pregnant woman presented to the emergency department with the complaint of sudden swollen neck and tongue in the morning. The patient stated that she has had swollen neck and tongue every month coincided with her ovulation for 3 years and relieved slightly with diphenhydramine syrup. In this episode, she started feeling neck swelling the day before without redness and she took diphenhydramine syrup as usual. However, in the morning, she noticed she had neck swelling along with angioedema associated with stridor and hoarseness of voice 10 min prior to arrival. There is no precipitating or aggravating factors related to recurrent episodes. She is not currently on ACE inhibitors or aldosterone receptor blocker. There is no recent illness, insect bite or newly prescribed medications. She has previous medical history of anxiety, gestational diabetes mellitus and pre-eclampsia.

The patient experiences 10–12 episodes of angioedema in the past 2–3 years prior to menstruation. However, it usually resolves after menstruation

and slightly relieved with diphenhydramine syrup. From time to time, she might come to the emergency department in the setting of angioedema and sudden respiratory distress. She was treated with epinephrine by autoinjectors, intravenous steroid and diphenhydramine injection. Later, she was discharged from the emergency department in 24 hours. Most events occur within the first week of menses. She has never done allergy testing and has not seen an allergist so far. There is no significant history of angioedema in her family or no recent illness, insect bite or newly prescribed medications.

INVESTIGATIONS

Complete blood count and basic metabolic panel are within normal limit. Serum C3, C4, C-1 esterase and IgE level are within normal limits. Serum tryptase at baseline and during anaphylaxis is normal. Twenty-four-hour urine 5-hydroxyindoleacetic acid (HIAA), vanillylmandelic acid (VMA) and catecholamine levels later showed within normal limits. However, skin test to medroxyprogesterone showed positive in our patient. Both Mallampati and modified Mallampati scoring are used to predict the ease of endotracheal intubation in the setting of angioedema or acute hypoxic respiratory failure and it showed that the soft palate, uvula and pillars are visible (class I).

DIFFERENTIAL DIAGNOSIS

- ▶ Angioedema secondary to allergens.
- ▶ Monosodium glutamate poisoning.
- ▶ Hereditary angioedema.
- ▶ Capillary leak syndrome.
- ▶ Globus hystericus.

TREATMENT

On arrival to the emergency department, the patient was able to provide the whole history. She can speak in one full sentence without getting shortness of breath but appeared to be in respiratory distress with respiratory rate of 26–28 breaths/min. After high-dose intravenous methylprednisolone, two doses of intramuscular epinephrine, intravenous diphenhydramine 50 mg along with intravenous ranitidine 50 mg stat, the angioedema and stridor have resolved in 30 min.

OUTCOME AND FOLLOW-UP

On the second day of in-hospital stay, the angioedema and neck swelling have resolved. The patient is discharged with epinephrine auto-injector

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for emergency use, per oral diphenhydramine and prednisone in short course. The patient was encouraged to follow up with an allergist-immunologist.

DISCUSSION

Catamenial or cyclical anaphylactic reaction is a rare but not uncommon anaphylactic syndrome ranging from dermatitis, urticarial, angioedema, asthma to anaphylactic shock usually in the luteal phase of menstruation, even just before menopause, after intrauterine device placement or even with single dose of emergency contraception (levonorgestrel) in a few cases. Catamenial anaphylaxis is diagnosed after other causes were excluded such as allergic reaction secondary to foods, non-steroidal anti-inflammatory agents, endocrine conditions such as pheochromocytoma, carcinoid syndrome, haematological malignancies such as systemic mastocytosis and hypersensitive reactions to exogenous and endogenous progesterone.^{1 2}

Proposed mechanisms for catamenial anaphylaxis are hypersensitivity to progesterone and due to vasoactive component in menstrual fluid such as prostaglandin.³ In a multicentre retrospective study done in three academic centres from 1998 to 2011, there are eight case series of catamenial anaphylaxis. The median age is 34 (14–40 years of age), median number of anaphylactic reaction during perimenstrual period is 10 per patient (4–24 episodes) and frequency of anaphylactic reaction that coincides with menstruation is 92% (15%–100%). One case was managed with high dose of cetirizine, second and fourth patients with leuprolide and bilateral salpingo-oophorectomy and third case with medroxyprogesterone.⁴ In a retrospective study of 24 cases of autoimmune progesterone dermatitis, symptoms were controlled in 8 out of 11 cases desensitised with intramuscular or oral progesterone.⁵

The common presenting symptoms are skin manifestations such as urticarial, allergic dermatitis, followed by cardiovascular, gastrointestinal or neurological symptoms and pulmonary systems in the setting of possible type I or IV hypersensitive reaction due to Th2 response. However, other causes that mimic anaphylaxis such as pheochromocytoma, carcinoid syndrome and systemic mastocytosis must always be ruled out by history, detailed examination, laboratory tests and imaging as needed.

Serum tryptase level can be used to confirm anaphylactic event but a normal level cannot rule out anaphylaxis as elevation in tryptase is transient and variable. In a cohort study of eight cases of catamenial anaphylaxis, serum tryptase level during anaphylaxis is high (46.9 ng/mL) only in one case.⁴ Normal serum IgE level cannot rule out the diagnosis either. Twenty-four-hour urine 5-HIAA, VMA and catecholamine level can also be checked during the anaphylactic event to rule out other possible differential diagnoses such as pheochromocytoma and carcinoid syndrome. Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin for menstrual cramps are underlying factors to precipitate catamenial anaphylaxis in some cases.⁵

After other causes of anaphylaxis are ruled out, management should be addressed to improve the quality of daily life and symptoms relieved with antihistamine with or without combined contraceptive pill to suppress monthly ovulation. Usually after 3 months of trials on medications such as antihistamine, corticosteroids and oral contraceptive pills, desensitisation can be considered on patients' request or preference of allergists or immunotherapists. In a case series of 24 cases of catamenial anaphylactic patients, near 50% of the patients responds to medications starting from high-dose antihistamines, corticosteroids, combined oral contraceptive pills to IgE monoclonal

antibody such as omalizumabs and depot GnRH analogue such as leuprolide.⁶ In the literature, two patients are managed with oral conjugated oestrogen.^{7 8}

Recently, a case of a 12-year-old girl with progesterone-induced anaphylaxis is managed successfully with omalizumab 300 mg subcutaneously monthly for 6 months and skin prick test with progesterone showed negative results after 6 months of treatment with recombinant humanised immunoglobulin G1 (IgG1) monoclonal antibody (omalizumab). It is approved by the US Food and Drug Administration for severe allergic asthma and severe chronic cutaneous urticaria.⁵ Therefore, similar biological agents, bradykinin B2 receptor antagonist and anti-CD20 monoclonal antibody might be used in selected complicated recurrent anaphylaxis in the future. In patients with anaphylactic shock or angioedema that requires intubation to protect airway and every other medical therapies failed, surgical castration of ovaries with or without total abdominal hysterectomy can be done as the last resort.⁹

In conclusion, catamenial anaphylaxis is a sole paradigm of menstrual-related disease in the female population. The very first case was reported in 1995. Catamenial anaphylaxis is also called cyclical anaphylaxis as recurrent episodes of hypersensitive reaction to progesterone occur during menstruation. Hence, the multidisciplinary approach between primary care physician, allergist, gynaecologist and patient is essential to prevent the recurrence, to relieve monthly progesterone hypersensitivity and to get efficient standardised therapy to get better physically and mentally healthy lifestyle.

Learning points

- Catamenial or cyclical anaphylaxis is a diagnosis of exclusion.
- A complex clinical syndrome with poorly reported incidence and prevalence in the literature review in the setting of progesterone hypersensitivity.
- It usually occurs in the luteal phase of the menstrual cycle but it can occur at any phase of menstruation and pregnancy.
- Omalizumab (recombinant humanised immunoglobulin G1 monoclonal antibody) might be used in catamenial anaphylaxis in the future.

Contributors KL and AR contributed equally in gathering information, writing introduction, case report and discussion. SL was involved in editing the case report. LG provided the management and proper diagnosis for this case report.

Competing interests None declared.

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