

Grave anaphylactic-like reaction in the course of menstruation

A case report

The case of a woman with a serious anaphylactic pattern during menstruation is described. The patient had a clinical picture of urticaria, angioedema and shock at each menstruation for a period of 2 years until hysterectomy was performed. The studies showed no hormonal or immunological change. The only relevant finding was the extraordinarily strong vasodilating action of the menstrual fluid in the patient, and not in the controls. The results of the study suggest the possibility of two mechanisms: 1) an IgE-mediated mechanism causing hypersensitivity to some metabolic substance in the menstrual fluid and 2) an excessive pharmacological vasodilatory action produced by the prostacyclin in the fluid itself.

Key words: menstrual anaphylaxis; menstrual angioedema; menstrual fluid; menstrual urticaria.

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Allergic or allergic-like symptoms have been described in relation to the female sexual cycle. Urticarial wheals, or exacerbation or worsening of a chronic urticaria coinciding with pre-menstruation are the best known clinical patterns (6, 15). Exacerbation of other clinical symptoms during menstruation has also been observed, including bronchial asthma and vasomotor rhinitis (1, 2, 3, 7, 11, 14, 15).

The etiology and mechanisms of these pre-menstrual or menstrual symptoms are not known, although some hypotheses have been suggested (6, 7, 8, 10, 12, 13, 15).

The present paper reports on a patient with a severe anaphylactic-like reaction in the course of menstruation. The studies conducted revealed no immunological origin of the symptoms, which totally disappeared after a hysterectomy.

CLINICAL CASE

The patient is a 40-year-old woman. Menarche at 13 years. At age 37 an acute urticaria attributed to sea-food is an antecedent of interest. Since that time, there have been minor, sporadic urticarial episodes.

Ten months prior to consultation, the patient showed, during menstruation, a pattern described as anaphylactic shock, with intense general urticaria, facial, glottal and genital angioedema and hypotension. This reaction has since coincided exclusively with menstruation, and in the form of generalized urticarial eruption, intense, facial and lingual angioedema, dysphagia, respiratory difficulty, dysphonia due to glottal edema, cholic epigastralgia and hypotension. The pattern systematically commenced a few hours before menses began, with intense genital inflammation, lasting approximately 24-48 h. This was controlled by administration of high

doses of antihistamines and steroids. Because of the intensity and severity of the symptoms, the subcutaneous administration of epinephrine was sometimes necessary and, for the same reason, the patient was hospitalized on several occasions.

The patient had always been menorrhagic, her menses lasting from 5 to 6 days, at regular intervals of 27–28 days. The patient did not use analgesics during menstruation, but otherwise she had shown no intolerance to analgesic medicines. The clinical gynecological examination was normal during the asymptomatic period. The hemogram was normal, with a relative eosinophilia of 3%. ESR, urinalysis, blood and coagulation biochemistry were normal, hepatitis markers negative. The components of the complement C3, C4, Clq and Cl-inactivator were normal. IgG of 911 mg, IgM 115 and IgA 301. The IgE was 340 mU/ml. A study of the circadian rhythm of cortisol secretion showed the following figures: basal cortisol at 8 h, 13 U/100 ml. Following stimulation with ACTH (1 h later), 33 U/dl. At 20 h, 4 U/dl. The elimination of corticoadrenal metabolites (17-cetosteroids and 17-hydroxycorticosteroids) was found within normal limits and a study of the gonadal function showed a normal ovarian cycle (pregnandiol and total estrogens) with the two phases being maintained.

Immunological studies

Prick tests and RAST with common inhalants (Dermatophagoides, pollens and fungi) and foods, were negative. The cutaneous reaction with female hormones (pregnandiol, allopregnanediol, estrone, estradiol and estriol) and chemical mediators of inflammation (histamine, acetylcholine, polycarpine, kalicein and saline solution) were similar to those obtained in three healthy women controls.

Menstrual fluid

Menstrual fluid was taken by a hematophore during the first 24 h of menstruation (in the course of the clinical pattern with anaphylactic symptoms). The fluid was centrifuged and the supernatant separated and filtered with a Milli-

pore filter and used for skin testing in the patient and the three controls. Using the 1/1000 dilution, the skin test with menstrual fluid was strongly positive in the patient, with an immediate reaction of a 70 × 60 mm papule, with pseudopodia. The reaction disappeared after 90 min. At 24 h only a small induration of 2 mm diameter remained at the injection site. The tests on the healthy controls were negative to the 1/1000, 1/100 and 1/10 dilutions.

RAST

Munkel No. 00H paper discs previously activated with ^{Br}CN (4) were sensitized with undiluted menstrual fluid. The sensitized paper discs were subsequently challenged with the patient's serum and that of two healthy subjects, following the usual RAST method, and subsequently with anti-IgE antiserum marked with ¹²⁵I, and radioactivity measured with a gamma-counter. The result in the patient's serum (cmp) was similar to that obtained with the sera of healthy controls, and was considered negative.

Course and follow-up

An anovulatory was administered during two complete cycles but did not prevent the appearance of symptoms in the following menstruation. In view of the gravity of the symptom pattern, and since no other impediments existed, an oophorohysterectomy was performed, resulting in the total disappearance of the symptoms. The patient was given periodic check-ups for 2 years, and no relevant pathology has been recorded since that time.

Comments

In the case under study, the symptoms suggested a serious anaphylactic or anaphylactic-like pattern, clearly related to menstruation. It was not possible to prove hormonal hypersensitivity and there was no previous history of analgesic hypersensitivity or food allergy. Neither was there evidence of toxic shock (9), which has been reported to stem from a *Staphylococcus aureus* infection.

The evidence is that the patient's menstrual fluid acted as a potent vasodilator, producing a significant wheal when injected subcutaneously at high dilutions. Inflammation of the genitals when in contact with menstrual fluid can be added to the pattern of angioedema, urticaria and shock. On the other hand, this fluid did not act as a vasodilator in the controls.

Two pathogenic possibilities could be involved:

- 1) An IgE-mediated mechanism, whose antigen would be a product of proteinic degradation contained in the menstrual fluid. Supporting this hypothesis would be the positive skin test result in the patient herself. The negative RAST does not exclude the possibility of this IgE mechanism.
- 2) A pharmacological mechanism mediated by prostaglandins, mainly PGI₂ (prostacyclin), which is a powerful vasodilator (5, 14). Since the test with menstrual fluid containing these pharmacologically active substances produced a positive skin reaction only in the patient, and not in the controls, it should be assumed (if this hypothesis were accepted) that the patient had a specific sensitivity to the pharmacological action of this substance.

At all events, the course after the hysterectomy confirms that some substance in the menstrual flow was responsible for the pattern, whatever the mechanism.

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