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

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Lodi A, Betti R, Cattaneo M, Rosti A, Masnada M C, Marmini A, Crosti C. A comparative study on peripheral blood lymphocyte subpopulations in different kinds of warts. Acta Derm Venereol (Stockh) 1987; 67: 169–172.

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 ± SE) of 36 patients with different clinical types of viral warts*

Figures within parentheses denote number of patients per group

Patient group	Lympho-cyte counts/mm^3	OKT3$^+$		OKT4$^+$		OKT8$^+$		OKT4$^+$/ OKT8$^+$
		Number	%	Number	%	Number	%	

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

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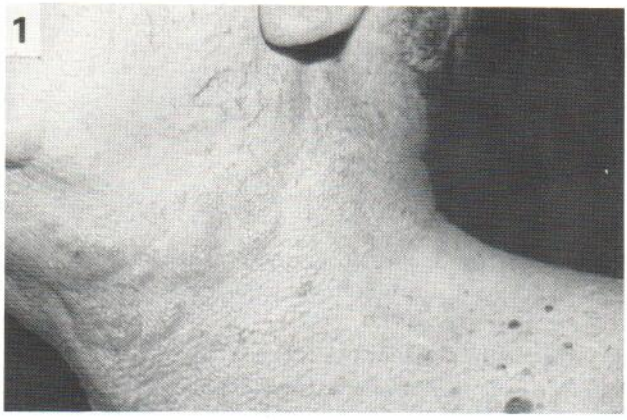
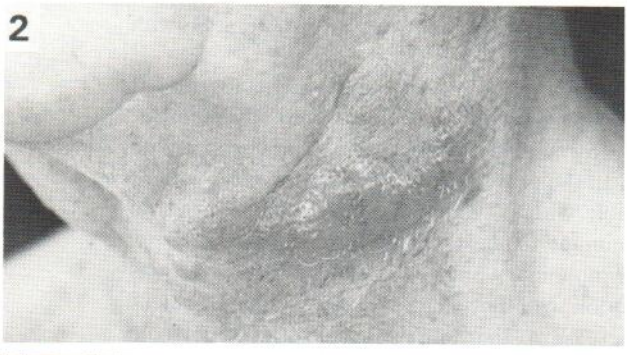
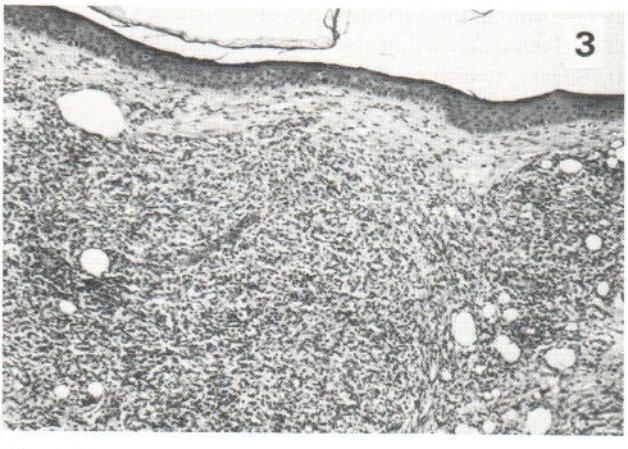
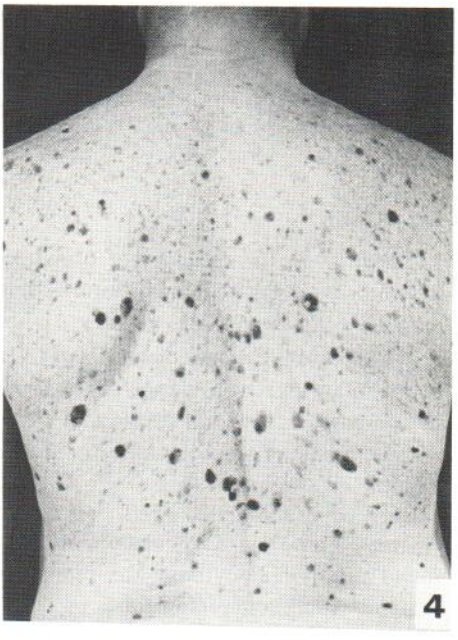
Halevy S, Sandbank M. Transformation of Lymphocytoma cutis into a malignant lympho-









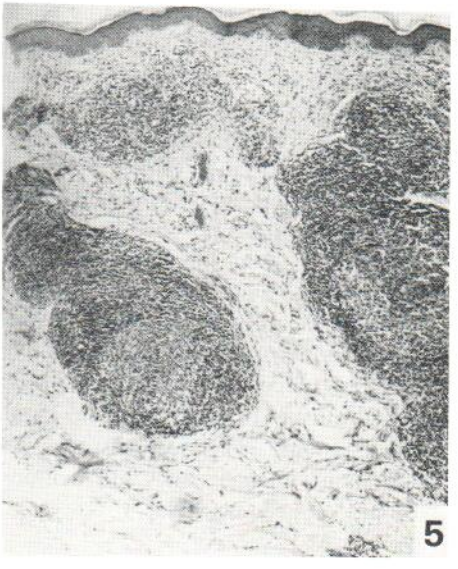


Fig. 1. Erythematous papular lesions on the left side of the neck.

Fig. 2. Tumoral masses on the left side of the neck consisting of firm red-violaceous nodules several centimeters in diameter.

Fig. 3. Second biopsy: Lymphoma of skin = dense diffuse infiltration of the dermis by small and large sized lymphocytes (H & E, ×315).

Fig. 4. Multiple seborrheic keratoses on the back giving a "splash effect".

Fig. 5. First biopsy: LC = patchy infiltration with formation of germinal centers (H & E, ×60).

infiltrate. The immunoperoxidase technique (PAP method) for the detection of light chains (kappa and lambda) as well as IgG and IgM was applied in the two biopsies and gave negative results. A thorough investigation of the patient revealed only enlargement of the liver and inguinal lymph nodes. Following radiotherapy for the skin lesions on the neck there was a complete regression of the tumoral masses, but no decrease in the number or size of the seborrheic keratoses.

DISCUSSION

LC belongs to the category of pseudolymphoma, a term applied to a group of benign dermatoses having histologic features that often make the distinction from lymphoma very difficult if not impossible.

In the present case the diagnosis of LC established in the first biopsy has been supported by the following: the presence of germinal centers, a paucity of medium-sized lymphocytes in comparison to both small and large lymphocytes, non-involvement of the deeper dermis, predilection of the infiltrate for perivascular areas, and vascular proliferation with endothelial swelling (3, 4).

Burg & Braun Falco (5) found B lymphocyte markers on the lymphocytes in LC whereas Van Hale & Winkelmann (6), using leukocyte monoclonal antibody staining, found that lymphocytoma was represented by nodular masses of B lymphocytes with peripheral and intervening zones of T cells. In the present case the morphological pattern of the lymphocyte infiltration was compatible with B lymphocyte infiltration (4) but no immunoglobulins were detected by the immunoperoxidase technique.

Transformation of LC into malignant lymphoma which occurs only rarely (1) was supported in the present case by the association with the sign of LT. The sign of LT refers to the sudden appearance and/or rapid increase in the number and size of seborrheic keratoses as a marker of internal malignancy (2). Among the various types of malignancy reported in association with the sign of LT are malignancies of the reticuloendothelial system, including mycosis fungoides (7, 8), Sezary syndrome (9), a well-differentiated lymphoma (7) and a poorly-differentiated lymphocytic lymphoma (10).

To the best of our knowledge, association of the sign of LT with malignant transformation of LC into a malignant lymphoma, diffuse, mixed small and large lymphocytes, as in our case, has not been reported previously. In the present case, as well as in another case of poorly-differentiated lymphocytic lymphoma associated with the sign of LT (10), the sign of LC preceded the discovery of the malignancy, and the clinical findings included a "splash effect" of the seborrheic keratoses and the abundance of hemangiomata and "mixed lesions". The mechanisms responsible for proliferation of seborrheic keratoses in association with malignancy and their possible regression following adequate therapy (7, 8) have not yet been clarified.

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Skin Tags: A Cutaneous Marker for Diabetes Mellitus

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Two hundred and sixteen non hospitalized patients with skin tags (ST) were studied for the presence of diabetes mellitus (DM) and obesity. Overt DM was found in 57 (26.3%) patients and impaired glucose tolerance test was found in 17 (7.9%) patients. Sixteeen new cases of DM were found among this group. All the diabetic patients in the study population had non-insulin dependent DM. Sixty-two (28.7%) of the patients were obese. No correlation was found between the localization, size, colour and number of the ST and the presence of DM. Our study indicates that ST are not associated with increased incidence of obesity compared to the general population. On the other hand, ST are associated with impaired carbohydrate metabolism, and may serve as a means for identifying patients at increasing risk of having DM. (Received September 2, 1986.)

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Skin tags (ST) are small, soft, pedunculated, often pigmented lesions, usually occurring on the eyelids, neck and axillae. The condition is very common, particularly in middle-aged and elderly women. Obesity is a factor that has been associated with the development of ST. Aside from their unsightly appearance, these lesions were thought to bear little clinical meaning (1). Recently, an association beween ST and acromegaly (2, 3) and colonic polyps (3–5) has been reported.

In 1976, Margolis & Margolis (6) reported the association between multiple ST and diabetes mellitus (DM). They examined prospectively 500 consecutive hospital admissions for the presence of ST. Approximately 75% of their 47 male patients with ST had elevated fasting and postprandial blood glucose in the diabetic range. Marglis & Margolis concluded that multiple, large, hyperpigmented, bilateral ST were predictive of DM in men. The association between ST and DM was briefly mentioned later (7, 8). However, no further studies confirming this relationship or relating it to the presence of obesity have been published. We therefore undertook our study to test these findings in non hospitalized population of both men and women.