SHORT REPORTS

Paraffin Section Light-chain Immunostaining of Large-cell Lymphocytoma

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Winkelmann RK, Banks PM. Paraffin section light-chain immunostaining of large-cell lymphocytoma. Acta Derm Venereol (Stockh) 1988; 68: 356–358.

Sixteen biopsy specimens from 11 patients with cutaneous large-cell lymphocytoma were studied by a peroxidase method using monospecific antisera to κ and λ Ig light chains. Five specimens had polyclonal presence of both κ and λ chains. Four specimens were graded as devoid of immunoreactivity, and eight were graded as non-specific because the albumin control staining was as intense as or more intense than the immunoglobulin light chains. Two specimens showing monoclonality for λ light chains had the cells in the interfollicular spaces only, and the patients have survived for 9 and 12 years without evidence of lymphoma. *Key words: Lymphoma; Dermatitis; Immunocytochemistry; Cutaneous lymphoma.* (Received November 17, 1987.)

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Criteria for malignant cells in cutaneous lymphoid infiltrates are few and often prove to be non-specific. Evans et al. (1) found only the extensive, destructive nature of the infiltrate and the medium size of the cells to be reproducibly present in clinically confirmed malignant cutaneous lymphoma. The number of mitotic figures per high-power field, monomorphism, vascularity, and inflammatory cells were unreliable features.

The development of methods for detecting lymphocyte receptors, gene rearrangements, and the presence of immunoglobulins has aided the diagnosis of lymphoma (2–5). It is generally accepted that monoclonal expression of κ or λ light chains in a B-cell lymphoma is confirmatory of malignancy (6). B-cell lymphomas are uncommon in the skin, but we studied large-cell lymphocytoma, a clinically benign nodular B-cell proliferation in the skin with many large follicular center type cells (7, 8), and found that monoclonality is rare and unrelated to a poor prognosis.

METHODS

We selected 16 skin biopsy specimens from 11 patients with large-cell lymphocytoma for study. Two patients had three biopsy specimens studied and one had two specimens studied. All 16 specimens were studied by an indirect, two-step peroxidase method using sheep monospecific antisera to human κ and λ light chains and albumin (Miles Laboratories). Swine anti-sheep Ig peroxidase conjugate was used as a secondary reagent (TAGO), and 3-amino-9-ethylcarbazole was used as a color substrate. The results were graded as negative (−), weakly positive (±), positive (1+), or strongly positive (2+). Non-specific staining was interpreted when the albumin stain was as strong as or stronger than the light-chain staining. Null staining was recorded when all staining was negative.

RESULTS

The results are shown in Table I. The results for cytoplasmic staining were polyclonal in five specimens: three showed polyclonal light chains in the large cells of the follicular and the

Table I. *κ and λ light chains in large-cell lymphocytoma*

Results	No. of biopsies
Polyclonal	5
Monoclonal	2
Non-specific	8
Null	4

small cells of the interfollicular zones and two showed polyclonal reactions in the small round cells in the interfollicular areas. Two patients showed small round cells with monoclonal λ staining in the interfollicular areas only. The follicular or nodular areas did not show monoclonal light chains. Eight specimens stained small round cells in interfollicular or large cells in follicular zones as intensely or more intensely for albumin as for κ or λ chains and were labeled non-specific. Four specimens were negative for reactants. One of the 2 patients with three biopsy specimens had a polyclonal reaction in one and non-specific results in two. The second patient with three specimens had monoclonal λ light-chain results in one and non-specific staining in the other two. The patient with two biopsy specimens had non-specific staining in both.

Follow-up information on all patients for 9 years or longer showed them to be alive and to have a good response to treatment, which consisted of local X-ray therapy or operation. No patient has developed lymphoma, although several patients developed local cutaneous tumors over several years (7).

DISCUSSION

The findings of an organized nodular structure in the skin lesion, large-cell lymphocytoma, are confirmed by T- and B-cell antibody studies. A large nodular B-cell mass is surrounded by a mantle of T-cells, or perivascular T-cell arciform masses may penetrate the nodule. The polyclonal B- and T-cell masses correlated with the benign course in all 28 cases reported to date (7–9).

The availability of high-specificity and high-sensitivity monospecific antisera for human Ig light chains, as well as the more recent development of monoclonal antibodies capable of demonstrating results in paraffin tissue, has extended the capacity for studying lymphoid tumors (2, 3). We found varying results comparable to those in the present study using frozen-section methods for immunoglobulin light chains in the study of large-cell lymphocytoma. Three patients previously showed frozen-section polyclonal results in two specimens and monoclonal κ staining in the third. Paraffin section staining from 2 of these same cases showed null and non-specific staining. Continued comparison of frozen and paraffin

Table II. *Comparison of large-cell lymphoid tumors of the skin*

Feature	Large-cell lymphocytoma (7)	Crosti's tumor (12)	Follicular center cell lymphoma (11)	Follicular lymphoma (13)
Location	Head	Back	Trunk	Head
B-markers	+	+	+	+
Light chains	Polyclonal (5/11)	Monoclonal (14/14)	Monoclonal (14/16)	Null (6/9)
T-cells	Mantle	Mantle	Perivascular	Mantle

methods is mandatory. We do not know how to give specific interpretation of interfollicular monoclonal staining.

The differential diagnosis of large-cell lymphocytoma of the skin includes large-cell lymphoma. We agree with Smolle et al. (10) that there is "a heterogeneous spectrum regarding clinicopathologic and immunologic features of cutaneous large-cell lymphoma". Both B- and T-cell lymphomas occur with large cells. We would extend this spectrum to include large-cell lymphocytoma with its large central follicular cell types, often interpreted as lymphoma by inexperienced investigators. Apparent concurrence was recently expressed by others that at least isolated cutaneous large-cell B lymphoid tumors are associated with a good prognosis (11). The concomitant or sequential presence of typical histologic features of classic lymphocytoma in such cases is reassuring that such large-cell tumors may be a form of lymphocytoma (7). Additional skin tumors that are similar are Crosti's lymphoma, shown recently by Berti et al. (12) to be a B-cell tumor, and the follicular center cell lymphoma of the skin reported by Willemze et al. (11). Comparing the features of these lymphomas, we find that, despite some differences, they are all B-cell lymphoid tumors of the skin with a good prognosis (Table II). Comparison with large-cell lymphocytoma shows some similar features. In particular, the 'follicular lymphomas' of the skin reported by Garcia et al. (13) are similar in many respects to large-cell lymphocytoma. The European series (11, 12) involved very constant monoclonal B-cell phenotype masses on the trunk and an associated good prognosis overall, but some cases had progression to systemic lymphoma.

Thus, despite a generally more favorable long-term outcome than in cases with corresponding morphologic and immunologic findings in lymph nodes, demonstration of a monotypic immunoglobulin expression is indeed an indication for fastidious staging evaluation and long-term clinical scrutiny.

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