circulating basement membrane zone and antibodies, and (5) direct immunofluorescence findings that reveal IgG, IgM, or both, and, often, IgA at the basement membrane zone. The bullous eruption in our patient fulfilled these criteria. The immune deposits localized to the lamina and sublamina densa were also identical to those present in the bullous eruption of SLE.[6] This is the same region where immunoreactants for epidermolysis bullosa acquisita are found. Results of indirect immunofluorescence studies have usually been negative in the bullous eruption of SLE. However, Gammon et al.[7] demonstrated circulating antibodies to the epidermolysis bullosa acquisita antigen in three of four patients with bullous SLE by use of 1.0 mol/L sodium chloride–separated human skin as a substrate in their indirect immunofluorescence assay. In contrast, with the same technique Camisa and Grimwood[8] found no staining in four cases of bullous SLE. Recently Gammon and Briggaman[9] suggested that there were at least two immunologically distinct subtypes of bullous SLE characterized by the presence or absence of circulating or tissue-bound basement membrane zone autoantibodies, or both that recognize type VII collagen. The bullous eruption of SLE shares histologic and immunopathologic features with both DH and epidermolysis bullosa acquisita; therefore there may be heterogeneous causative factors that explain the inconstant serologic findings.

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Porphyria cutanea tarda: Pregnancy versus estrogen effect

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We describe the worsening of porphyria cutanea tarda in a young woman while she was taking oral contraceptives. However, she did not have an exacerbation during two pregnancies. We conclude that estrogens produced during pregnancy do not exert the same effect as orally administered medications that contain estrogen. The pronounced effect of oral ethinyl estradiol on the liver may be attributed to its first-pass effect on that organ. (J AM ACAD DERMATOL 1994;31:390-2.)

Porphyria cutanea tarda (PCT) is a metabolic disorder of heme biosynthesis characterized by vesicles and bullae, hypertrichosis, skin fragility, hyperpigmentation, and sclerodermoid changes that occur predominantly in sun-exposed areas. A defect in the activity of uroporphyrinogen decarboxylase[1] results in the accumulation of specific porphyrins.

Many chemical agents and drugs have been implicated as precipitating factors in PCT. Although reduced activity of uroporphyrinogen decarboxylase is a specific and intrinsic defect in PCT, modulation

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Table I. Uroporphyrin and coproporphyrim levels in pregnant and nonpregnant states

Status	Date	Uroporphyrin level in urine (NL <28 μg/24 hr)	Coproporphyrin level in urine (NL 72-275 μg/24 hr)	Uroporphyrin level in feces (NL <1000 μg/24 hr)	Protoporphyrin level in feces (NL <1500 μg/24 hr)	Coproporphyrin level in feces (NL <200 μg/24 hr)
Taking oral contraceptives	10/83	307	279			
No oral contraceptives						
Conception	3/84					
	4/84	65	52			
	6/84	52	65			
	7/84	38	60	45	301	71
	9/84	46	71	8	409	108
	10/84	52	69			
	11/84	52	83			
	4/85	52	65			
Delivery	11/85					
	7/86	72	73			
	10/86	29	54			
	11/86	52	83			
Conception	3/87					
	8/87	26	44			
	10/87	35	65			
	11/87	40	129			
Delivery	12/87					
	4/88	24	29			
	3/91	18	27			
	5/91	22	31			
	9/93		Fluorescent porphyrin spectrum scanning: serum porphyrin <1 μg/dl (NL <1 mg/dl)			
	11/93	22	17			

NL, Normal level.

of porphyrin synthesis by extrinsic factors is required for full biochemical expression of the disease.[2] Use of oral estrogens for contraception in women and in men treated for prostatic cancer has been reported to exacerbate the disease.[3, 4]

We describe a woman with PCT that was clinically active while the patient was taking oral contraceptives and who had a remission when she discontinued use of oral contraceptives. The patient had two term pregnancies without any clinical or biochemical evidence of recurrence.

CASE REPORT

In July 1983 a 30-year-old Oriental woman had vesicles, crusts, and milia on the dorsum of the hands and facial hypertrichosis. A biopsy specimen revealed a subepidermal blister with sharp separation of the epidermis from the papillary dermis with preservation of papillae, and a sparse infiltrate around the vessels of the superficial plexus. Urine uroporphyrin, urine coproporphyrin, and serum iron levels were elevated. A diagnosis of PCT was made. The patient had given birth several years before and was given an oral contraceptive (Ortho-Novum). Before the use of oral contraceptives, the patient denied having any skin lesions and first noticed blisters and increased facial hair about 1 year after she started using the oral contraceptive. She was instructed to stop taking the oral contraceptive, to avoid iron supplements, and to use an alternative birth control method. The patient discontinued use of oral contraceptives, underwent phlebotomy, and noted marked clinical improvement.

Six months later the patient was 1 month pregnant and the urine uroporphyrin level was normal. The patient gave birth to a healthy male infant. A year later, in the nongravid state, urine uroporphyrin levels were again normal. The next year the patient was 5 months pregnant and the urine uroporphyrin level was again normal. A normal female infant was delivered at term. Urine uroporphyrin levels were normal 4 months post partum (Table I).

During pregnancies the patient remained free of symptoms. The mother and her children were healthy as of September 1993. Serum porphyrin fluorescent scanning and total porphyrin levels (<1 μg/dl) were normal.[5]

DISCUSSION

During pregnancy a woman cannot avoid increases in estrogens. Therefore pregnancy might be

expected to precipitate the clinical manifestations of PCT. This did not occur in our patient. Orally administered estrogens significantly increase renin substrate, thyroxine-binding globulin, and cortisol-binding globulin, all substances produced by hepatic metabolism.[6] Studies performed to compare oral versus transdermal delivery of estrogens revealed that the latter did not show this augmentation effect on hepatic proteins.[7] Because transdermal delivery of estrogens bypasses the liver's first-pass effect, it does not augment the liver's metabolic processes. This supports the concept that in PCT, the route of administration of estrogens determines their effect on liver metabolism. In pregnancy there is endogenous production of estrogens that bypasses the liver's first-pass effect; this might explain why our patient had an exacerbation of her disease while taking oral contraceptives, but not during her two pregnancies.

Studies have demonstrated that diethylstilbestrol can induce δ-aminolevulinic acid synthetase in chick embryo liver.[8] The induction of this enzyme would lead to an increase in substrate for uroporphyrinogen decarboxylase that is already low in PCT, or the hepatic effects of orally administered estrogens may inhibit the already reduced activity of uroporphyrinogen decarboxylase.

There have been other case reports that also demonstrate the clinical and biochemical inactivity of the disease during pregnancy.[9, 10] One patient had an exacerbation of the disease during the first trimester and a remission during the second and third trimesters.[11] The authors attributed this to iron depletion that occurs in the latter part of pregnancy. A second pregnancy in one of the above patients was not accompanied by biochemical or clinical recurrence of the disease. All patients had worsening of their disease while they were taking oral contraceptives.

Our patient's disease activity was clearly related to her intake of oral contraceptives. When these agents were discontinued clinical and biochemical remission occurred. The elevation in endogenous estrogens during the patient's two pregnancies did not precipitate a recurrence of her disease. It may be that transdermal delivery of estrogens is safe for patients with PCT.

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