A Case of Estrogen Dermatitis

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Sensitivity to estrogen has been described previously. The clinical picture is varied with pruritus, either generalized or localized or as urticaria. The hallmark of estrogen dermatitis is the cyclic premenstrual flare. The patient reported here had cyclic erythema multiforme-like lesions and showed a positive intradermal skin test to estrogen. A 20-year-old female patient presented with a periodic 5 year duration of skin lesions on both hands. The eruption commenced in the second half of the menstrual cycle, worsened through the luteal phase but the lesion almost disappeared during menstruation. An intradermal skin test to estrone showed positive results. However, a skin test with medroxyprogesterone acetate was negative. After systemic steroid and antihistamine therapy, the lesions were found to be significantly improved.

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Key Words : Erythema multiforme, Estrogen

In 1995, Shelley et al,[1] reviewed 6 cases diagnosed initially as autoimmune progesterone dermatitis. However, they had a positive intradermal skin test to estrone and a negative test to progesterone. The authors suggested the term "estrogen dermatitis" rather than " autoimmune estrogen dermatitis" to include diseases in which immune modulation by estrogen occurs rather than by direct sensitivity to estrone. The hallmark of estrogen dermatitis is the cyclic premenstrual flare. The patients will complain premenstrually, but the lesions will usually subside during menstruation. The clinical picture varies like in autoimmune progesterone dermatitis and consists of localized pruritus, urticaria, or inflammatory vesicles and papules. However, the lesions tend to involute during pregnancy and at menopause. Herein, we describe a patient with cyclic premenstrual flare of erythema multiforme-like skin lesions showing a positive intradermal test to estrogen.

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REPORT OF A CASE

A 20-year-old woman presented with a 5 year history of cutaneous eruptions occurring every month, beginning mid-cycle and resolving within a few days of menstruation. Figure 1 shows a schematic diagram of the relationship of the eruption to the menstrual cycle of the patient. The lesions seemed to be aggravated after taking oral contraceptives. Her past and family history were not significant. The lesions comprised of pruritic erythematous macules and papules on both hands(Fig. 2A,B,C). All routine laboratory tests were negative or within normal limits. The biopsy taken from the hand lesion showed a mixed dermal-epidermal type of erythema multiforme with mononuclear infiltration and hydropic degeneration on the dermal-epidermal junction with individual necrotic keratinocytes in the epidermis(Fig. 3A,B). Duplicate intradermal skin tests on the forearm of the patient were done; medroxyprogesterone(Depo-Provera^{R}, 0.1ml, 1mg/ml) was injected and the response was interpreted at 15 minutes, 2 hours and at 24 hours; estrone(Theelin Aqueous^{R}, 0.1ml, 1mg/ml) at 15 minutes, 2 hours and at 24 hours(Table 1). The response at the site of the estrogen injection at 15 minutes compared to the control site(normal saline, 0.1ml) showed an im-

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Table 1. Results of provocative intradermal skin test

Time after intradermal injection	Estrone(Theelin Aqueous, 0.1ml, 1mg/ml)	Medroxyprogesteron(Depo-Provera, 0.1ml, 1mg/ml)
15 minutes	Positive	Negative
2 hours	Positive	Negative
24 hours	Positive	Negative

mediate wheal reaction(Fig. 4A). The estrone skin sites remained indurated for more than 24 hours(Fig. 4B), immediate and delayed responses after the skin test with progesterone showed a negative result(Fig. 4C). A diagnosis of estrogen-induced erythema multiforme was made and treatment with systemic steroid and systemic antihistamine had some benefit.

DISCUSSION

Erythema multiforme can be due to a wide variety of causes[2]. When associated with menstruation it can be a manifestation of autoimmune progesterone dermatitis[3]. Autoimmune progesterone dermatitis is characterized by a recurrence of a skin eruption in association with the hormonal changes of the menstrual cycle[4]. Since Shellys et al[6] demonstrated a case of severe generalized erythema multiforme that was caused by progesterone sensitivity, many cases have been reported. Autoimmune progesterone dermatitis develops cyclic and recurrent eruptions with polymorphic manifestations of eczematous[7], and erythematous patches[5], urticarial[8,9], and erythema multiforme-like eruptions[4], and papulopustular lesions[6]. In these cases, positive skin tests with progesterone have shown immediate reactions[5], and delayed hypersensitivities[6,7]. However in our case, although the clinical picture may resemble progesterone dermatitis, a cyclic premenstrual flare with positive estrogen skin test led us to think of the diagnosis of estrogen dermatitis. There are reports of progesterone dermatitis in Korea. However, estrogen dermatitis has not been re-

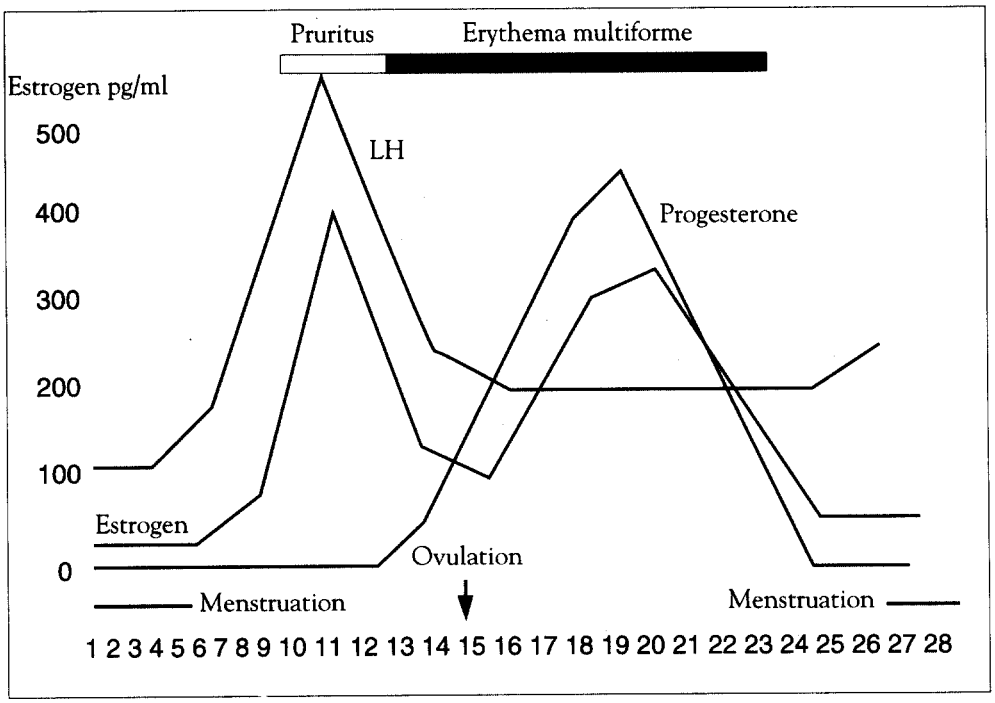

Fig. 1. A schematic diagram of the relationship of the eruption to the hormonal cycle of the patient.

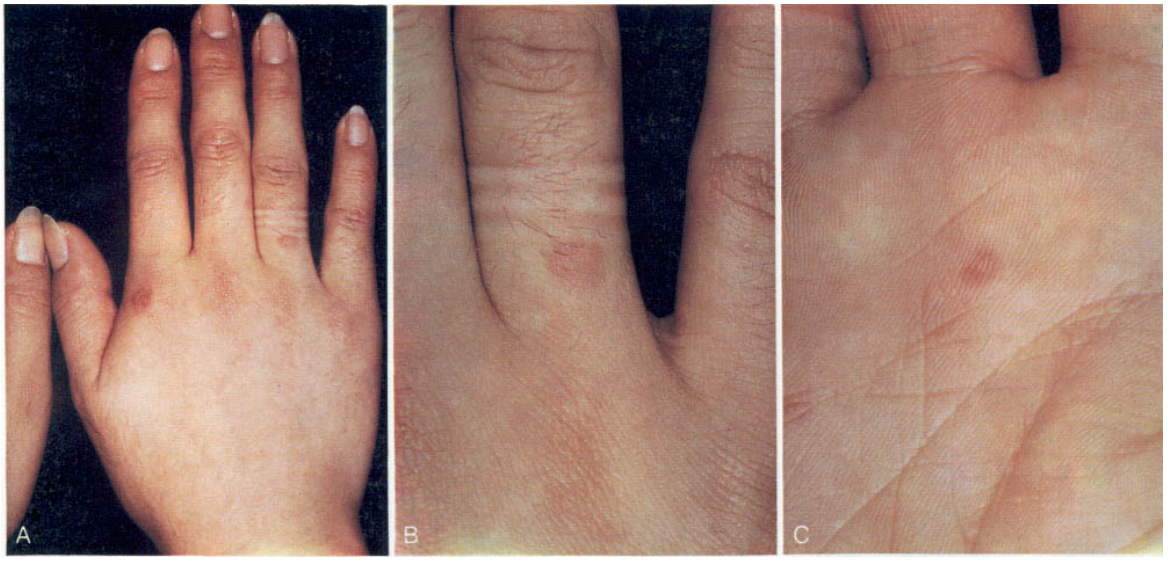

Fig. 2. Clinical picture of erythema multiforme.
A: Match-head to rice sized erythematous macules and papules on both hands.
B: Close -up view of the lesion on the finger.
C: Close -up view of the lesion on the palm.

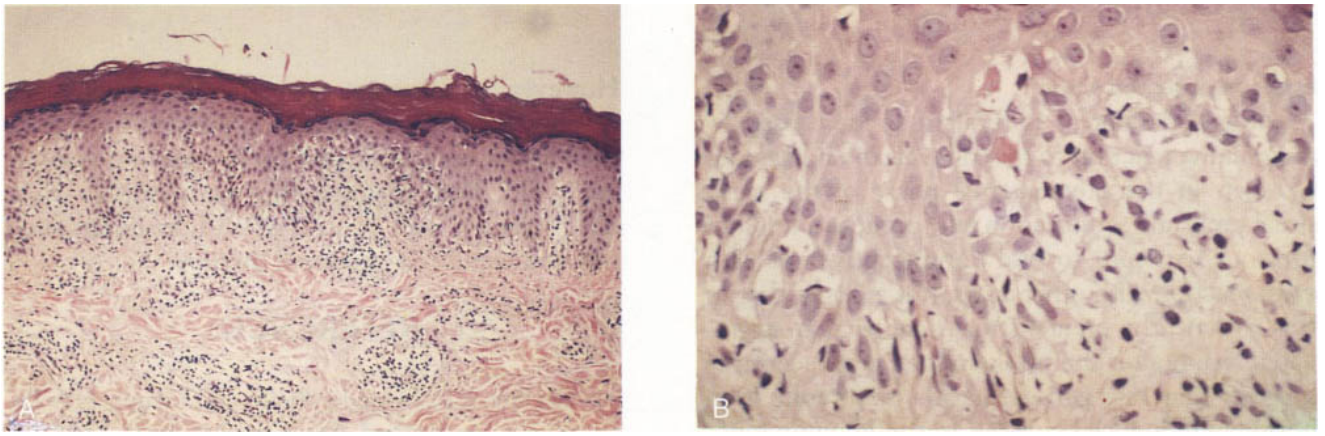

Fig. 3. Mixed dermal-epidermal type of erythema multiforme.
A : Mononuclear cell infiltrates are present along the dermal-epidermal border. The basal cells show hydropic degeneration(× 100).
B : The epidermis contains individual necrotic keratinocytes with eosinophilic cytoplasm(× 400).

ported yet.

Intradermal skin tests are necessary to establish the diagnosis of estrogen dermatitis. It is essential that intradermal test material be injected subepidermally to raise a superficial bleb and minimize rapid lymphatic removal. A 0.1 ml of 1:1,000 dilution (1mg/ml) of Theelin^{R} (aqueous estrone) was injected with a tuberculin syringe with a 27-gauge needle. Persistence of a papule for more than 24 hours is considered a positive test. An oral challenge may also be done with ethinyl estradiol, but a positive result supports only an estrogen aggravated dermatitis[1]. The estrogen skin test of our patient showed an immediate wheal reaction on the test site which remained indurated after 24 hours, whereas, negative results were shown on the prog-

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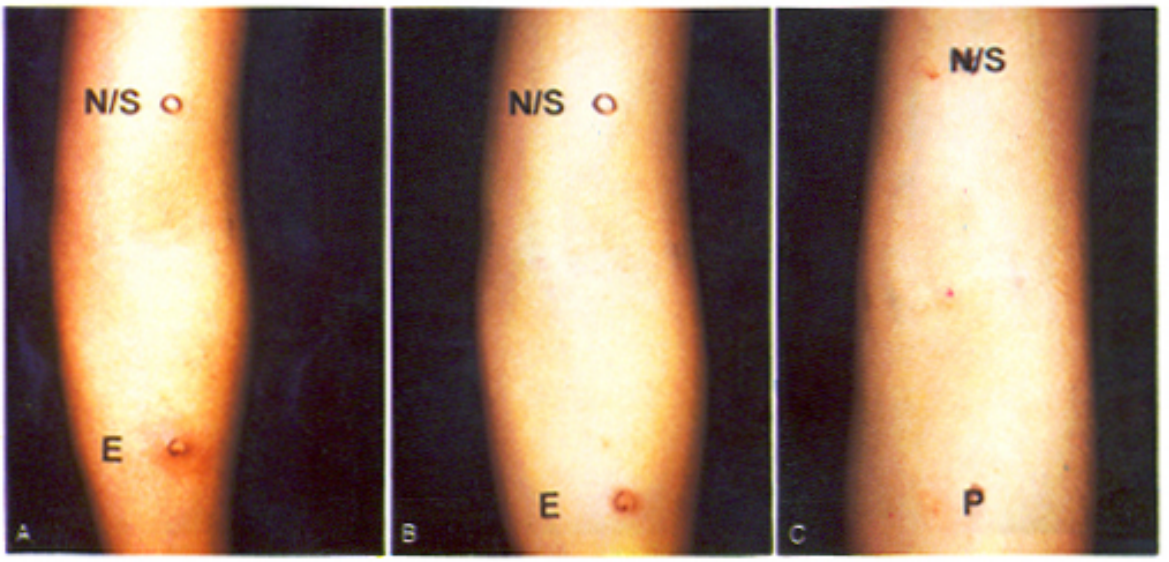

Fig. 4. Intradermal skin test reaction.
A : Immediate reaction of the intradermal skin test with estrogen. Response at the site of the estrogen injection at 15 minutes compared to the control site.
B : Positive intradermal skin test at 24 hours after the estrogen injection.
C : Negative response after the skin test with progesterone.

esterone injected site.

Estrogen dermatitis is thought to be caused by an immune reaction to raised levels of endogenous estrogen in the premenstrual phase of the menstrual cycle and sensitization may occur as a result of previous exposure to oral contraceptives or as a cross-reaction with other drugs. It is thought that in this patient, the premenstrual flare with an aggravated lesion after the intake of oral contraceptives suggests that estrogen dermatitis may result from hormonally induced changes in the immune function.

Therapy of estrogen dermatitis can vary from systemic antihistamine, corticosteroids, progesterone and oophorectomy. A specific treatment is antiestrogen, tamoxifen[R](10mg one to three times a day for 10 to 14 days before each period). Tamoxifen[R] interferes with the clinical expression of estrogen sensitivity, possibly via its competitive binding of the estrogen receptors[1]. The drug must be kept at the minimal effective level and given intermittently as briefly as possible. Desensitization requires intradermal injection of premenstrual serum every other day for 1 to 2 months. The injections are given four successive times in the same skin site. However, in our case, tamoxifen therapy was refused by the patient since she wanted to have children in the near future and the lesions were considered mild, disappearing during menstruation. Now the patient is well controlled with systemic antihistamine and corticosteroid therapy.

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