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A Comparative Study on Peripheral Blood Lymphocyte Subpopulations in Different Kinds of Warts

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Peripheral blood T-cell subpopulations were evaluated in 36 patients with clinically different types of warts, subdivided in 4 groups (common, genital, flat and plantar warts). A significant decrease was found in OKT3 and OKT4 subsets total count and in OKT4/OKT8 ratio in patients with common and genital warts as compared with controls. Only in common and genital warts did we also observe a significant decrease of percentage of OKT4 subset. No significant difference of considered parameters was observed in flat and plantar warts as compared to controls, apart from a significant increase in number of OKT8 subset in flat warts. We then discuss this different status of C.M.I. in patients with different clinical warts, stressing the importance of various types of HPV. *Key words: T-cell subpopulations.* (Received July 23, 1986.)

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The role of cell-mediated immunity (CMI) in wart infections has been well documented by several reports (1, 2). The identification of many antigenically different types of human papilloma viruses (HPV) (3) and the observation that clinically and histologically different types of warts are mostly associated with particular types of HPV (3, 4) suggest that the studies so far performed on the immune response to HPV should be reconsidered.

New interest arises from immunological studies performed on groups of patients with clinically well-characterized and antigenically well-differentiated lesions. As early as in 1980, Obalek & Jablonska (2) showed, with a classic method, the difference of CMI defect in patients with different clinical types of warts. The use of monoclonal antibodies specific for human T lymphocytes allows us a new approach to this problem.

PATIENTS AND METHODS

Monoclonal antibodies specific for surface markers of human T lymphocytes were used to evaluate the peripheral blood T lymphocyte subsets in 36 patients with clinically different types of warts

(common warts: 8 patients—3 males, 5 females; genital warts: 10 patients—7 males, 3 females; flat warts: 10 patients—7 males, 3 females; plantar warts: 8 patients—6 males, 2 females). The study included 14 healthy, sex and age matched subjects tested at the same time.

The ages of patients ranged from 18 to 72 years (mean 31.18 ± 18.24). The number of warts per patient varied from 6 to 25 (mean 13.45 ± 4.5) and their history from 12 to 36 months (mean 16.45 ± 6.6). For all these parameters no significant difference was observed among the group of patients.

All subjects were evaluated by standard laboratory tests: blood count, urinalysis, ESR, protein electrophoresis and immunoglobulins. No patient had ever received immunosuppressive or immunomodulating therapy. Monoclonal antibodies directed against various human T cell antigens were produced as previously described (5). Three monoclonal antibodies were employed: OKT3 reacting with all peripheral T cells, OKT4 with cells having helper-inducer function, OKT8 identifying cells with suppressor-cytotoxic activity. The absolute number of T cell subsets was calculated using the peripheral blood lymphocyte count.

The observed percentages of positive cells were corrected for non-lymphocyte contamination of the mononuclear fractions. This was achieved by cytochemical staining with non-specific esterase (α -naphthyl-acetate esterase) on smears of mononuclear cells. Results were analysed using the Mann-Whitney U test and the Student's *t*-test.

RESULTS

Results are summarized in Table I. Only patients with common and genital warts show a decrease in total lymphocyte count, although not significant, as compared to the control group. A significant decrease ($p < 0.05$) is shown in OKT3 and OKT4 subpopulations and OKT4/OKT8 ratio of these two groups as compared with the control group. With regard to T subsets percentages, the same significant decrease is observed only in OKT4 subset of common and genital wart groups ($p < 0.05$). No significant difference of considered parameters is observed in flat and plantar wart groups compared to the control group, apart from a significant increase in number of OKT8 subset in flat warts group.

Table I. Lymphocyte number and T-lymphocyte subsets (number and percentage; mean $\pm$ SE) of 36 patients with different clinical types of viral warts

Figures within parentheses denote number of patients per group

Patient group	Lymphocyte counts/mm ³	OKT3 ⁺		OKT4 ⁺		OKT8 ⁺		OKT4 ⁺ /OKT8 ⁺
		Number	%	Number	%	Number	%	
(8) Common warts	1 856.2 ± 139.3 NS	1 134.2 ± 116.0 $p < 0.05$	61.2 ± 4.3 NS	622.5 ± 84.9 $p < 0.05$	32.8 ± 3.1 $p < 0.05$	514.6 ± 47.6 NS	29.5 ± 2.7 NS	1.2 ± 0.12 $p < 0.05$
(10) Genital warts	2 010.0 ± 203.5 NS	1 175.6 ± 81.8 $p < 0.05$	62.0 ± 2.4 NS	683.7 ± 71.3 $p < 0.05$	35.5 ± 2.3 $p < 0.05$	520.2 ± 25.2 NS	27.9 ± 1.5 NS	1.29 ± 0.10 $p < 0.05$
(10) Flat warts	2 588.0 ± 175.8 NS	1 863.6 ± 118.4 NS	72.5 ± 1.6 NS	1 078.6 ± 80.4 NS	41.5 ± 1.1 NS	795.2 ± 56.3 $p < 0.05$	27.7 ± 2.1 NS	1.36 ± 0.06 NS
(8) Plantar warts	2 887.5 ± 328.3 NS	1 831.7 ± 289.9 NS	62.7 ± 4.4 NS	1 091.5 ± 168.7 NS	37.5 ± 2.9 NS	731.3 ± 125.3 NS	25.8 ± 2.3 NS	1.49 ± 0.11 NS
(14) Control	2 421.4 ± 209.7	1 624.0 ± 156.1	67.0 ± 2.1	1 048.5 ± 161.0	42.2 ± 1.8	632.5 ± 53.1	26.5 ± 1.3	1.62 ± 0.11

p = significance vs. control group, NS = not significant vs. control group.

DISCUSSION

Humoral immunity is thought to play a small role in infectiveness of warts; on the contrary CMI has a major importance in it. Monoclonal antibodies, now available against distinct blood T lymphocyte subsets, give us a new and interesting approach to the study of CMI in wart infections. In previous works many authors stressed the importance of certain parameters in this pathology.

The duration of viral infection is of capital importance as demonstrated by Thivolet et al. (1), Morrison (6) and Chretien et al. (7). Mohanty (8) demonstrated a significant reduction of total T cells in patients who had had genital warts for at least 12 months. In another study performed on T lymphocyte subsets we confirmed these data also in common warts (9). Another point of importance is the extent of the lesions. This concept was suggested by Morrison (6), then observed by Obalek et al. (2) and confirmed by us.

Furthermore, clinically different types of papillomata are mostly associated with distinct types of papilloma viruses and this makes such studies all the more complex. For all these considerations it seems necessary to study the immunity in patients with clinically well characterized warts. In the light of this the comparative studies of Obalek & Jablonska (2) on CMI in patients with different warts are of primary importance.

We have tackled the problem studying a population of patients with clinically different warts, of sufficiently long duration (more than one year) and sufficiently great number (more than six lesions), so as to observe homogeneous groups of patients. Our data show a non-significant reduction of lymphocyte total count and a significant decrease in the total count of OKT3, OKT4 subsets and OKT4/OKT8 ratio only in common and genital warts. OKT8 total number show a significant increase versus controls only in the group of flat warts.

These data therefore show a different response of CMI—studied with monoclonal antibodies against various blood T lymphocyte subsets—in patients with clinically different warts. We can only give a speculative explanation of this difference. The variability is probably determined by different antigenicity or different host response to various types of HPV. Furthermore, the number of virions produced by each wart differs according to the type of virus (10), thus conditioning the immunological response. Our data partially differ from those of Obalek et al. (2). This could be accounted for by the fact that they used different methods, such as in vitro lymphocyte response to PHA and in vivo sensitization to DNCB. We believe that the interest of our study lies mainly in the approach. A further interesting subject of research could be the correlation between the CMI response in all its aspects and the virological type of clinical warts.

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Transformation of Lymphocytoma cutis into a Malignant Lymphoma in Association with the Sign of Leser-Trélat

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Halevy S, Sandbank M. Transformation of Lymphocytoma cutis into a malignant lymphoma in association with the sign of Leser-Trélat. *Acta Derm Venereol (Stockh)* 1987; 67: 172-175.

A patient is described in whom transformation of lymphocytoma cutis (LC) into malignant lymphoma, diffuse, mixed small and large lymphocytes, occurred in association with the sign of Leser-Trélat (LT), which is a marker for internal malignancy. To the best of our knowledge, such an association has not been reported previously. (Received May 26, 1986.)

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Lymphocytoma cutis (LC) is essentially benign in nature and only rarely becomes malignant (1). We present a case in which malignant transformation of LC into a malignant lymphoma, diffuse, mixed small and large lymphocytes, was associated with the sign of Leser-Trélat (LT), which is a marker for internal malignancy (1, 2).

CASE REPORT

A 64-year-old male presented with erythematous papular lesions on the left side of the neck (Fig. 1). The diagnosis of LC was established based on the following histologic findings. The epidermis was unaffected. Below the epidermis there was a thin grenz zone, and in the upper and middle dermis there were foci of mononuclear cell infiltration, mainly in perivascular areas. The cellular infiltrate was composed mainly of mature lymphocytes with a few large lymphocytes and histiocytes. A few germinal centers were seen. There was small vessel proliferation with prominent swollen endothelial cells. The skin adnexa were preserved and did not show any cellular infiltration (Fig. 5). In addition to these, there were several pigmented seborrheic keratoses (histologically confirmed) on the trunk, with a predilection for the back.

Seven years later the patient reported having noticed a rapid increase in the number of the seborrheic keratoses as well as in the size of those already existing. The seborrheic keratoses on the back were seen to have a "splash effect" (Fig. 4) and there was an abundance of senile hemangiomas as well as "mixed lesions" composed of both seborrheic keratosis and hemangioma. Within 19 months the neck lesions were also observed to have changed markedly, with an accompanying pruritus. Now present were firm, non-tender nodules several centimeters in diameter with smooth overlying skin of a red-violaceous colour (Fig. 2). Histological examination of a nodule revealed findings compatible with malignant lymphoma, diffuse, mixed small and large lymphocytes. The epidermis was normal and a thin grenz zone was seen beneath it. All of the dermis and subcutaneous fat was invaded by a dense homogenous cellular infiltration composed of small and large-sized lymphocytes (Fig. 3). No germinal centers were found. No skin adnexa were found in the biopsy specimen. Reticulum stains showed thin, small broken reticulum fibers interspersed in the cellular