CASE REPORT

Chronic vulvovaginal pruritus treated successfully with GnRH analogue

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A Medline search shows that this is the first reported case where vulvovaginal pruritus was treated successfully with a GnRH analogue. The report describes a patient with chronic premenstrual vulvovaginal pruritus thought to be attributable to autoimmune progesterone dermatitis.

A 35 year old, white woman, presented with intractable, chronic premenstrual vulvovaginal itching and discharge of six years' duration, which began after she started the combined contraceptive pill (CCP). The symptoms persisted despite withdrawal of the CCP and treatment with various agents including antimycotic creams and pessaries, oral fluconazole, and ketoconazole. Medical history and gynaecological clinical examination were unremarkable. A full blood count, urea and electrolytes, liver function test, random blood glucose, and a high vaginal swab (HVS) were normal. A clinical diagnosis of chronic premenstrual non-albican candidial vulvovaginitis was made and treatment with local povidone-iodine 10% solution (Betadine, SSL) paint application, oral ketoconazole, and premenstrual fluconazole was started. After an initial improvement her symptoms persisted 2.5 years with this regimen. A repeat HVS was negative. Considering her premenstrual symptoms medical suppression of ovulation was discussed and empirical treatment with four weekly intramuscular injection (depot) of a GnRH analogue (leuporelin acetate, Wyeth, 3.75 mg) was started. Her symptoms disappeared as soon as menstruation stopped. She continued with this for six months. A presumptive diagnosis of autoimmune progesterone dermatitis (APD)¹ was made. She declined a progesterone challenge test and add-back treatment on the basis that the progestogen in the CCP might have started the pruritus. She resumed normal menstruation without the vulvovaginal pruritus soon after completing the treatment. She remained symptom free over 18 months after stopping the GnRH analogue. She opted to be sterilised.

DISCUSSION

This is the first case report where cyclical vulvovaginal pruritus was treated with GnRH analogue. A possible diagnosis of APD was made in this patient on the basis of the luteal phase vulvovaginal pruritus, which was recurrent on cyclical basis.²

Initial diagnosis of fungal infection remains one of the most common causes of vulvovaginal itching. However, non-albicans species are found in around 20% of patients with recurrent infection where an HVS could be negative.³ Conventional antimycotic treatment is not as effective against these species as against *Candida albicans*. On presentation we thought this was a case of non-albicans candida infection and therefore, treatment with a

combination of local povidone-iodine 10% solution and oral antifungal preparation, was started.

APD is a rare and unusual premenstrual cyclic reaction to progesterone produced during the luteal phase of the menstrual cycle with polymorphic clinical manifestations including erythema multiforme, eczema, urticaria, angioedema, and anaphylaxis.⁴⁻⁵ Geber⁶ in 1921, reported the first case of APD and since then around 50 cases have been published. The pathogenesis of APD is unclear. Hypothetically, an autoimmune phenomenon or allergy to progesterone or progestogens (type I or IV hypersensitivity reactions) may occur by exposure to raised concentrations of endogenous hormone during pregnancy or menarche or an exogenous hormone (CCP).²⁻⁴⁻⁵ A case of anaphylaxis-like reaction during menstruation in a patient with no history of hormone therapy has been reported.⁷ Ideally diagnosis of APD should be confirmed by the detection of antibodies to progesterone, but such immunofluorescence tests have been reported to be negative in many cases and therefore not essential to make a diagnosis.⁸ This test was indeed considered in this case soon after she became amenorrhoeic. The immunologist suggested the demonstration of progesterone sensitivity by means of oral, intradermal, or intramuscular administration of progesterone as challenge tests has been reported as negative in several cases.²⁻⁵ In this case, the patient declined a progesterone challenge test knowing the risk of recurrence of her vulvovaginitis and test related anaphylactic reaction.⁵ Stephens *et al*⁹ felt that no further investigation is justified in patients who are controlled with agents that create anovulation and low progesterone concentrations. Although spontaneous remission has been reported, this is usually after a prolonged period of expectant management.⁵ Other treatment options that have been described with variable effects includes ethinylestradiol, conjugated oestrogen, danazol, tamoxifen, and surgical oophorectomy.⁴⁻⁵

In our case amenorrhoea induced by the GnRH could have had placebo effects. But in this patient we cannot explain the prolonged benefit of GnRH therapy. Research has been proposed that within the thymus leutinising hormone releasing hormone (LHRH) plays a unique part of immunomodulator, contributing to the sex dependent changes in the immune responses during the menstrual cycle as well as pregnancy.¹⁰ It also seemed that LHRH as a peptide may act as an immunological response modifier in the brain-pituitary-lymphoid-gonadal axis.¹⁰ In this case GnRH analogue may

Lesson to learn

Intractable cyclical vulvovaginitis despite prolonged antifungal treatment and negative microbiology should prompt autoimmune progesterone dermatitis as a possible cause and treatment with a GnRH analogue may be considered.

have worked by removing the repeated progesterone stimulus and helping to repair the malfunction of local immune response or desensitisation.

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