

Homozygous compared with homozygous		
First mole	Second mole	
	P ₁ P ₁	P ₂ P ₂
P ₁ P ₁	x	o
P ₂ P ₂	o	x

A

Heterozygous compared with heterozygous				
First mole	Second mole			
	P ₁ P ₁	P ₁ P ₂	P ₂ P ₁	P ₂ P ₂
P ₁ P ₁	x	o	o	o
P ₁ P ₂	o	x	x	o
P ₂ P ₁	o	x	x	o
P ₂ P ₂	o	o	o	x

B

Homozygous compared with heterozygous				
First mole	Second mole			
	P ₁ P ₁	P ₁ P ₂	P ₂ P ₁	P ₂ P ₂
P ₁ P ₁	x	o	o	o
P ₂ P ₂	o	o	o	x

C

Fig. 2. Combinations of allelic patterns indistinguishable from a truly different mole on an informative locus. **A.** Homozygous–homozygous allelic pattern. **B.** Heterozygous–heterozygous pattern. **C.** Homozygous–heterozygous pattern. P₁ and P₂, two paternal alleles with different repeat numbers; open circle, distinguishable; X, indistinguishable.

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than $(1/2)^n$. In the case of a homozygous mole and a heterozygous mole, the probability of misjudgment is given simply by $(1/4)^n$ (Fig. 2C). The combination of

alleles is given by $(P_1P_1, P_2P_2) \times (P_1P_1, P_1P_2, P_2P_1, P_2P_2)$ for homozygous and heterozygous moles, respectively, and their distinction is impossible in one-quarter of cases. Again, the possibility of misjudgment is quite low. Collectively, distinction of the origins of two moles in one person by short tandem repeat analysis is highly reliable, as for the diagnosis of trophoblastic disease.

The accuracy of the polymerase chain reaction-based DNA analysis depends on the purity of the DNA sample. This is especially true if a tiny amount of possibly mixed tissues is used. In the present case, stereomicroscopic dissection was performed to identify chorionic tissues and eliminate possible contamination with maternal cells. In conclusion, DNA analysis appears to be useful for the differential diagnosis of consecutive moles separated by a short time interval.

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Progesterone Autoimmune Dermatitis With Positive Autologous Serum Skin Test Result

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BACKGROUND: Progesterone autoimmune dermatitis is a rare disease attributable to hypersensitivity to endogenous progesterone and characterized by cyclic derma-

tologic manifestations at the end of the luteal phase that disappear some days after menses.

CASE: A 35-year-old woman experienced cyclic premenstrual urticaria and angioedema occurring from 4 days before to 5 days after menses. The diagnosis of progesterone autoimmune dermatitis was made by a progesterone-positive skin test. Autologous serum skin test, using sera from estrogenic and luteal phases, also elicited a positive response. The patient became pregnant with near-clearance of the urticaria.

CONCLUSION: Skin tests with progesterone and autologous serum, which are easy to perform, convenient, and

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inexpensive, are highly useful for establishing the diagnosis of progesterone autoimmune dermatitis and ruling out other skin disorders.

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Progesterone autoimmune dermatitis is a rare disease caused by hypersensitivity to endogenous progesterone and characterized by cyclic dermatologic manifestations at the end of the luteal phase of the menstrual cycle that disappear a few days after menses.¹ Clinical symptoms include urticaria, eczematous eruptions, vesicles, pustules, erythema multiforme, and anaphylaxis.² The diagnosis is clinically suspected and confirmed by progesterone-positive skin tests or intramuscular progesterone challenge or both.^{2,3} The definitive etiologic treatment consists of ovulation inhibition by drugs or oophorectomy.^{1,4}

CASE

A 35-year-old woman with a clinical history of dust mite allergic rhinitis and mild intermittent asthma and no history of dysmenorrhea, menstrual irregularities, or oral contraceptive use was evaluated for recurrent urticaria and angioedema. At the age of 28, she started to experience generalized erythematous, pruritic wheals, and areas of edema on the face and limbs, which appeared exclusively from 4 to 5 days before to 5 days after menses and had poor response to antihistamines and corticosteroids. Between the ages of 31 and 34, she was treated with Diane-35 (cyproterone acetate 2 mg plus ethinyl estradiol 0.035 mg) for polycystic ovary syndrome and symptoms markedly improved; however, 6 months before the visit she decided to attempt pregnancy. The hormonal treatment was withdrawn and she switched to herbal homeopathy. Physical examination performed on day 5 of her menstrual cycle revealed multiple itchy maculopapular wheals and areas of edema on the face and lower limbs. Skin prick tests to determine sensitivity to common inhalant allergens were positive for dust mites and grass pollen; skin prick tests to determine sensitivity to foods were negative. Blood count, erythrocyte sedimentation rate, biochemistry, and thyroid-stimulating hormone were normal. Ethinyl estradiol-17 β , progesterone, and 17-hydroxyprogesterone were within normal limits. Antinuclear antibodies and anti-nDNA were negative. Serum tryptase, immunoglobulin (Ig) G, IgM, IgA, and complement factors (C3, C4) were within normal limits. Immunoglobulin E was 488 international units/mL (less than 100 international units/mL). A basophil activation test and a lymphoproliferative stimulation test to progesterone were negative. The biopsy result of affected skin demonstrated mild perivascular dermatitis with minimal mixed interstitial inflammation consistent with urticaria.

With the suspicion of progesterone autoimmune dermatitis, prick tests and intradermoreactions with medroxyprogesterone acetate (Farlutal) were performed. After a negative prick test, an intradermoreaction with 0.002 mg/mL produced a strong, itchy wheal and flare response at 20 minutes, persisting at 2 hours (Fig. 1A). Autologous serum skin tests performed during the estrogenic phase using 0.05 mL of patient serum collected in both estrogenic and luteal phases showed strong positive responses (erythematous wheals more than 8 mm) at 30 and 60 minutes (Fig. 1B). The diagnosis of progesterone autoimmune dermatitis manifesting clinically as recurrent urticaria was made. One month later, the patient became pregnant and symptoms almost disappeared, with only occasional mild wheals on lower legs that have required no treatment until present (week 32 of gestation).

COMMENT

Progesterone autoimmune dermatitis is a rare disease, with approximately 60 cases described to date. Atopy and familial aggregation are not risk factors, although a report of three sisters was recently published.⁴ In some cases, the condition has been associated with polycystic ovary disease.⁵

Age at onset is variable but always between menses and menopause. In many cases a history of exogenous progesterone administration has been recorded² and in others the disease began during pregnancy⁴ or soon after delivery,¹ whereas in some patients none of these factors was observed.⁶ Some women became disease-free during pregnancy,^{3,7} with a natural desensitizationlike phenomenon developing, probably because of a slow gradual increase in progesterone levels, as seems to have occurred in our patient, whereas pregnancy resulted in exacerbation of symptoms in the majority.^{4,8} In one pregnant patient with severe progesterone autoimmune dermatitis manifested with urticaria, angioedema, and dyspnea, delivery by cesarean was complicated with anaphylactic shock, requiring immediate treatment with vasopressors.⁵ On occasion the disease may resolve spontaneously,¹ but in general the clinical course is chronic, long-lasting, and described as highly distressing for the patient. Urticaria, sometimes accompanied by angioedema, is the most common manifestation of progesterone autoimmune dermatitis, although other clinical manifestations including anaphylaxis,⁵ laryngeal edema, erythema multiforme,⁸ eczematous or vesicular eruptions, erythema annulare centrifugum,⁷ purpura, and fixed drug eruption may occur.

The diagnosis of progesterone autoimmune dermatitis, whatever the clinical manifestations may be,



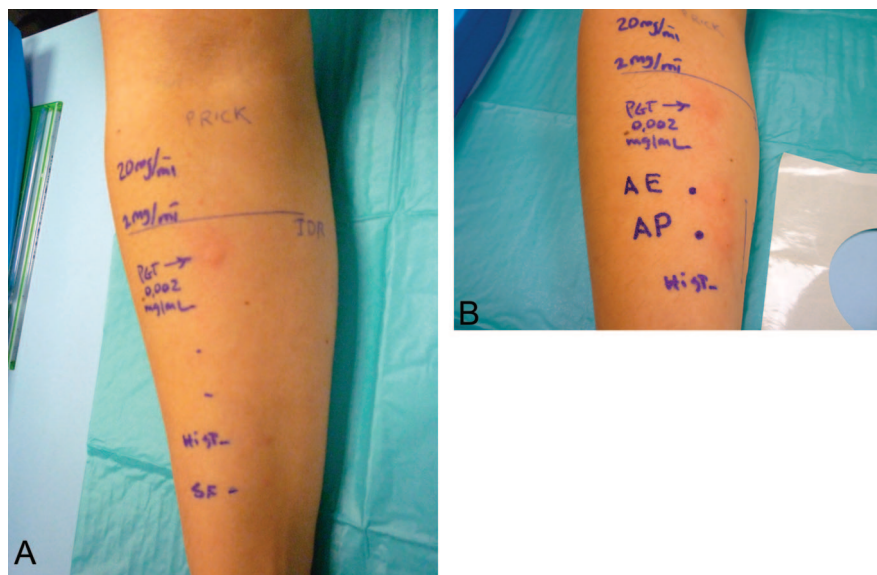


Fig. 1. A. Positive skin test with progesterone in a patient with progesterone autoimmune dermatitis. Picture taken 20 minutes after performance of intradermoreaction. From top to bottom: prick tests to progesterone 20 and 2 mg/mL; intradermoreaction to medroxyprogesterone 0.002 mg/mL. Hist, histamine 10 mg/mL (positive at the 15-minute reading); SF, phenolated saline. **B.** Positive skin tests with progesterone and with autologous serum in a patient with progesterone autoimmune dermatitis. Picture taken 30 minutes after performance of autologous serum intradermoreactions. From top to bottom: prick tests to progesterone 20 and 2 mg/mL; intradermoreaction to medroxyprogesterone 0.002 mg/mL (still positive). AE, autologous serum skin test with estrogenic-phase sample; AP, autologous serum skin test with luteal-phase sample; Hist, histamine 10 mg/mL (positive at the 15-minute reading).

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is based on the typical cyclic symptoms pattern, demonstration of progesterone-positive skin test results,^{1,2,4,7} reproduction of symptoms with progesterone challenge,³ or detection of purified antibodies to progesterone or its derivatives,⁸ or a combination of these. Different concentrations of progesterone and vehicles, ranging from 0.1 to 50 mg/mL, have been used for skin tests^{1,2,6}; the reactions can be immediate⁷ or delayed (from 6 to 96 hours).^{1,6} We recommend the use of a small volume (0.02 mL) from 0.2 to 20 mg/mL of medroxyprogesterone in aqueous suspension, which we proved to be nonirritant in two controls, to avoid false-positive results. Patch tests to test sensitive for progesterone have been repeatedly reported as negative.² In occasional patients, specific IgG anti-progesterone or anti-17-hydroxyprogesterone⁸ or T-cell sensitization to progesterone after the development of a specific interferon- γ release assay⁷ have been demonstrated.

Most patients with progesterone autoimmune dermatitis are unresponsive to the different treatments assayed, including antihistamines, corticosteroids, danazol, stanazolol, doxepin, azathioprine,² or even thalidomide,⁶ and some of these are too toxic to be

used in the long-term. Thus, suppression of ovulation with oral contraceptives,² estrogens,² tamoxifen,⁶ or GnRH analogs such as leuprolid acetate⁶ have been used as etiologic treatment. In the 1960s, some desensitization procedures were attempted in occasional patients, resulting only in temporary improvement or being directly unsuccessful,¹ although successful desensitization was performed recently in a patient with progesterone autoimmune dermatitis and ovarian cancer who had progesterone-induced urticaria develop after starting progesterone supplements after oophorectomy.³ Nevertheless, long-term side effects of all these drugs and procedures also should be taken into account, and bilateral oophorectomy has been established as the only curative treatment for patients with unacceptable side effects of hormonal treatment or in whom significant symptoms remain.^{4,6}

Autologous serum skin test has proved useful in the detection of skin autoreactivity in some autoimmune urticarias, such as autoimmune thyroid-associated urticaria or anti-IgE autoimmune urticaria.⁹ We suggest that this simple, convenient, and inexpensive diagnostic tool is useful in the diagnosis of progesterone autoimmune dermatitis and indicates an autoimmune mechanism⁸ in this rare disease.



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Parathyroid Adenoma With Hypertensive Crisis and Intracerebral Hemorrhage Mimicking Hemolysis, Elevated Liver Enzymes, Low Platelets Syndrome

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BACKGROUND: Hyperparathyroidism is seldom encountered during pregnancy. Moreover, when the disease does occur, it is typically masked until late pregnancy or after delivery.

CASE: A previously healthy multiparous woman presented with sudden-onset severe preeclampsia with hemolysis, elevated liver enzymes, low platelets syndrome at 37 weeks of gestation. Acute intracerebral hemorrhage and disseminated intravascular coagulopathy developed 24 hours after cesarean delivery and persisted after craniotomy. Hypercalcemia and hyperparathyroidism were noted, and imaging studies revealed parathyroid tumor. The patient recovered from severe preeclampsia

after resection of a hemorrhagic parathyroid adenoma and was fully rehabilitated after 3 months.

CONCLUSION: This patient exhibited a concealed hyperparathyroidism with acute hypertensive crisis, probably attributable to hemorrhagic parathyroid adenoma. The presentation mimics acute late-onset preeclampsia and requires vigilant diagnosis followed by surgery.

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Hyperparathyroidism in pregnancy is rare.¹ Manifestations of this condition can be countervailed by the physiological changes in pregnancy and are typically masked until term or after delivery. Parathyroid adenoma is the main cause of primary hyperparathyroidism.³ Clinical presentations can involve typical or atypical preeclampsia, creating difficulties in diagnosis. We report a case of initial presentation of severe preeclampsia developing into hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome and worsening to intracerebral hemorrhage after emergent cesarean delivery. The condition of the patient improved markedly after removal of the tumor.

CASE

A 32-year-old multiparous woman underwent regular and uneventful antepartum care until week 37 of her pregnancy, when she exhibited sudden-onset dull epigastric pain and elevated blood pressure (185/95 mm Hg). She had previously experienced two normal vaginal deliveries without morbidity. Physical examination revealed epigastric tenderness and a 3+ deep tendon reflex with no pitting edema. Obstetrics sonography revealed no evidence of placental abruption. Her blood pressure increased to 190–215/100–115 mm Hg, and two doses of nifedipine 10 mg sublingual were administered without result. Laboratory studies revealed total bilirubin/direct bilirubin of 4.6/1.4

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