Phospholipase A₂ Activity of Peripheral-Blood Mononuclear Leukocytes in Psoriasis

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Ten years ago, Forster et al. [1] demonstrated increased phospholipase A₂ (PLA₂) activity in nonlesional skin of psoriasis patients [2], possibly due to downregulation of the lipocortin 1 inhibitor [3, 4] and resulting in an overly active arachidonic acid cascade [5]. The possibility of upregulated PLA₂, an inflammatory mediator [6], as a phenotypic expression of psoriasis suggested a series of experiments using peripheral-blood mononuclear leukocytes (PBMLs) from control and psoriatic blood, with or without challenge. Hopefully, these experiments would suggest a noninvasive test that might be used to detect latent psoriasis in subjects as yet without clinical symptoms. Two general methods to assess PBML activity were used.

Following Goppelt-Strube [7], normal and psoriatic PBMLs were isolated using a Ficoll gradient and prelabeled with ³H arachidonic acid before exposure to one of the following: calcium ionophore A23187 (1 µg/ml), thrombin (1 µg/ml) or lipoteichoic acid (from *Staphylococcus aureus*; 5-100 ng/ml). Without any of these, the amount of ³H released to the supernatant by control cells was 23.1 ± 6.4% (SD; n = 15), and this figure was 67.3 ± 8.9% (n = 9) when A23187 was used or 32.5 ± 8.1 (n = 5) with thrombin; lipoteichoic acid had no effect. These figures were not significantly different when psoriatic PBMLs were used.

According to Etienne and Polonovski [8], aliquots of sonicated cell suspensions were incubated with L- α -dioleoylphosphatidyl-2-¹⁴C-ethanolamine, followed by separation of extracted lipids by thin-layer chromatography.

The distribution of ¹⁴C on the plates was monitored and quantified by β -radiation scanning and visualization. Figure 1 shows the results with a nonenzymatic control (a), two positive controls (b) using pancreatic PLA₂

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Fig. 1. Separation by thin-layer chromatography of the PLA₂ product lysophosphatidylethanolamine (arrow) from the substrate after treatment with pancreatic PLA₂ (b) or PBML sonicates (c) or neither (a). Lipids were visualized with iodine vapor.

References

Forster S, Ilderton E, Summerly R, Yardley HJ: Epidermal phospholipase A2 activity is raised in the uninvolved skin of psoriasis. *Br J Dermatol* 1983;109(suppl 25):30-35. Cartwright PH, Ilchyshyn A, Ilderton E, Yardley HJ: Modulation of phospholipase A2 activity in extracts of lesion-free psoriatic epidermis by alkaline phosphatase and a protein phosphatase inhibitor. *Br J Dermatol* 1988; 118:333-338.

Ilchyshyn A, Ilderton E, Kingsbury J, Yardley H: Evidence that the raised level of PLA2 in the uninvolved skin of psoriasis is caused by hyperphosphorylation of an inhibitor. *Br J Dermatol* 1984;111:721-722. Cartwright PH, Ilderton E, Sowden JM, Yardley HJ: Inhibition of normal and psoriatic epidermal phospholipase A, by picomolar concentrations of recombinant human lipocortin I. *Br J Dermatol* 1989;121:155-160.

and two typical experimental patterns (c). The spot (arrow) corresponding to the reaction product lysophosphatidylethanolamine was satisfactorily separated from other products with higher Rf values. After deducting the nonenzymatic control counts, the percent hydrolysis was 0.55 ± 0.28 (n = 13) for controls and 0.28 ± 0.17 (n= 11) for psoriatics (n.s.).

Thus we have found that the PLA2 activity and responsiveness in psoriatic PBMLs, despite diverse degrees of disease severity, are comparable to controls. It is possible that factors upregulating PLA2 in the epidermis are present in serum [9] but do not survive cell isolation. Alternatively, such factors may differentially affect keratinocytes and PBMLs. A third interpretation is that endogenous epidermal factors activate keratinocyte PLA2 without effect on circulating cells.

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Dennis EA: The regulation of eicosanoid production: The role of phospholipases and inhibitors. *Biotechnology* 1987;5:1296-1300. Pruzanski W, Vadas P: Phospholipase A₂ – A mediator between proximal and distal effectors of inflammation. *Immunol Today* 1991; 12:143-147.

Goppelt-Struebe M: Phospholipase A2 activity in T lymphocytes. *FEBS Lett* 1986;202: 45-52.

Etienne I, Polonovski J: Phospholipase A2 activity in rat and human lymphocytes. *Biochem Biophys Res Commun* 1984; 125: 719-724.

Kobayashi S: Phospholipase A2 activating factor in sera of patients with psoriasis vulgaris. *Jpn J Dermatol* 1990;100:1017-1021.

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Multiple Eruptive Dermatofibromas in an AIDS Patient: A New Differential Diagnosis of Kaposi's Sarcoma

The clinical differential diagnosis of Kaposi's sarcoma is large with more than 35 possibilities [1]. Multiple eruptive dermatofibromas in HIV-infected persons have not previously been reported before Murphy et al. [2]. This entity is probably underestimated and can mimic Kaposi's sarcoma as it is illustrated in the following case report.

A 37-year-old homosexual Caucasian was known for AIDS disease (stage C3) with prior Candida esophagitis and a very low CD4 count (5 cells/mm³). He was treated with zidovudine

and zalcitabine associated with a fluconazole and trimethoprim-sulfamethoxazole prophylaxis. He consulted our clinic for evaluation of asthenia, anorexia and abnormal liver tests. Finally, disseminated infection with *Mycobacterium genavense* was suspected [3], and the symptoms disappeared with a combination of clarithromycin, etham-butol and clofazimine. At the initial physical examination, 7 firm, purple-brown nontender papules ranging in size from 2 to 6 mm were noted on the skin (4 on the back, 2 on the anterior left thigh and 1 on the right foot). A very light desquamation was seen at the top of the

lesion. All lesions except that of the foot were recent and were not pruriginous. Our first diagnosis was Kaposi's sarcoma. Biopsy firmly excluded this diagnosis and showed a typical dermatofibroma with an ill-defined dermal tumor. Characteristically the epidermis above the lesion was hyperplastic and hyper-pigmented. A grenzzone was present immediately under the epidermis. The dermal part was composed of interlacing fascicles of slender spindle cells and collagen. Histio-cytes were scattered between the spindle cells, and thin-walled blood vessels were rare within the lesion and dilated at the periphery. Multinucleated giant cells, neovascularization with angulated vascular channels, extravasated red blood cells or mitotic figures were absent. Diagnosis of multiple eruptive dermatofibromas was made, and no specific treatment was proposed.

This case shows that eruptive dermatofibroma is not rare in AIDS patients and can mimic Kaposi's sarcoma. It should be considered in the clinical differential diagnosis. Multiple eruptive dermatofibromas in AIDS can help the dermatologist to understand the pathogenesis of this common tumor of the skin. In this regard, the concept developed by Nestle et al. [4], which explains dermatofibroma as an abortive immunoreactive process, featuring dermal dendritic cells as initiators of the disease is very interesting.

References

Martin RW, Hood AF, Farmer ER: Kaposi sarcoma. *Médecine* 1993;72:245-261. Murphy SC, Lowitt MH, Kao GF: Multiple eruptive dermatofibromas in an HIV-positive man. *Dermatology* 1995;190:309-312. Pechère M, Opravil M, Wald A, Chave JP, Bessesen M, Sievers A, Hein R, Overbeck J, Clark RA, Tortoli E, Emler S, Kirschner P, Gabriel V, Böttger EC, Hirschel B: Clinical and epidemiology features of infection with *Mycobacterium genavense* infection. *Arch Intern Med*, in press.

Nestle FO, Nickoloff BJ, Burg G: Dermatofibroma: An abortive immunoreactive process mediated by dermal dendritic cells? *Dermatology* 1995;190:265-268.

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