Demonstration of Clonal Immunoglobulin Gene Rearrangements in Cutaneous B-Cell Lymphomas and Pseudo-B-Cell Lymphomas: Differential Diagnostic and Pathogenetic Aspects

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Twenty-five patients with a benign or malignant cutaneous B-cell lymphoproliferative disease, including seven cutaneous pseudo-B-cell lymphomas, eight primary cutaneous B-cell lymphomas (CBCL), and 10 secondary cutaneous B-cell lymphomas, were investigated for the presence of clonal immunoglobulin (Ig) gene rearrangements using Southern blot hybridization analysis. The selection of pseudo-B-cell lymphomas was based on the presence of polyclonal light-chain expression with immunohistochemical analysis. All cases of CBCL demonstrated monotypic light-chain expression or absence of detectable Ig on $CD20^+$ B cells. Clonal rearrangements of one or more Ig genes were demonstrated in four of seven cases of cutaneous pseudo-B-cell lymphomas, six of eight cases of primary CBCL, and in all cases of secondary CBCL. The observation that cutaneous pseudo-B-cell lymphomas as defined by immunohistochemical criteria often contain occult monoclonal B-cell populations implies that differentiating between pseudo-B-cell lymphomas and CBCL is not always possible by means of gene-rearrangement analysis. These findings may support the concept that cutaneous pseudo-B-cell lymphomas and primary CBCL are part of a continuous and progressive spectrum of B-cell lymphoproliferative skin disorders. *J Invest Dermatol 99:749-754, 1992*

Differentiation between pseudo-B-cell lymphomas and cutaneous B-cell lymphomas (CBCL) is one of the most difficult problems in dermatopathology. It is well established that clinical and histologic criteria are insufficient to differentiate between both conditions in all cases [1]. In recent years the results of immunophenotypical analysis of lymphoid infiltrates have become a decisive criterion for differentiating between both conditions. Demonstration of monotypic immunoglobulin light chain (IgL) expression or the presence of an immunoglobulin (Ig)-negative B-cell population is considered indicative of a malignant B-cell lymphoma, whereas pseudo-B-cell lymphomas contain polytypic B cells [2-4]. However, the interpretation of staining for IgL chains may be difficult and in some cases a definite diagnosis cannot be made. Recent studies have demonstrated that T-cell receptor- and Ig gene-rearrangement analysis by Southern blot hybridization is a more objective and sensitive technique that may detect clonal T- and B-cell populations that are not demonstrable by immunohistochemical analysis. With this technique clonal rearrangements of Ig genes have been demonstrated in primary CBCL [5], and also in some cases of pseudo-B-cell lymphomas [6,7]. Therefore the value of Ig gene-rearrangement analysis in differentiating between CBCL and pseudo-B-cell lymphomas has not been established. In this study, analysis of rearrangements of Ig genes was performed on skin biopsies of a large group of pseudo-B-cell lymphomas and primary as well as secondary CBCL. The results of gene-rearrangement analysis were correlated with histologic, immunohistochemical, and clinical data. The aim of the study was to determine the value of Ig gene-rearrangement analysis in the differential diagnosis of cutaneous B-cell lymphoproliferative disorders and to gain insight in the pathogenetic relationship between pseudo-B-cell lymphomas and primary CBCL.

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Abbreviations:
B-CLL: B-cell chronic lymphocytic leukemia
CBCL: cutaneous B-cell lymphoma
EDTA: ethylenediaminetetraacetic acid
Ig: immunoglobulin
IgH: immunoglobulin heavy chain
IgL: immunoglobulin light chain
SDS: sodium dodecyl sulfate
sIg: surface immunoglobulin

PATIENTS AND METHODS

Patients Twenty-five patients with a cutaneous B-cell lymphoproliferative disease, including seven patients with pseudo-B-cell lymphoma (cutaneous lymphoid hyperplasia), eight patients with primary CBCL, and 10 patients with secondary CBCL, were studied. The clinical and histologic data of these patients are summarized in Table I. The diagnosis pseudo-B-cell lymphoma (seven cases) was based on clinical, histologic, and immunophenotypical criteria. All cases showed polytypic light-chain expression on representative cryostat sections. Histologic examination showed nodular

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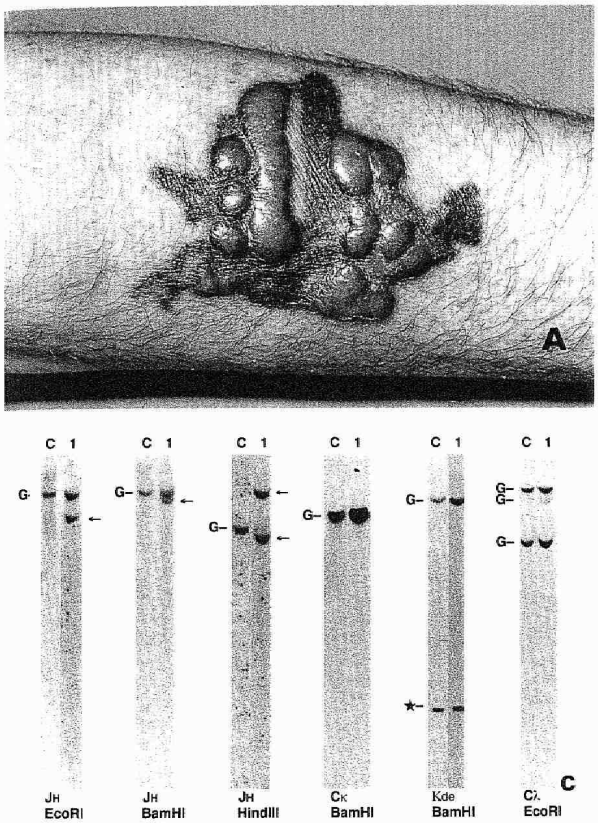
Table I. Clinical, Histologic, and Follow-Up Data of 25 Patients with a Pseudo-B-Cell Lymphoma, Primary Cutaneous B-Cell Lymphoma, and Secondary Cutaneous B-Cell Lymphoma

Patient	Age (years)	Sex	Clinical Features at Presentation[a]	Diagnosis[b]	Treatment[c]	Follow-Up (months)[d]
Pseudo-B-Cell Lymphomas						
1	53	M	Nodules in red part of tattoo. DTH to mercury products in tattoo.	Pseudo-B	Excision	A^0, 66
2	69	M	Tumor scalp since 6 months.	Pseudo-B	RT	A^0, 43
3	35	M	Tumor trunk since 3 months.	Pseudo-B	Excision	A^0, 19
4	46	F	Multiple papules and tumors on trunk and extremities.	Pseudo-B	Topical steroids	A^+, 60
5	48	F	Subcutaneous tumor left upper arm.	Pseudo-B	Intralesional steroids	A^0, 24
6	82	F	Tumor scalp.	Pseudo-B	RT	A^0, 46
7	54	M	Two small tumors on right arm.	Pseudo-B	Excision	A^0, 18
Primary CBCL						
8	88	F	Localized plaques and tumors on chest since 4 years.	CB/CC	Excision	A^0, 14
9	50	F	Tumor scalp since 9 months.	CC	Excision	A^0, 29
10	43	F	Tumor and nodules on back since 6 years.	CB/CC	RT	A^0, 6
11	65	M	Tumor chest since 12 years.	CB/CC	RT	A^0, 13
12	69	M	Since 40 years tumors trunk.	CC	COP	A^+, 18
13	47	F	Tumor scalp since 2 months. Pseudolymphoma scalp 6 years ago.	CB/CC	RT	A^0, 6
14	91	M	Multiple tumors on right leg.	CB	RT	D^+, 7[e]
15	56	M	Tumor right lower leg. Since 12 months multiple tumors with spontaneous regression.	CB/CC	RT	A^+, 13
Secondary CBCL						
16	73	M	Since 10 years solitary tumor left arm. Since 6 months generalized tumors, bone marrow and LN involvement.	Immunocytoma	COP	D^0, 31
17	70	M	Tumor trunk. Bone marrow, spleen, and LN involvement.	CB/CC	COP	D^+, 12
18	75	F	Tumors face and trunk. Bone marrow and spleen involvement.	Immunocytoma	none	D^+, 42
19	67	F	Tumors on both legs. CC-lymphoma bone marrow and peripheral blood.	CB	CHOP	A^0, 20
20	66	F	Subcutaneous swelling upper lip. B-CLL peripheral blood.	B-CLL	RT (lip)	A^+, 14
21	61	M	Tumor right cheek. LN involvement.	CB/CC	CHOP	A^0, 12
22	65	F	Tumors and plaques on trunk and right arm. Lung involvement.	CB/CC	COP	A^+, 18
23	63	M	Multiple nodules on face and trunk. LN involvement.	Immunocytoma	CHOP	A^0, 20
24	66	F	Tumors on both legs after CHOP for lymphoma of LN and bone marrow.	CB/CC	Chemotherapy	A^0, 10
25	82	M	Tumors on scalp and trunk. LN and bone marrow involvement.	Immunocytoma	Prednisone	A^0, 6

[a] LN, lymph node.
[b] CB, centroblastic lymphoma; CC, centrocytic lymphoma; CB/CC, centroblastic/centrocytic lymphoma; B-CLL, B-cell chronic lymphocytic leukemia.
[c] RT, radiotherapy; COP, cyclophosphamide, vincristine, and prednisone; CHOP, cyclophosphamide, adriamycin, vincristine, and prednisone.
[d] A^0, alive, no evidence of disease; A^+, alive, ongoing disease; D^0, died of unrelated disease; D^+, died of lymphoma.
[e] Local plus extra cutaneous relapse.

to diffuse infiltrates throughout the entire dermis with a distinct B- and T-cell compartment. In six cases (cases 1–5 and 7), secondary lymphoid follicles were present. In two cases (cases 6 and 7) histologic examination had been suggestive of a malignant lymphoma, but because of polytypic light-chain expression these cases were classified as pseudo-B-cell lymphomas. Only in one of the seven patients could a probable cause be identified. This patient (case 1), who has been described in detail elsewhere [8], presented with a pseudo-B-cell lymphoma in the red parts of a tattoo that was associated with a strong delayed-type hypersensitivity to the mercury products present in the tattoo dye (Fig 1*A*). At present six of the seven patients have no evidence of disease; case 4 has ongoing disease. None of the patients developed signs of cutaneous or systemic lymphoma. Median follow-up is 43 months (range 19–66 months).

The selection criterion for the eight patients with a primary CBCL was monotypic light-chain expression or absence of surface immunoglobulin (sIg) in a $CD20^+$, $CD22^+$ B-cell infiltrate. Histologic examination showed a diffuse large cell lymphoma of cleaved and non-cleaved cells (centroblastic/centrocytic, according to the Kiel classification) in all cases [2]. With extensive staging procedures including complete blood cell counts, chest radiography, bone marrow biopsy, computed abdominal tomography, and/or lymphangiography no extracutaneous disease was detected in these patients. These patients had solitary (four cases) or localized (four cases) tumors on various parts of the skin. Patients were treated with excision, radiotherapy, or polychemotherapy. All patients were in complete remission after the initial treatment. At present five patients are in complete remission, two patients have ongoing disease, and one patient died because of systemic spread of his skin lymphoma. The median follow-up is 13 months (range 6–29 months). The ten patients with a secondary CBCL presented with concurrent cutaneous and systemic disease or developed skin lesions after the diagnosis systemic B-cell lymphoma was made. Histologic examina-



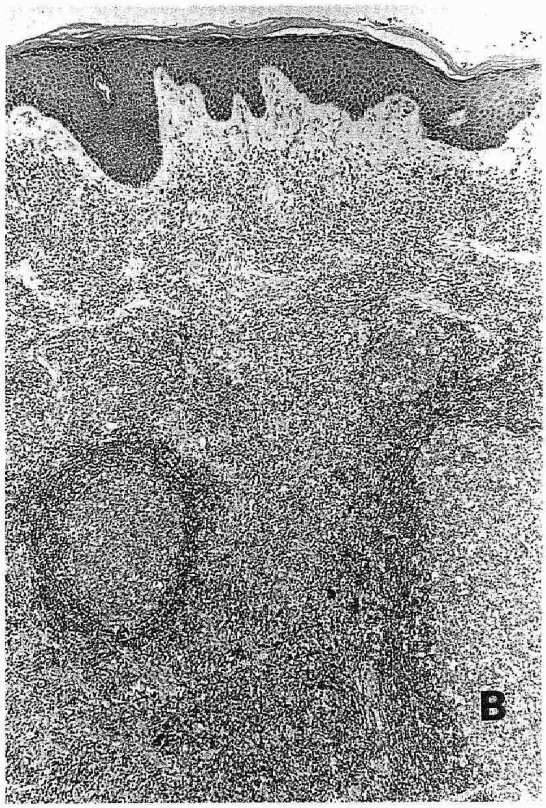


Figure 1. *A*) Pseudo-B-cell lymphoma in the red parts of a tattoo on the left arm (case 1). *B*) Histologic section of case 1 showing a dense cellular infiltrate throughout the entire dermis, with large secondary follicles. *C*) Immunoglobulin gene-rearrangement analysis using DNA isolated from a skin-biopsy specimen of case 1. C, control germline configuration (G) of human placenta DNA. *Arrows,* rearranged bands in EcoRI; BamHI, and HindIII-digested DNA, after hybridization with the JH probe. *Asterisk,* extra band due to cross hybridization of the κde probe to sequences on the long arm of chromosome 2 (2q11). With the Cκ, κde, and Cλ probe no rearrangements were detected. (*A* and *B* courtesy of Am J Dermatopathol 10:518-523, 1988.)

tion showed a diffuse large cell lymphoma of large cleaved and non-cleaved cells in five cases, an immunocytoma in four cases, and in one case a cutaneous localization of B-cell chronic lymphocytic leukaemia (B-CLL).

Southern Blot Analysis Liquid nitrogen-stored skin biopsies were used for gene-rearrangement studies. About 30-40 frozen sections of 20 μm were cut for DNA extraction. Five-micrometer sections for routine histology were cut prior and after the sections used for DNA extraction, to check whether the biopsy specimens contained sufficient characteristic lymphoid infiltrate. High-molecular-weight DNA was prepared according to standard procedures [9]. Fifteen micrograms of DNA was digested to completion with EcoRI and BamHI restriction endonucleases (Pharmacia LKB, Sweden), size fractioned by 0.6% agarose-gel electrophoresis and transferred to nylon membranes (Biotrace, Gelman sciences, USA) by a modification of Southern diffusion blotting [10] in 0.5 N NaOH and 1.5 M NaCl. Membranes were saturated with 2 × SSC (1 × SSC is 0.15 M NaCl, 0.015 M sodium citrate) and prehybridized in a solution containing 0.5 M sodium phosphate (pH 7.4), 7% sodium dodecyl sulphate (SDS), and 1 mM ethylenediaminetetraacetic acid (EDTA) [11]. Membrane-bound DNA was hybridized in the same solution with probes labeled by random priming. Membranes were washed (up to 0.1 × SSC; 0.5% SDS) at 65°C and hybridizing DNA was visualized by autoradiography (Kodak Royal X-Omat) with intensifying screens. After exposure, membranes were stripped in 0.4 N NaOH at 42°C, neutralized, and used for rehybridization. Sensitivity experiments using diluted cells proved that our Southern blot analysis can detect 1-2.5% of clonal DNA [12].

Probes The JH probe, kindly provided by Dr. T. Honjo, Kyoto University, Japan, is a 2.5-kb EcoRI-BgIII genomic fragment containing the JH region that detects rearrangements of IgH genes in BamHI and EcoRI digests [13]. The Cκ light-chain probe is a 2.5-kb EcoRI genomic fragment that allows detection of rearrangements of IgL κ genes in BamHI digests [14]. The Cλ light-chain probe is a 0.8-kb BgIII-EcoRI genomic fragment that was used to identify rearrangements in the IgL λ genes in EcoRI digests [15]. Both light-chain probes were a gift of Dr. Ph. Leder, Harvard Medical School, Boston, MA. The κde probe is a 2.5-kb BamHI-HindIII genomic fragment of the κ deleting element that rearranges on one or both alleles in cells that have progressed to λ light-chain gene rearrangement [16,17]. This probe was kindly provided by Dr. S.J. Korsmeyer, Howard Hughes Medical Institute Laboratories, St. Louis, MO.

RESULTS

Gene Rearrangement Analysis The results of gene rearrangement analysis are summarized in Table II. Hybridization of BamHI- and EcoRI-digested DNA with the JH probe showed clonal rearrangements in four of seven pseudo-B-cell lymphomas, an example

Table II. Results of Immunoglobulin Gene-Rearrangement Analysis on Skin Biopsies Using a JH Probe, Cκ Probe, κde Probe, and Cλ Probe[a,b]

Case	JH		Cκ	Kde	Cλ	Immunohistochemical Analysis	Diagnosis[c]
	BamHI	EcoRI	BamHI	BamHI	EcoRI		
Pseudo-B-cell lymphomas							
1	R	R	G	G	G	polyclonal	Pseudo-BCL
2	G	G	G	G	G	polyclonal	Pseudo-BCL
3	G	G	G	G	G	polyclonal	Pseudo-BCL
4	G	G	G	G	G	polyclonal	Pseudo-BCL
5	R	—	G	G	G	polyclonal	Pseudo-BCL
6	G	R	R	G	G	polyclonal	Pseudo-BCL
7	R	R	G	R	G	polyclonal	Pseudo-BCL
Primary CBCL							
8	G	G	G	G	G	sIg^-	CB/CC
9	G	G	G	G	G	sIg^-	CC
10	G	—	R	G	G	sIg^-	CB/CC
11	G	G	R	G	G	sIg^-	CB/CC
12	G	R	R	G	G	sIg^-	CC
13	R	R	G	R	R	λ	CB/CC
14	R	R	G	R	R	λ	CB
15	R	R	R	G	G	κ	CB/CC
Secondary CBCL							
16	R	G	G	R	R	λ	Immunocytoma
17	R	R	R	G	G	κ	CB/CC
18a[d]	G	G	R	G	G	κ	Immunocytoma
b[e]	R	R	R	G	G	κ	
19	R	R	R	R	G	κ	CB
20	R	R	G	R	G	λ	B-CLL
21	R	R	G	R	R	λ	CB/CC
22	R	R	R	R	G	κ	CB/CC
23	R	R	R	G	G	κ	Immunocytoma
24	R	R	R	R	G	κ	CB/CC
25	R	R	R	G	R	λ	Immunocytoma

[a] For further details see text.
[b] R, rearranged band; G, germline.
[c] CB, centroblastic lymphoma; CC, centrocytic lymphoma; CB/CC, centroblastic/centrocytic lymphoma; B-CLL, B-cell chronic lymphocytic leukemia.
[d] Biopsy 1987.
[e] Biopsy 1991.

of which is shown in Fig 1. Rearrangement of IgL chain genes was found only in case 6 using the Cκ probe that detected a clear rearranged band in BamHI-digested DNA. To examine the state of IgL chain gene rearrangement more thoroughly we used the κde probe. This probe detects the κ deleting element that mediates the deletion of the Cκ gene region on one or both alleles in cells that progress to λ light-chain gene rearrangement. In that case the Cκ locus is eliminated on one or both alleles and, as a consequence, non-functionally rearranged Cκ gene(s) cannot be detected by the Cκ gene probe [16,17]. In case 7, BamHI-digested DNA showed a faint rearranged band after hybridization with the κde probe, indicating a deletion of the constant region of the κ gene. In this case the Cλ probe did not detect a rearrangement of the λ light-chain gene, indicating that the usual progression to λ gene rearrangement had not yet occurred.

In primary CBCL the JH probe demonstrated clonal rearrangements in four of eight cases on BamHI- and/or EcoRI-digested DNA. Using the Cλ and the Cκ probe rearrangements of one or both, IgL genes were found in six of eight cases. In two cases no rearranged Ig genes could be detected. In these two cases immunohistochemical analysis did not show sIg either. In cases 13 and 14, hybridization of BamHI-digested DNA with the Cκ probe showed germline configuration. However, in both cases BamHI-digested DNA showed a strong rearranged band after hybridization with the κde probe, indicating a deletion of the Cκ gene locus. In these cases progression to rearrangement of the λ gene was shown using the Cλ probe (Fig 2). In cases 13–15, who showed monotypic light-chain expression, the results of gene rearrangement and immunohistochemical analysis showed identical light-chain restriction.

In the 10 patients with a secondary CBCL hybridization with the JH probe on BamHI digested DNA showed clonal rearrangements of one or two alleles in ten of the 11 samples, whereas hybridization of EcoRI-digested DNA with the JH probe showed clonal rearrangements in nine of the 11 samples.

In patient 19, who presented with a cutaneous centroblastic lymphoma and a small cell centrocytic lymphoma of the bone-marrow and peripheral blood, gene-rearrangement analysis demonstrated different clonal rearrangements in both lymphomas. In patient 20, who had a skin manifestation of a B-CLL, identical clonal rearrangements were found in DNA isolated from a skin-biopsy specimen and peripheral blood mononuclear cells. In all secondary cutaneous lymphomas the results of gene-rearrangement analysis and immunohistochemical analysis showed identical light-chain restriction.

DISCUSSION

In the present study, clonal rearrangements of one or more Ig genes were detected in four of seven pseudo-B-cell lymphomas, six of eight primary CBCL, and all ten secondary CBCL. Thus, there was a good correlation between the genotypic and phenotypic results in 19 of 25 cases. Discordant results were noted in six cases, including two patients with a CBCL and four patients with a pseudo-B-cell lymphoma.

There are several possible explanations for the lack of clonal Ig gene rearrangements in cases that have been classified as malignant B-cell lymphoma by means of immunohistochemical criteria. One explanation might be that the material used for DNA analysis was not representative. Because it is known that primary CBCL may contain considerable numbers of reactive T cells [18] it is feasible that the number of clonal cells in such a sample is insufficient. However, this possibility can be excluded as serial sections of the biopsy material we used contained a considerable proportion of monotypic B cells. Because both primary CBCL that failed to show

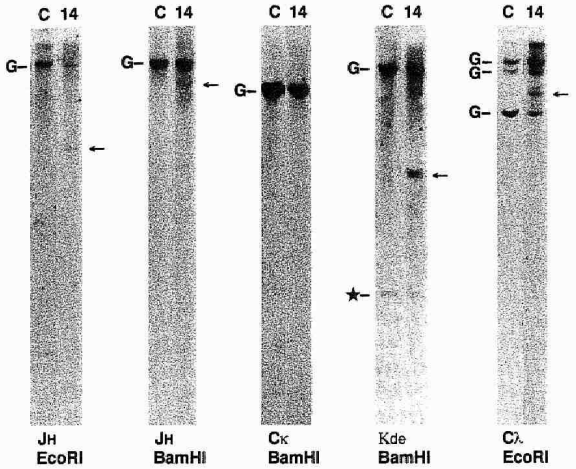


Figure 2. Immunoglobulin gene-rearrangement analysis of a λ light-chain expressing primary cutaneous B-cell lymphoma (case 13) illustrating the use of the κde probe. This probe detects the κ deleting element that mediates the deletion of the Cκ gene region on one or both alleles before progression to λ light-chain rearrangement occurs. Rearranged bands were detected on EcoRI- and BamHI-digested DNA after hybridization with the JH probe. Because of deletion of the Cκ gene region no rearrangements were detected with the Cκ probe, whereas both the κde and the Cλ probe detected a clear rearranged band. C, control germline configuration (G) of human placenta. DNA. *Arrows*, rearranged bands. *Asterisk*, extra band due to cross hybridization of the κde probe to sequences on the long arm of chromosome 2 (2q11).

clonal rearrangement of Ig genes were lymphomas in which the atypical $CD20^+$, $CD22^+$ B cells did not express sIg, deletion of Ig genes may be another explanation for the absence of clonal Ig gene rearrangements as well as the absence of detectable surface immunoglobulin. The absence of clonal Ig gene rearrangements has also been reported in systemic Ig^- B-cell lymphoma [19].

The finding of a clonal B-cell population in four of seven pseudo-B-cell lymphomas is consistent with the results of Wood et al [7], who observed clonal Ig gene rearrangements in five of 14 patients with cutaneous lymphoid hyperplasia, as defined by clinicopathologic and immunophenotypical criteria. The presence of clonal B-cell populations in pseudo-B-cell lymphomas can be explained in several ways. First, it may indicate the presence of a reactive clonal B-cell population selected by antigenic stimulation. This might be the reason for the monoclonality of IgH genes in case 1. In this patient with a pseudo-B-cell lymphoma in the red parts of a tattoo, there were no clinical, histologic, or immunohistochemical signs suggestive of a CBCL (Fig 1). The presence of a clonal B-cell population reactive to the mercury containing tattoo dye can be postulated, although on theoretical grounds an oligoclonal rather than a monoclonal B-cell proliferation is expected in such a B-cell response. Secondly, some cases of pseudo-B-cell lymphomas may actually represent early-stage CBCL, in which the number of clonal B cells is still insufficient to be identified by immunohistochemistry, whereas with a more sensitive technique, such as gene-rearrangement analysis, clonality may be demonstrated. This might be a valid explanation in patients 6 and 7, in whom clinical and histologic features were suggestive of a CBCL, but immunohistochemistry failed to show a monoclonal B-cell population. However, in the other two clonal pseudolymphomas the clinical and histologic findings were characteristic of a pseudolymphoma, and suspicion of an (early) CBCL was completely lacking. The few studies published thus far do not allow any conclusion as to the relationship between the different groups of cutaneous B-cell proliferative disorders. It is possible that pseudolymphomas, as defined by immunohistochemistry, consist of two separate groups, those with and those without occult clonal B-cell populations. Alternatively, one may conclude that the division between cutaneous pseudo-B-cell lymphomas and CBCL is not absolute, but that a continuous spectrum from polyclonal and clonal reactive B-cell proliferations towards malignant B-cell lymphomas exists [20]. In this concept the pseudolymphomas containing occult clonal B-cell populations may be considered as an initial step in tumor progression. Clonal Ig gene rearrangements have been reported in several other benign conditions, including benign lymphoid hyperplasia, at noncutaneous extranodal sites such as the orbit, the thyroid gland, and the salivary gland [21] and hyperplastic lymph nodes of patients with AIDS [22]. It has been suggested that the frequent occurrence of clonal B-cell proliferations in these conditions, which do not represent overt malignant lymphomas themselves, may be related to the increased incidence of malignant lymphomas in these patients [21]. Similarly the transition of cutaneous pseudo-B-cell lymphomas into malignant lymphoma has been described frequently [7,23,24] and not all cases can be explained by the fact that the pseudolymphoma represented an incorrectly diagnosed malignant lymphoma. One of our cases (case 13) presented with a tumor on the scalp, polyclonal with immunohistochemistry, that cured completely with local steroids, and after 6 years developed an identical tumor that showed clonality with both immunohistochemistry and Ig gene-rearrangement analysis. This patient illustrates very nicely the close relationship between pseudo-B-cell lymphomas and primary CBCL.

Thus, the concept that cutaneous pseudo-B-cell lymphomas and primary CBCL represent a continuous and progressive spectrum of B-cell neoplasia does not only explain the existence of clonal pseudolymphomas, but also provides a theoretical basis for the transition of cutaneous pseudo-B-cell lymphomas to CBCL. Furthermore this concept explains why it never has been possible to formulate indisputable clinical and/or histologic criteria for the differentiation of cutaneous pseudo-B-cell lymphomas and CBCL.

Previous studies have described that clonal pseudo-B-cell lymphomas may be cured with topical or intralesional steroids or even may disappear spontaneously [7]. This observation suggests that, whereas these clonal pseudo-B-cell lymphomas may be considered as an initial step in tumor progression, subsequent steps, that is, somatic mutation of cellular genes, are required before transition to overt malignancy occurs. The molecular basis of these further steps in the development of primary CBCL is unknown. There is one report of t[14;18] translocation involving the bcl-2 oncogene in a small percentage of cutaneous CBCL, but it is not clear whether these cases were primary or secondary CBCL [25]. In another study of 14 cases of primary CBCL no involvement of the bcl-2 and the c-myc oncogenes nor the Epstein-Barr virus was found [5]. The clinical relevance of the finding of clonal Ig heavy- and light-chain gene rearrangements in pseudo-B-cell lymphomas is difficult to evaluate because of the excellent prognosis of both cutaneous pseudo-B-cell lymphomas and primary CBCL. It must be emphasized that only one of nine clonal pseudolymphomas reported thus far—including the four cases of the present study—developed a CBCL. More important, none of these patients developed systemic lymphoma. We therefore agree with Knowles et al [21] that reclassification of these clonal pseudo-B-cell lymphomas as malignant lymphomas does not appear warranted at this time. It appears more appropriate to continue to designate these cases according to their histologic and immunophenotypical characteristics pseudo-B-cell lymphomas or cutaneous lymphoid hyperplasia, because these terms communicate the idea that these are essentially benign conditions. The chance that these clonal pseudo-B-cell lymphoma patients have systemic lymphoma at the time of first presentation is probably very low. Nevertheless, because only a few cases have been published thus far, the safest therapeutic approach for these patients is to establish that there is no concurrent extracutaneous disease, irradiation of the skin lesions, and careful monitoring of the patient for the development of malignant lymphoma.

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MEETING ANNOUNCEMENT

The Division of Dermatology, University of British Columbia, is sponsoring a research meeting entitled "The Physical Organization of Stratum Corneum Lipid," to be held February 28 to March 2, 1993 in Vancouver, British Columbia. The focus will be the physical properties of stratum corneum intercellular membranes, and we hope to attract interested basic scientists from both stratum corneum biology and membrane biophysics. The meeting will be in workshop format, attendance is expected to be about 50, and proceedings will not be published. For more information please contact Neil Kitson, Division of Dermatology, Department of Medicine, University of British Columbia, 855 West 10th Ave., Vancouver, BC Canada V5Z 1L7. Phone, (604)875-4747; Fax, (604)873-9919.