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Catamenial Anaphylaxis: A Case Report with Cyclical Issue

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Abstract

Catamenial anaphylaxis, a scarcity subtype of menstrual cycle-associated allergic reactions, characterized by a spectrum of manifestations ranging from mild cough or the severe angioedema and loss of consciousness due to hypersensitivity reactions occurring predominantly during the first days of menstruation. The precise pathophysiology remains elusive, although fluctuations in progesterone appear to play a dominant role. We present a case of an 18-year-old female who experienced recurrent exacerbation episodes of anaphylaxis coinciding with her menstrual cycles. Regarding the rarity of evidence on Catamenial anaphylaxis, it is critical to do further investigations into the clinical presentation, triggering factors, and therapeutic modalities for improved diagnostic clarity and treatment outcomes in affected patients.

Background

Allergic reactions or hypersensitivity can occur at any age and phase of the menstrual cycle in a woman's life, a phenomenon that is relatively rare and often underdiagnosed with less than 200 reported documented cases. Catamenial or Cyclical Anaphylaxis (CA), an unusual condition characterized by allergic reactions in association with the menstrual cycle, is thought to be influenced by the endogenous or exogenous progesterone and estrogen hormones at the onset of the menstruation.

This phenomenon presents with complex and variable array of clinical symptoms, including pruritus, urticarial, angioedema, diarrhea, abdominal pain, anaphylactic shock. Prostaglandins seem to proposed as one of probable potential mechanisms involved in its pathogenesis [1]. Through a comprehensive evaluation and management approach, we aim to shed light on the clinical presentation, diagnostic challenges, and treatment considerations associated with CA.

Case presentation

An 18-year-old young female with a history of asthma childhood, sought medical attention in the hospital emergency department six months ago during her menstrual cycle's second day with complaining of spontaneity urticarial, generalized itching, coughing, shortness of breath, generalized angioedema, and a drop in oxygen saturation level. She claimed to have taken one Ibuprofen tablet daily for the preceding two days. Following evaluation, Anti-histamine and Epinephrine were prescribed for her and she was advised to from Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) to prevent potential complications in subsequent menstrual cycles.

Six months later, she experienced a recurrence of severe symptoms, including urticarial, pruritus, angioedema, diarrhea, intensive abdominal pain, coughing, and dyspnea, also decreased the level of oxygen saturation and consciousness so she was admitted to require admission to the Intensive Care Unit (ICU) for one day, despite abstaining from any medication in that menstrual period. There were no other known triggers for the patient's allergic reactions including food and drug, and she denied having a considerable medical history or taking medications. Subsequently, she was referred to an allergist for a further comprehensive assessment.

Initial investigations involved drug allergy testing with 10% and 90% doses of celecoxib and other essential evaluation were negative. Furthermore, a progesterone prick test was conducted to assess potential triggers of anaphylactic reactions which

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was negative, either. As a precautionary measure, the patient was advised to carry an Epinephrine Auto-Injector Pen (EpiPen) for self-administration in case of anaphylactic reactions.

Currently, the patient is being treated with Rokin for one year without experiencing any recurrence of anaphylactic episodes.

Discussion

Catamenial anaphylaxis remains an enigmatic and under-recognized entity, often presenting significant diagnostic and therapeutic challenges for clinicians. While the exact pathophysiology of catamenial anaphylaxis remains elusive, hormonal fluctuations during the menstrual cycle are believed to play a pivotal role in triggering allergic reactions in susceptible individuals.

Progesterone levels typically begin to rise 24 to 48 hours before ovulation and reach their peak on 20 to 21-days of a 28-day cycle. Hence, the majority of individuals with endogenous progesterone hypersensitivity exhibit symptoms during the luteal phase, occurring several days before menstruation, approximately a week prior to menstruation. Of note, it is crucial to distinguish Progesterone Hypersensitivity (PH) from CA, as the former appears one day prior to or on the first day of the menstrual cycle, albeit the latter can occur at any time throughout the follicular phase and even commence as early as one day before or during the menstrual [2-4]. In a case report, Brander et al. highlighted its important differential diagnosis by describing a 17-year-old woman experienced pruritus, flushing, and angioedema in her second day of mensuration cycle. Positive results from a medroxyprogesterone acetate test led to the diagnosis of progesterone hypersensitivity, prompting treatment with high-dose antihistamines and no epinephrine administration [5]. In 2017, Lin et al. expressed a case of CA in a 48-year-old non-pregnant female with neck edema and angioedema persisting for 3 years, which was exacerbated by voice hoarseness and stridor, fortunately her symptoms were controlled after high-dose methylprednisolone, epinephrine, and diphenhydramine [6]. However, in our case, the suppressive medications as a conventional therapy proved ineffective so she had to take oral contraceptive pill or synthetic progesterone as a routine management strategy. While high-dose suppressive medications may be considered as an interim measure by some experts and desensitization with appropriate medications and dosages, such as monoclonal antibodies, presents a more favorable long-term approach [2,7,8].

Eight women in a Bauer et al. cohort with catamenial anaphylaxis showed heterogeneity in clinical manifestation and treatment; the majority of cases experienced gastrointestinal and cutaneous symptoms, had a median age of 34 years (range: 14-40 years) at the onset, and a median of 10 premenstrual anaphylactic episodes at presentation (range: 4-24 per patient). Progesterone skin tests yielded negative in all but one of four cases. Notably, high-dose systemic steroids, oral contraceptives, and certain NSAIDs failed to elicit improvement in any patient, while just one person was alleviated with antihistamines, and others responded positively to GnRH agonist and progesterone synthetic treatment highlighting the variable response to suppressive medications in a pattern that considered CA has a heterogeneous paradigm along numerous mechanisms and mediators as a role player in pathogenesis [9]. Furthermore, intriguing hypotheses persist regarding the etiology of catamenial anaphylaxis and it's unclear that IgE-mediated reactions triggered by the absence of progesterone at the onset of menstruation or in response to its fluctuations while it's noteworthy that in our case, the progesterone prick test was negative so it is possible to assume progesterone IT as a healing choice for the patients.

An alternative theory positing the involvement of Prostaglandins (PG), a vasoactive component of menstrual fluid, in catamenial anaphylaxis has gained traction. Research indicates that PGF2a synthesizes by the endometrium regulates mediator release in uterine mast cells, Additionally, PGI2, a potent vasodilator hormone at day 1 of the menstrual cycle in those who are vulnerable, may elicit systemic effects [1,9]. Verdolini et al. conducted a comprehensive evaluation with suspected prostaglandin hypersensitivity. The patient was also found to be hypersensitive to progesterone injection, prostaglandin-F2 analogue (carboprost tromethamine), andestradiol cream, she had a limited response to GnRH agonist and the PG inhibitor, demonstrating that CA was caused by endogenous prostaglandin in the menstrual fluid so hysterectomy was ultimately the last resource [10]. Overall, further research is imperative to elucidate the underlying mechanisms and optimize management strategies such endeavors are essential for enhancing the quality of life for affected individuals.

Conclusion

Catamenial anaphylaxis represents a unique and demanding subset of menstrual cycle-associated allergic reactions. Through meticulous evaluation and management, clinicians can adeptly identify and attend to the needs of patients afflicted by this rare condition. However, ongoing research efforts are essential to enhance our understanding of pathogeneses' catamenial anaphylaxis and improve patient outcomes.

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