Acta Derm Venereol (Stockh) 1985; 65: 313–318

Polymorphic Eruption of Pregnancy: Histopathologic Study

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Moreno A, Noguera J, de Moragas JM. Polymorphic eruption of pregnancy. Histopathologic study. Acta Derm Venereol (Stockh) 1985; 65: 313–318.

The microscopic findings in 31 biopsies of patients with polymorphic eruption of pregnancy are reported with a literature review. Cutaneous changes include edema, dermal lymphohistiocytic infiltrate and epidermal lesions. We have found a correlation between the intensity of the inflammatory response and the presence of epidermal involvement. In our opinion, the histopathological changes may allow an accurate diagnosis with the adequate clinical information. Direct immunofluorescence did not reveal immunoglobulin or complement deposits in the ten cases studied. It may help in the differential diagnosis with non-bullous herpes gestationis. (Received September 26, 1984.)

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Polymorphic eruption of pregnancy is a term coined by Holmes & Black (1) which encompasses the specific dermatosis of pregnancy characterized by urticarial eruptions. The term includes lesions previously called toxaemic rash of pregnancy (2), late onset prurigo of pregnancy (3), pruritic urticarial papules and plaques of pregnancy (4) and toxic erythema of pregnancy (5).

The clinical picture and evolutionary course of the disease have been well delineated in previous reports (4, 6, 7, 8) and can be summarized as follows: a cutaneous rash composed of papules and urticarial plaques, occurring in the third trimester of pregnancy, pruritus, location on abdomen and proximal aspects of the thighs, disappearance of the lesions before or in a few weeks after delivery, and absence of materno-fetal risks.

The morphologic picture of polymorphic eruption of pregnancy has been the subject of controversies since the first histological description reported by Lawley et al. (4). They described two different histological presentations, one with a superficial perivascular infiltrate and the other with superficial and deep perivascular infiltrate.

In this paper we report the microscopic findings in 31 biopsies from 28 patients with polymorphic eruption of pregnancy.

MATERIAL AND METHODS

Twenty-eight patients diagnosed as polymorphic eruption of pregnancy in the Hospital de San Pablo, Barcelona, form the basis of this study. Fourteen patients, found in a retrospective study from 1975 to 1981, have been reported previously (8). The other cases were diagnosed in a prospective study since 1981.

All the patients were pregnant women having a cutaneous rash during the third trimester of pregnancy that met the above mentioned criteria for the diagnosis of the disease. Clinical findings are summarized in Table 1. Both kinds of lesions, papules and urticarial plaques, were biopsied. In three patients two punch biopsies, one from a papule, the other from an urticarial plaque, were examined. Thirty-one cutaneous specimens were available for study.

All were fixed in Bouin's medium, and processed and stained by routine methods. In ten cases a direct immunofluorescence technique was used to detect the presence of immunoglobulins or complement in the lesions.

RESULTS

Three kinds of changes were demonstrated on light microscopic examination: dermal edema, inflammatory infiltrate and epidermal lesions (Figs. 1–3).

Dermal edema was present in all the specimens. It was usually mild to moderate except in three cases in which it was classified as severe, resulting in subepidermal vesiculation in two of these.

Inflammatory infiltrate was also evident in all the specimens. Lymphocytic and histiocytic cells were seen around dermal blood vessels involving the superficial plexus in 20 biopsies and both superficial and deep seated vessels in the remaining ones.

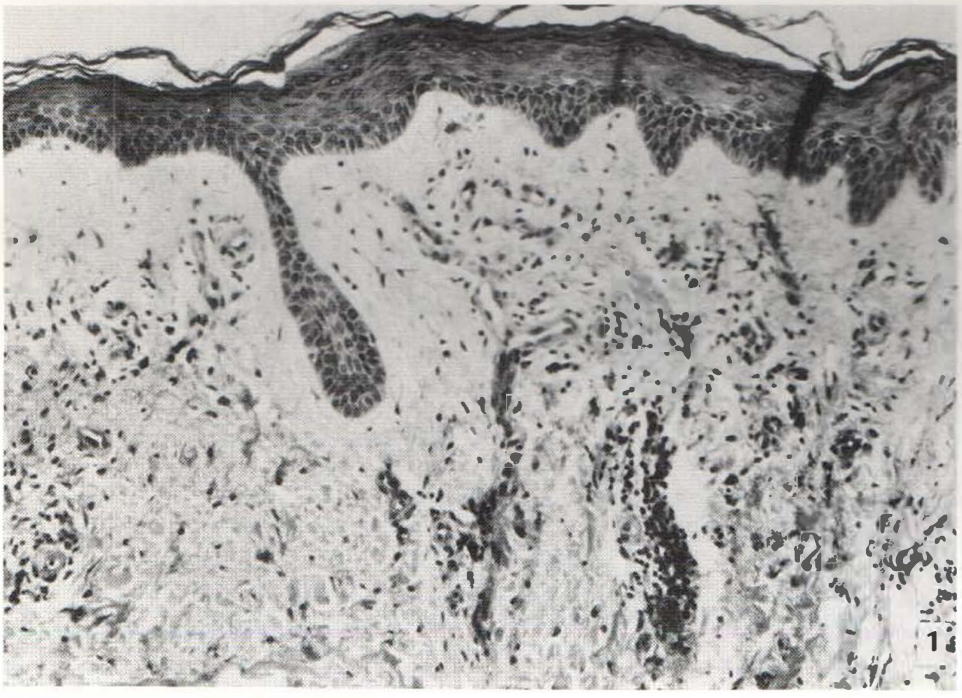
Eosinophils were present in all the cases, but predominated only in six. In those cases the eosinophils were identified either in the superficial or the deep layer of the infiltrate.

Epidermal involvement was inconstant, being present in 20 biopsies (64%). Spongiosis and acanthosis were the most frequent epidermal changes, being found in 17 specimens (54%). Intraepidermal spongiotic vesicles were seen in only six cases (19%), and parakeratotic foci were recorded in seven (22%). The epidermis was considered to be normal in the remaining eleven specimens.

Table I. *Clinical findings*

T = trunk, B = buttocks, AR = arms, TH = thighs, A = abdomen, L = legs, BC = back, S = papules over striae

Case	Age	Onset (month)	Pruritus	Distribution	Clearing after delivery (days)
1	17	8	++++	T A B L	7
2	22	7	+++	T A	4
3	30	9	+++	T A	2
4	29	8	+++	A	7
5	20	8	++++	A B L	7
6	26	8	++	A	6
7	25	8½	++	T A	7
8	25	8½	++++	T A	6
9	30	8	++++	T A B L	10
10	21	9	+++	T A B	3
11	20	8	++	A	3
12	32	9	+++	T A	5
13	22	9	++++	T A B L	7
14	23	9	++	T A	3
15	31	8½	+++	T A	15
16	22	9	++	L A	2
17	25	8½	+++	A TH BC	14
18	30	9	++++	A AR B TH	7
19	30	9	++	A S	5
20	39	8½	++	A S	3
21	23	9	++++	A L	7
22	25	8	++	A L	21
23	27	8½	++	A	7
24	30	9	++	A S	3
25	27	9	++++	A L	7
26	21	8½	++++	T A	10
27	24	9	+++	A B L	5
28	37	8	++++	A	15



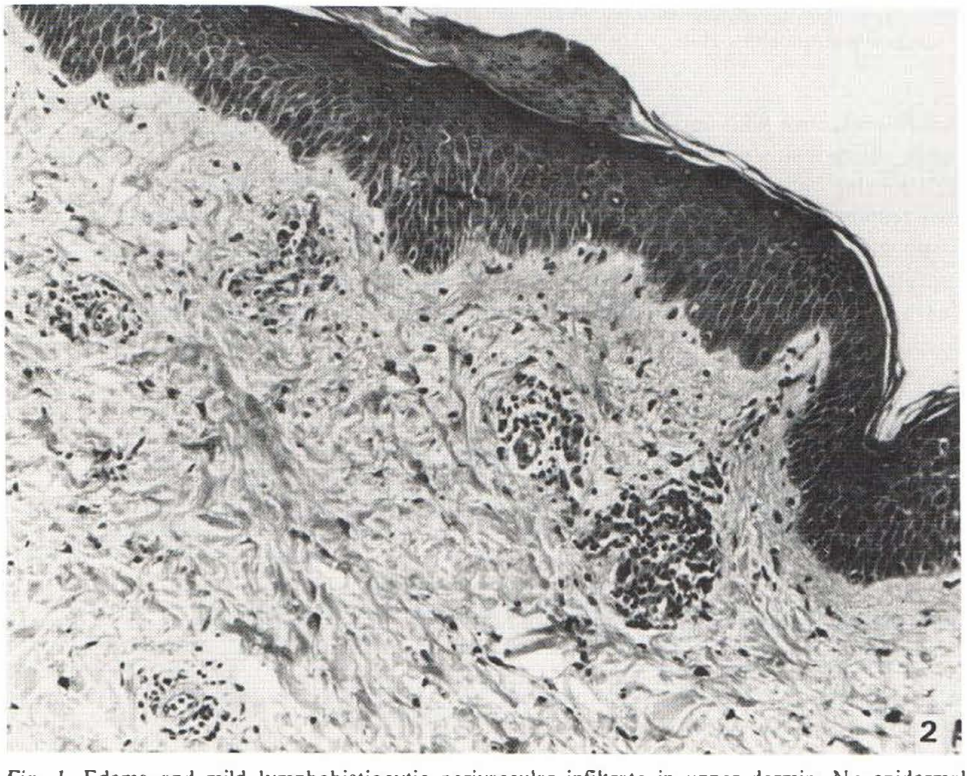


Fig. 1. Edema and mild lymphohistiocytic perivascular infiltrate in upper dermis. No epidermal involvement. H–E, ×90.

Fig. 2. Edema and inflammatory infiltrate are less intense. The epidermis shows a parakeratotic focus. H–E, ×90.

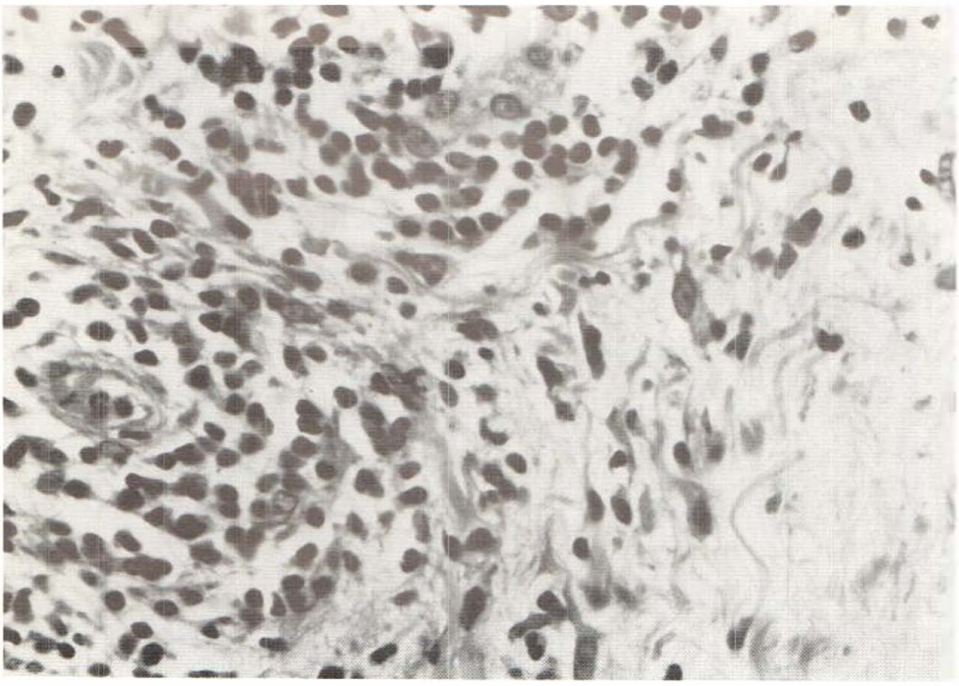


Fig. 3. A high power view showing edema and inflammatory infiltrate. It is formed by lymphohistiocytic cells with occasional eosinophils. H–E. ×320.

Direct immunofluorescence with anti-IgG, anti-IgA, anti-IgM and anti-C3 was negative in the ten cases in which it was performed.

A possible relationship between the epidermal changes and the location and intensity of the inflammatory response has been looked for (Table II). Although a small predominance of acanthosis, spongiosis and parakeratosis was noted in cases with superficial and deep inflammatory infiltrate, no statistical differences could be demonstrated using the chi-square test. Cases with epidermal lesions were associated with a more intense inflammatory response.

DISCUSSION

The histopathology of polymorphic eruption of pregnancy has been a matter of speculation in the dermatological literature. Lawley et al. (4) described two morphologic patterns, one characterized by dermal edema, superficial lymphohistiocytic infiltrate and focal epider-

Table II. *Relationship between epidermal changes and inflammatory response*

	Parakeratosis	Acanthosis	Spongiosis	Vesicles
Infiltrate superficial	3/20	8/20	7/20	3/20
Infiltrate superficial and deep	4/11	9/11	10/11	3/11
χ^2	NS	NS	NS	NS

NS = non-significant.

mal involvement, the other by superficial and deep inflammatory infiltrate and edema, lacking epidermal involvement. Sasseville et al. (9) and Winton & Lewis (10) reviewed the specific dermatoses of pregnancy and quoted the paper by Lawley et al. in their description of pruritic urticarial papules and plaques of pregnancy. Callen & Hanno (7) found epidermal involvement in 61% of their biopsies (similar to our figures). Five patients showed marked papillary edema and three of these also had numerous eosinophils. Ahmed & Kaplan (6) did not find epidermal changes in their cases. Faber et al. (11) reported epidermal involvement in seven patients diagnosed a late prurigo of pregnancy.

Holmes et al. (5) reported histopathologic findings in 16 patients with toxic erythema of pregnancy. Epidermal involvement with spongiosis was found in 31% of biopsies and parakeratosis in 25% of the cases. In a later paper, Holmes et al. (12) described the morphological findings in 25 patients. Parakeratosis and acanthosis were found less frequently than in our series, but spongiotic vesicles were found in 36% of their cases as compared to 22% in ours. They proposed that different histopathological patterns correlate with the clinical stage of the eruption, edema and perivascular lymphocytic infiltrate being the morphologic findings of the early lesion. Vesicular spongiosis is, according to their paper, the hallmark of the papulovesicular stage, and crusting and scaling are the findings of the resolving phase.

Wood (13) found a correlation between clinical and histological severity.

Finally, Yancey et al. (14) reported epidermal involvement in 10 cases from their series (55%), exocytosis and parakeratosis being the most usual epidermal alterations.

In our study we have found no correlation between the presence of epidermal involvement and the superficial or deep location of the lymphohistiocytic infiltrate. Some of the patients in our series did not present vesicles throughout the entire course of the disease. The presence of spongiotic vesicles and spongiosis does not reflect only a clinical stage as suggested by Holmes et al. (12), but rather the intensity of the inflammatory response in a given patient. In our experience, the intensity of the inflammatory infiltrate correlates well with the presence of epidermal changes, both being a manifestation of the severity of the disease rather than the clinical stage. However, biopsies showing mild acanthosis and parakeratosis may represent the residual stage of vesicular lesions.

Except for occasional reports of C_3 deposits in the vessel walls (4, 14), there is a general agreement that immunofluorescence is negative in polymorphic eruption of pregnancy (1, 8, 12, 13, 15). This finding is important in the differential diagnosis with the urticarial lesions of herpes gestationis.

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