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SHORT REPORTS

Immunofluorescence Study in Purpura Pigmentosa Chronica

Keiji Iwatsuki, Tadahiro Aoshima, Hachiro Tagami, Masatoshi Ohi and Mizuho Yamada

Department of Dermatology, Hamamatsu University School of Medicine, Hamamatsu, Japan

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Abstract. Purpura pigmentosa chronica comprises a group of vascular disorders of unknown etiology. In biopsied specimens obtained from 8 patients, we observed vascular changes such as fibrinoid degeneration and occlusive damage occasioned by a hyalinized substance as well as swollen endothelia in 3. However, in all biopsied specimens, direct immunofluorescence studies demonstrated depositions of C3 or C1q with or without immunoglobulins, and of fibrin in papillary vessels. These findings suggest the possibility that immunological processes are involved in producing the histopathologic features of this disorder.

Key words: Purpura pigmentosa chronica; Immunofluorescence findings; Vascular alterations; Mononuclear cell vasculitis

Purpura pigmentosa chronica (PPC) or purpura pigmentosa progressiva is a group of dermatoses characterized by petechiae and brownish pigmentation, particularly on the lower extremities, without any associated hematologic disorders or obvious venous insufficiency; thus progressive pigmentary disease (Schamberg), purpura annularis telangiectodes (Majocchi) and pigmented purpuric lichenoid dermatitis (Gougerot-Blum) are clinical entities which can be grouped together as PPC because of the similarities of their clinical as well as histopathological features (10).

Although the etiology of PPC remains obscure, a disturbance of peripheral circulation and a weakness of the blood vessels have been suggested as a possible cause; in some cases, the cutaneous fragility test (Rumpel-Leede) has been reported to be positive (4). Furthermore, its occurrence in members of the same family has been described (2) and a manifestation of an autosomal dominant trait has been suspected (6).

On the other hand, pigmented purpuric lesions similar to those of PPC have been reported to develop as a result of sensitivity to wool oil (7) or of carbromal (8). On the basis of these facts and the histopathologic picture which is characterized by a mononuclear cell infiltration around the capillaries in the dermal papillae, diapedesis of red blood cells and spongiosis of the lower epidermis with deposition of hemosiderin in old lesions, Illig & Kalkoff (8) suggested the involvement of cellular immunity, possibly with humoral immunity, in the pathogenesis of PPC.

However, to our knowledge, no specific immunological findings have been reported in PPC. Recently we have found interesting immunohistopathological evidence in all 8 patients with PPC studied, which prompted the present report.

MATERIAL AND METHODS

Biopsy material from 8 patients with skin findings characteristic of PPC was studied in the form of hematoxylin and eosin (H-E) sections and immunofluorescence technique. Clinically, 5 patients belong to Schamberg's disease, one to Majocchi's purpura and 2 to eczematide-like purpura of Doucas and Kapetanakis. Each half of the biopsy specimens taken from fresh lesions was prepared for ordinary H-E sections and for frozen sections for direct immunofluorescence studies.

Non-fixed, snap-frozen specimens were studied with FITC-labelled anti-human IgG, IgA, IgM, C1q, C3 and fibrinogen sera produced by MBL* (Medical and Biological Laboratories, Nagoya, Japan), partly by Behring**. Each fluorescein/protein ratio was as follows; FITC-labelled anti-human IgG (1.9*, 1.6*), IgA (1.8**), IgM (2.1**, 1.1*), C1q (1.4*), C3 (2.9**, 1.5*), and fibrinogen (1.3*, 1.5*).

RESULTS

Table 1 presents the pertinent clinical, histopathological and immunohistopathological data on the 8 patients.

Clinical findings

Brown or dusky red macules containing pinhead-sized petechia were seen mainly on the legs of 5

Table I. *Summary of findings in 8 patients with purpura pigmentosa chronica*

S: Schamberg's disease, M: Majocchi's disease, D-K: Eczematide-like purpura of Doucas-Kapetanakis, N.D.: not done, mos.: months, ( )*: immune deposits at the dermo-epidermal junction, ±: faint, +: mild, ++: moderate, +++: severe

Case no./ Age/Sex	Type of lesion	Symptom	Distribution	Duration (mos.)	Epidermal change (H-E section)	Vascular damage (H-E section)	Immunoglobulin (vessel wall)	Complement (vessel wall)	Fibrin
1/60/♀	S	(−)	Legs	3	±	+++	IgM	C3	+
2/53/♂	S	Itching	Legs, planta	4	+	+	(−)	C3	+
3/58/♂	S	(−)	Legs, foot	20	±	++	IgM	C3	+
4/47/♀	S	Itching	Legs	2	+++	±	(−)	C3	+
5/71/♂	S	(−)	Legs	9	+	+	(−)	C3 (C3)*	+
6/50/♂	D-K	(−)	Legs, abdomen	2	++	++	(−)	C3	N.D.
7/77/♂	D-K	Itching	Legs, abdomen	1	+	+	IgM	C1q (C3)*	+
8/29/♂	M	(−)	Legs	12	+	±	IgA	C3	+

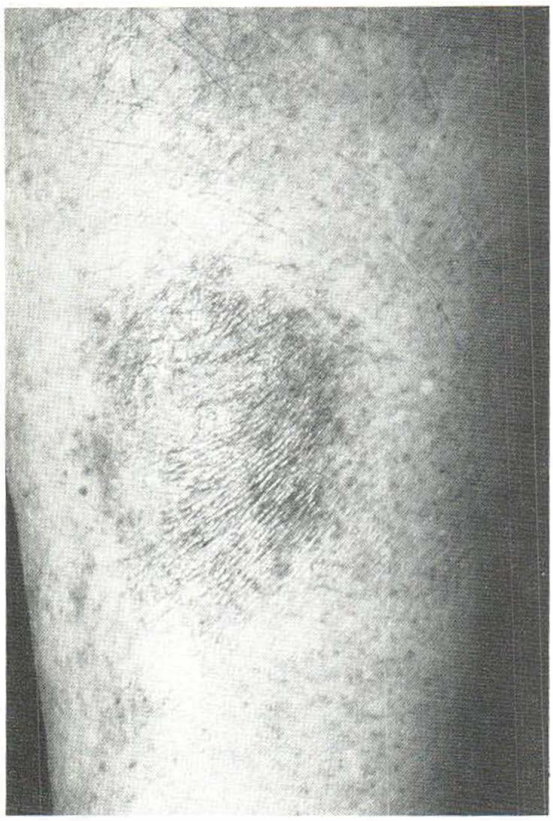

Fig. 1. Brownish pigmented macules studded with petechiae on the lower legs in case 5.

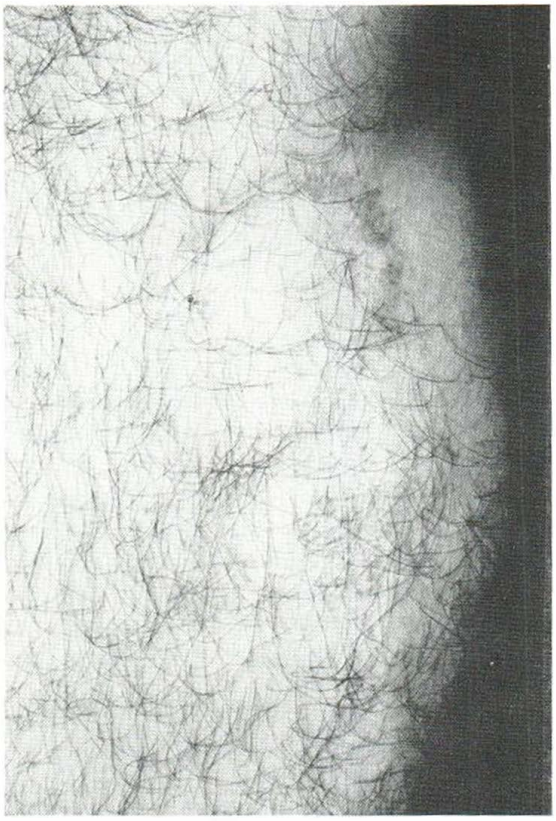

Fig. 2. Annular pigmented lesion composed of punctiform purpura in case 8, clinically diagnosed as Majocchi's purpura.

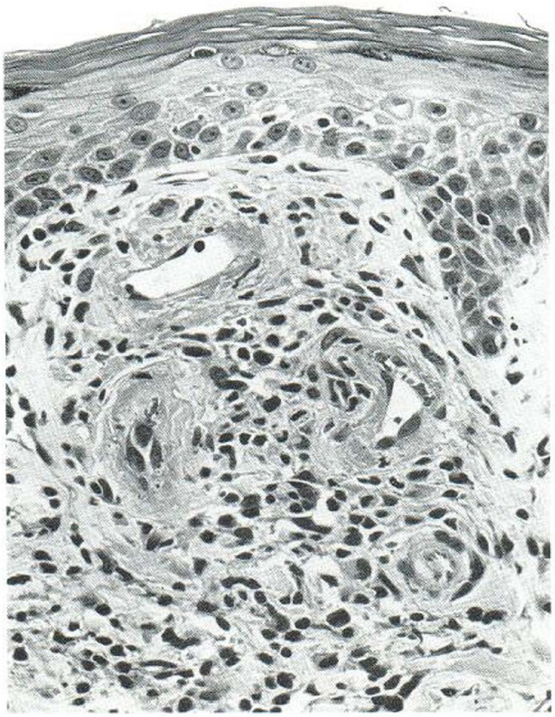

Fig. 3. Remarkable fibrinoid degeneration of the vascular walls of the dermal papilla with a perivascular lymphohistiocytic infiltration in case 1. Note the presence of nuclear dust.

patients (cases 1–5) (Fig. 1). In cases 6 and 7 punctiform purpura spread over the lower limbs and abdomen and then faded in a course of a few weeks leaving brownish pigmentation behind, thus being clinically diagnosed as eczematide-like purpura. In patient no. 8, who was diagnosed clinically as having purpura annularis telangiectodes, the primary lesion was brownish pigmented macules composed of punctiform petechiae, which later formed an annular configuration due to fading of the pigmented central portion (Fig. 2).

Histopathology

A perivascular lympho-histiocytic infiltration and extravasated erythrocytes were observed in the upper dermis in all the cases, with varying degrees of epidermal exocytosis and accompanying spongiotic bulla formation. Close examination of the vasculature in such areas revealed swollen endothelia in 5 cases. Moreover, it is remarkable that fibrinoid degeneration was observed in cases 1, 3 and 6 (Fig. 3). However, there was no correlation between the vascular damage and epidermal changes.

Immunofluorescence studies

All biopsy specimens showed granular or dense globular deposits of C3 or C1q, with or without immunoglobulins, in the walls of the blood vessels in the papillary dermis. Furthermore, in 2 patients (cases 5 and 7) granular deposits of C3 were also demonstrated at the dermo-epidermal junction (Figs. 4 and 5). The immunoglobulins detected in the lesions were IgM in 3 cases and IgA in one.

In addition, deposits of fibrin were found in the papillary vessels in all the studied cases (Fig. 6).

DISCUSSION

The present study disclosed the characteristic histopathologic picture of PPC in all 8 cases. In addition, swelling of the endothelia was noted in 5 cases

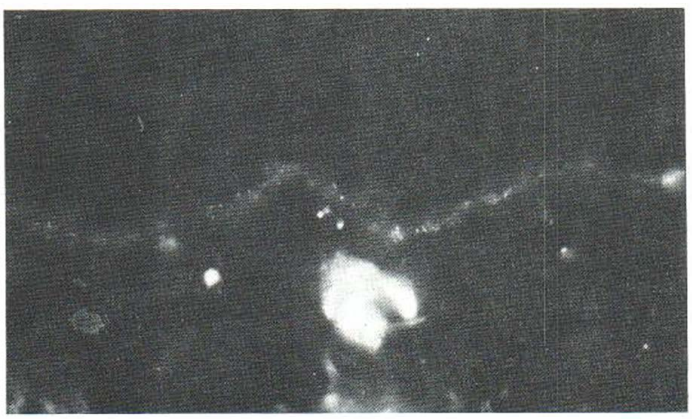

Fig. 4. Granular deposits of C3 along the dermo-epidermal junction and a dense globular deposition in the vessel wall in case 5.

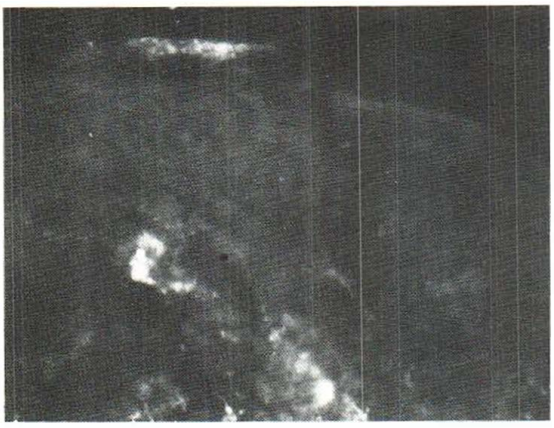

Fig. 5. The presence of C3 in both the papillary vessels and the horny layer (*right above*) was found with simultaneous depositions at the dermo-epidermal junction in case 5.

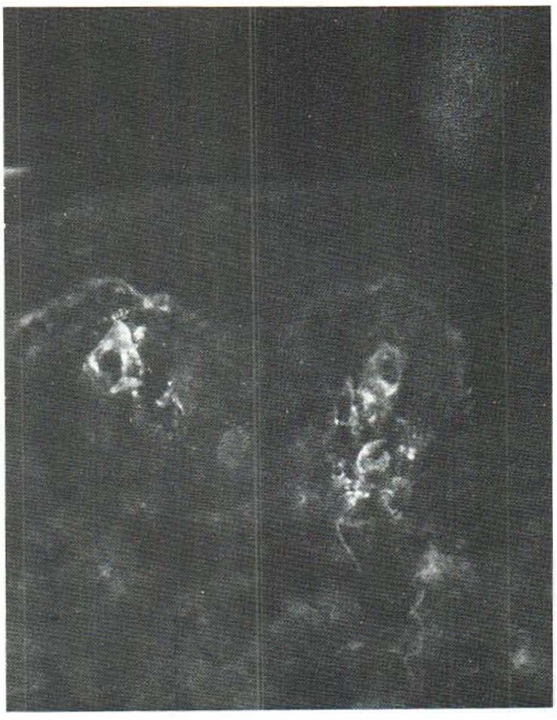

Fig. 6. Dense deposition of fibrin in the walls of the blood vessels, almost encircling the vascular lumina and at the dermo-epidermal junction in case 2.

and fibrinoid degeneration with occlusive change further noted in 3. Pinkus & Mehregan (11) regarded such fibrinoid degeneration of vessel walls, which might be observed only in favorable sections, as the hallmark of PPC (11). Furthermore, it is noteworthy that our immunofluorescence study demonstrated the deposition of C3 and fibrin, occasionally associated with IgM or IgA, in the vessel walls or along the dermo-epidermal junction of the lesions. No such findings have been made in PPC, so far as we know.

The immune deposits in vessel walls are a characteristic feature of cutaneous necrotizing vasculitis and their presence constitutes firm evidence that immune complexes play an important role in this kind of vasculitis. If a similar mechanism also underlies the development of PPC, it is of interest that the histologic feature of PPC is distinct from that of leukocytoclastic vasculitis. However, even in necrotizing vasculitis, it is reported that patients with normocompletemia exhibited predominance of lymphocytes as compared with those with hypocomplementemia, where neutrophils predominate among the infiltrating cells (12). This might be due to the difference in membrane receptors for immunoglobulins and complement, e.g. receptors for C3d are noted on B lymphocytes and those for C3b are present on neutrophils, which accounts for the differing histologic appearance of mononuclear cell vasculitis and leukocytoclastic vasculitis, as suggested by Kazmierowski & Wuepper for erythema multiforme; they found deposits of IgM and C3 in papillary vessels, but only in early lesions (9). Furthermore, in lupus erythematosus, a dense lymphocytic infiltration rather than that of polymorphonuclear leukocytes is predominant in spite of the deposits of immunoglobulins and complement.

We must consider if another possibility that these immune deposits might represent only a secondary event to a cell-mediated immune response. In lichen planus, which reveals a dense mononuclear cell infiltration in the upper dermis, probably as a manifestation of a cell-mediated immune reaction, deposits of immunoglobulins chiefly of IgM and fibrin were also demonstrated (1, 3).

Recently, Duncan & Winkelmann (5) noted a perivascular lymphocytic infiltrate with a focal area of lymphocytic epidermal invasion in addition to the feature indicating that lymphocytes may be a primary inflammatory cell early in many forms of vasopermeable conditions (5). Thus, we cannot completely exclude the possibility that the mononuclear cell infiltration may be an event secondary to increased vasopermeation and that the deposits

of immunoglobulins and complement are simply trapped in fibrin deposits (13), although such a possibility seems to be rather unlikely because of the selectivity of immunoglobulins and of the specific site of deposition, viz. vessel walls and dermo-epidermal junction, the sites most frequently involved in the deposition of immune complexes in the skin.

Although there is much yet to be studied before a definite process of the pathogenesis for PPC is established, our findings seem to indicate at least a new direction of research in this disorder.

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Autosensitization to DNA

F. Brauner, W. Brenner and F. Gschnait

Department of Dermatology I, University of Vienna, Vienna Austria

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Key words: Gardner-Diamond syndrome; Autoerythrocyte sensitization syndrome; Painful bruising syndrome; Differential diagnosis

The spontaneous occurrence of widespread ecchymoses in a patient not exhibiting coagulopathy leads to a spectrum of differential diagnoses including amyloidosis, anaphylactoid purpura, pseudoxanthoma elasticum, Ehlers-Danlos syndrome, autoerythrocyte sensitization and autosensitization to DNA (11). This paper reports on a patient exhibiting the characteristic clinical findings and skin reactivity indicative of DNA autosensitization. The syndrome will be discussed briefly with particular reference to the differential diagnosis to autoerythrocyte sensitization.

CASE REPORT

A 48-year-old female patient presented with widespread, well circumscribed ecchymoses on the buttocks and extensor and flexor sites of her extremities. The lesions, which erupt spontaneously, are not preceded by trauma and appear initially as red, tender, macular to slightly raised patches, 1–2 cm in size, which sometimes disappear quickly or more often spread peripherally within a few hours, becoming surrounded by a well defined blue ring-shaped area about 1–2 cm in width. Some hours later numerous ecchymoses develop in these sites, which become confluent and finally resemble widespread hematomas (Fig. 1 *a, b*).

The first attack leading to these skin changes occurred 5 months prior to admission and recurrent eruptions appeared at intervals of 2 to 3 weeks. There were no systemic symptoms such as fever, arthralgia or malaise.

The patient was strumectomized 18 years ago. Seven years ago vitiligo developed on the hands and knees. The patient is now in otherwise good health, she appears emotionally well balanced; the family history is unremarkable.

The general physical examination, ophthalmological examination, chest roentgenogram and thyroid scintigraphy showed no abnormalities. Platelet count, fibrinogen, prothrombin time and partial thromboplastin time were within normal ranges, as were ESR, urinalysis, complete blood count, serum analysis for glucose, blood urea nitrogen, creatinine, sodium, potassium, chloride, calcium, phosphate, uric acid, iron, cholesterol, triglycerides, alkaline phosphatase, SGOT, SGPT and LDH.