SBH-1, a Novel Reed-Sternberg–Like Cell Line Capable of Inducing Tumors in SCID Mice: Immunophenotypic, Cytogenetic, and Cytokine Expression Profiles

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A new cell line, SBH-1, with the morphologic, immunophenotypic, and karyotypic features consistent with those of Reed-Sternberg (RS) and Hodgkin (H) cells, has been established from the pleural effusion of a patient. The cytologic appearance of SBH-1 cells is characteristic of multinucleate RS and mononuclear H cells, all containing inclusion-like nucleoli. The SBH-1 cells express CD30, CD15, CD25, CD71, CD45, CD20, CD22, and bcl-2 protein and are negative for epithelial membrane antigen. Cytogenetic analysis showed multiple clonal abnormalities with breakpoints at 14q32, 6q21, and 11q23. The Ig heavy chain genes and both Ig light chain genes were rearranged in SBH-1 cells, whereas the bcl-2 gene was in germline configuration. Messages for the cytokines interleukin-1β (IL-1β), tumor necrosis factor-α, and transforming growth factor-β and the cytokine receptors IL-2R, IL-4R, IL-6R, and IL-7R were detected by reverse transcription-polymerase chain reaction analysis. Xenotransplantation of SBH-1 cells into severe combined immunodeficient (SCID) mice led to local and disseminated tumor growth. The cytologic, histologic, and immuno histochemical features of SBH-1 cells in SCID mouse tumors were typical of RS and H cells. The SBH-1 cell line will be useful in the study of RS and H cell biology, inasmuch as it represents a cell line obtained from a previously untreated patient.

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REED-STERNBERG (RS) and Hodgkin (H) cells are considered as representing the neoplastic cells in Hodgkin’s disease (HD), a subtype of malignant lymphomas that share common clinical and histologic features. The characterization of RS cells and their mononuclear variant H cells is difficult because they usually comprise only a small proportion of tumor cells. As a result, little is known about the origin of RS and H cells or how they contribute to the unique histopathologic and clinical features of HD.1,3

The use of established RS- and HD-derived cell lines can overcome the problem of low numbers of RS and H cells in diagnostic tissues by providing a continuous source of these cells for study. Despite numerous attempts to culture HD tumor cells, only 14 lines have been established that are likely to represent RS and H cells. All but 1 of these cell lines were obtained from patients with recurrent disease after chemotherapy or combined modality treatment.4-18 Cell lines established from untreated patients would be of particular interest because they have not acquired therapy-related alterations and are not end points of iatrogenically induced selection events.

We report here the establishment of a growth factor-independent RS-like cell line, SBH-1, derived from the pleural effusion of an untreated patient. Despite the fact that no tumor tissue was available for histologic assessment, the atypical cells in the pleural effusion and the SBH-1 cells showed morphologic, immunophenotypic, and karyotypic characteristics of RS and H cells.

MATERIALS AND METHODS

Case report. A 78-year-old woman presented to Sunnybrook Health Science Centre with a 6-month history of fever, lassitude, anorexia, and night sweats. Clinical, computer tomography (CT), and ultrasound examinations showed pancytopenia, bilateral pleural effusions, enlarged supraclavicular, subcarinal, para-aortic, mesenteric and portal lymph nodes, and a 5-cm mass in the left lobe of the liver. The pleural fluid contained numerous activated, atypical lympho-histiocytic cells, many with an RS cell appearance (Fig 1) characteristic of HD. After receiving informed consent from the patient, cells were collected from the pleural effusion and separated for morphologic and immunophenotypic analysis and for cell culture. Shortly after the initial investigations, the patient deteriorated, suffered a respiratory arrest, and died before a lymph node biopsy was performed. Consent for autopsy was denied.

In vitro culture of the pleural effusion. Cells from the pleural effusion were isolated by Percoll density centrifugation and resuspended in α minimal essential medium (αMEM) supplemented with antibiotics and 10% human serum, at a final concentration of 1 × 10⁶ cells/mL. Two milliliters of the suspension was placed into individual wells of a 24-well tissue culture plate. Cultures were maintained at 37°C in a humidified atmosphere with 5% CO₂ and fed with fresh medium every 3 to 5 days.

Colony-forming assays. Serial dilutions of SBH-1 cells from a maximum of 5 × 10² cells/mL to a minimum of 3 × 10⁶ cells/mL were suspended in 0.8% methylcellulose in αMEM with 10% fetal calf serum (FCS) and plated in duplicate into Petri dishes. After 7 days in culture, the dishes were inspected and colonies containing greater than 20 cells were enumerated. Colony-forming efficiency was expressed as the mean percentage of cells plated producing colonies.

Xenotransplantation of tumor cells in SCID mice. A total of 5 to 25 × 10³ viable SBH-1 cells were injected by either intravenous (IV; 8 mice) or intraperitoneal (IP; 9 mice) routes into 6-week-old female CB-17 SCID/SCID mice (Charles River, Quebec, Canada). The animals were housed in sterilized microisolator cages in the animal colony at the Sunnybrook Health Science Centre.

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Fig 1. Cytologic features of cells from the pleural fluid (A) and of the SBH-1 cells (B and C). Classical Reed-Sternberg (RS), mononuclear variant (H), and multinucleated RS cells; Romanowsky stain (original magnification × 400 for [A] and × 1000 for [B] and [C]).
**Morphology of the pleural effusion cells and SBH-1 cell line.**

The morphology of cells obtained directly from the initial pleural effusion and from the established cell line was evaluated by light microscopy using standard Romanowsky, Papanicolaou, and cytochemical staining methods. Histologic sections of formalin-fixed organs or tissue samples obtained from SCID mice injected with SBH-1 were stained with hematoxylin and eosin (H&E).  

**Immunophenotypic analysis.** Direct or indirect immunofluorescence studies of surface and cytoplasmic antigen expression were performed using flow cytometry (EPICS Profile; Coulter, Hialeah, FL) or microscopic examination of acetone-fixed cytospin slides.  

Paraffin sections were immunostained by use of the avidin-biotin-peroxidase complex method (Vector Laboratories, Burlingame, CA).  

The antibodies used in these studies included anti-CD45 (Hle-1), anti-CD15 (LeuM1), anti-CD71 (transferrin receptor), and anti-CD25 (interleukin-2 receptor [IL-2R]) (Becton Dickinson, Mountain View, CA); anti-CD19 (B4), anti-CD20 (B1), anti-CD22 (B3), anti-CD2 (T11), anti-CD3 (T3), anti-CD7 (3A1), anti-CD14 (My4), anti-CD13 (My7), anti-CD33 (My9), anti-CD10 (J5), and anti-HLA Dr (Is) (Coulter); anti-CD45 (LCA), anti-CD20 (L-26), anti-CD45RO (UCHL-1), anti-CD30 (BerH2), –bcl-2 (bcl-2,124), antihuman κ and antihuman λ light chains, and anti-epithelial membrane antigen (EMA, E29) (DAKO, Carpinteria, CA); and anti-p53 (DO-7) (Novocastra, Newcastle, UK).  

**Cytogenetic analysis.** Chromosomes were prepared from the pleural effusion cells after 3 weeks in culture and from the SBH-1 cell line after 6 months in culture. Cells were incubated at 37°C in a humidified atmosphere in 5% CO₂ overnight and then arrested in metaphase by treatment with 10 μg/mL of colchicine for 30 minutes. Cells were then suspended in hypotonic KCl solution and fixed according to standard methods.  

**Gene rearrangement studies.** Southern blot analysis was performed according to standard methods. Genomic DNA was extracted from cell lines and normal human peripheral blood mononuclear cells. Ten micrograms of DNA was then digested with the restriction enzymes BamHI, EcoRI, and HindIII (Boehringer Mannheim, Mannheim, Germany) and electrophoresed on 0.8% agarose gels; transferred to nylon membranes; and hybridized with α²P-labeled probes. The following probes were used: (1) J₄, a 3.1-kb EcoRI-HindIII genomic fragment containing the Ig heavy chain joining gene segments; (2) Cₓ, a 2.5-kb EcoRI genomic fragment containing the constant region of the Ig κ gene; (3) Cₓ, a 1.2-kb EcoRI genomic fragment containing Ig λ light chain constant region sequences; (4) Cₓ, a 400-500-bp Bgl III cDNA fragment containing the Cₓ region of the T-cell receptor β chain; (5) genomic fragments corresponding to the major breakpoint (MBR) and minor cluster (MCR) regions of bcl-2; and a cDNA that included sequences from exon 1 upstream of these regions; (6) p140, corresponding to sequences within the FVT-1 gene, and p76/1 and p53/6 that map to regions 5' and 3' of the FVT-1 gene, respectively. The filters were washed and autoradiographed at −7°C for 1 to 7 days in the presence of intensifying screens.  

**Polymerase chain reaction (PCR) analysis.** DNA extracted from SBH-1 and controls was amplified in search of bcl-2 Igk gene fusion and the presence of Epstein-Barr virus (EBV) genomic sequences. For the bcl-2-Igk fusion gene, 2 μg of purified DNA was subjected to 30 cycles of amplification using synthetic oligonucleotide primers MC4, MC5, and MC8. Oligonucleotide MC4 is complementary to a sequence common to all six Igk regions, whereas MC5 and MC8 correspond to sequences immediately 5' to the MBR and MCR regions of the bcl-2 gene, respectively. Consists of control DNA from cases of follicular lymphoma with known translocation t(14;18) involving MBR and MCR. Amplification conditions included denaturation at 95°C for 1 minute, annealing at 55°C for 2 minutes, and extension at 72°C for 3 minutes using 2.5 U Taq polymerase (Perkin-Elmer, Branchburg, NJ) in a total volume of 100 μL. After amplification, Southern blots were prepared and hybridized to α²P-labeled synthetic oligonucleotides MC6 and MC12 that correspond to sequences within the anticipated PCR products from MBR and MCR, respectively. PCR studies for EBV genomic sequences used primers and a probe derived from the EBNA 1 region of EBV, as previously described. DNA was subjected to 42 amplification cycles that included denaturation at 95°C for 45 seconds, annealing at 50°C for 45 seconds, and extension at 72°C for 1 minute. PCR products were electrophoresed through 1.5% agarose gels and blotted onto nylon filters. Filters were hybridized to α²P-labeled oligonucleotide probes, washed under high stringency conditions, and autoradiographed.  

**Expression of mRNA species for cytokine and cytokine receptors was determined by an RT-PCR technique using synthetic DNA as an internal positive control standard, as previously described. Total cellular RNA was isolated from SBH-1 cells and denatured at 65°C for 10 minutes. Single-stranded cDNA was then prepared from 5 μg of total cellular RNA by reverse transcription at 37°C for 6 minutes in a total volume of 40 μL containing 0.5 μg oligo dT (12–18mer, Pharmacia, Piscataway, NJ), 1 mmol/L dithiothreitol, 0.5 mmol/L dNTP, 80 U of RNA guard (Pharmacia), and 100 U of recombinant Moloney murine leukemia virus reverse transcriptase (GIBCO BRL, Burlington, Ontario, Canada). After heating at 65°C for 10 minutes, the cDNA was amplified. SBH-1-derived cDNA produced from 125 ng of total cellular RNA and 2 μg of internal standard DNA were amplified with 1 U of Taq polymerase (Perkin-Elmer) 50 mmol/L dNTP and 0.1 mmol/L of each of the 5' and 3' primers in a total volume of 50 μL. Amplification conditions included denaturation at 95°C for 1 minute, annealing at 54°C for 45 seconds, and extension at 72°C for 1 minute. The cDNA and the internal standard DNA use identical target sequences for the primers but yield PCR products of different sizes that are easily separated by gel electrophoresis. At the end of 30 cycles, 10 μL of PCR product was electrophoresed through 6% polyacrylamide gels in TBE buffer. Gels were then stained with ethidium bromide. The sequences of the primers used for this study have been published elsewhere. Negative controls were prepared by performing the reverse transcription reaction in the absence of reverse transcriptase to exclude false positive results caused by contaminating genomic DNA.  

**RESULTS**

**Establishment of the SBH-1 cell line.** After a period of 3 weeks, cells from the pleural effusion were transferred from 24-well tissue culture plates into a tissue culture flask and aliquots were removed for cytogenetic and immunophenotypic analysis. One month after initial plating, the cells could be maintained in flasks in αMEM supplemented with 10% fetal calf serum. After 5 weeks in culture, limited dilutions were performed. Cells were plated at a concentration of 1 cell per well into 96-well microtiter plates. A single clone was picked from one of the wells, expanded, and named SBH-1. SBH-1 cells have been passaged more than 100 times in culture without feeder layers or supplemental cytokines. The SBH-1 cell line grows as single, nonadherent cells or in small clusters, with a doubling time of 2 to 3 days and a colony-forming efficiency in methylcellulose of 2.0%.  

**Cytologic findings.** Pleural effusion cells and SBH-1 cells showed marked heterogeneity with diameters between 20 and 120 μm. Seventy percent of the cells were mononuclear, 20% to 25% were binucleate, and the remainder were
cells were found to express CD15 but to a variable degree, cells. There was little cell to cell variability in fluorescence the cells expressed CD45, B-lineage-associated markers common the chromosomal abnormalities del(3)pl lp25), culture showed a stemline and several sublines having in ranging from weakly to very strongly.

tetraploid karyotype.

tetraploid karyotype. The effusion cells had a RS and H cell phenotype. In addition, whereas the other positive markers were expressed by all HLA-DR, and p53 (Table 1). Mononuclear and multinuclear for myeloid markers CD13, CD33, and CD14; and for CD10, CD19, CD20, and CD22 and the bcl-2 oncoprotein. They obtained from the original pleural effusion after 3 weeks in culture and on established EMA consistent with a RS  and H cell phenotype. In addition, CD30, membrane-associated CD15, CD25, and both Ig k light chains. Expanded immunophenotyping performed on pleural cells after 3 weeks in culture and on established SBH-1 cells showed expression of CD30, CD15, CD25, CD71, and k and l light chains and lack of expression of EMA consistent with a RS and H cell phenotype. In addition, the cells expressed CD45, B-lineage—associated markers CD19, CD20, and CD22 and the bcl-2 oncoprotein. They were negative for T—lineage markers CD3, CD5, and CD7, for myeloid markers CD13, CD33, and CD14; and for CD10, HLA-DR, and p53 (Table 1). Mononuclear and multinuclear SBH-1 cells showed an identical pattern of antigen expression. Eighty percent of SBH-1 cells were positive for CD30, whereas the other positive markers were expressed by all cells. There was little cell to cell variability in fluorescence intensity for all markers, with the exception of CD15. All cells were found to express CD15 but to a variable degree, ranging from weakly to very strongly. 

**Cytogenetic analysis.** Cytogenetic analysis of the cells obtained from the original pleural effusion after 3 weeks in culture showed a stemline and several sublines having in common the chromosomal abnormalities del(3)(p11p25), del(4)(p12p15), del(4)(q21q28), del(6)(q21), +7, +dup(8) (q13q22), dup(9)(p13p22), del(11)(q23), add(12)(p13), i(15)(q10), and t(14;18)(q32q21). Cytogenetic analysis performed on the SBH-1 cell line after 6 months in culture showed a single clone only with the chromosomal abnormalities listed above (Fig 2). Several metaphases had a near tetraploid karyotype.

**Molecular genetics.** Southern blot analysis showed biallelic Ig heavy chain gene rearrangement (Fig 3). An identical Jk rearrangement pattern was seen in all six secondary cell lines obtained from SCID mice injected with SBH-1 that were tested (not shown). BamHI-digested SBH-1 DNA showed one deleted and one rearranged Ig k light chain gene, as well as rearrangement of the Ig l light chain genes. Germline configuration was detected with probes for the TCR b-chain, bcl-2, and FVT-1 genes (not shown).

**PCR analysis.** No PCR amplifiers were obtained from SBH-1 DNA with primers specific for Jk and the MBR or MCR regions of the bcl-2 gene or with primers specific for the EBV genome. A nonquantitative PCR method used to determine the presence of cytokine and cytokine receptor mRNAs in SBH-1 cells showed constitutive expression of the cytokines interleukin-1β (IL-1β), tumor necrosis factor α (TNFa), transforming growth factor-β (TGF-β), and the cytokine receptors IL-2R, IL-4R, IL-6R, and IL-7R (Table 2).

**Xenotransplantation of SBH-1.** Eight to 10 weeks after the injection of SBH-1 cells into SCID mice, tumor growth or deterioration in condition was observed, at which point the animals were killed for autopsy. Large intra-abdominal masses were present in all animals injected IP and some injected IV, whereas bone marrow lesions were observed in six mice injected IV. Other common sites of disease included lymph nodes, liver, spleen, and lung, with route of administration not predictive of pattern of organ involvement. The histologic appearance of SBH-1 cells in infiltrated SCID mouse tissue was typical of diagnostic RS cells and mononuclear H variants, with all cells containing inclusion-like nucleoli (Fig 4). Most tumors consisted of large collections of SBH-1 cells that replaced SCID mouse tissue. In a few instances, SBH-1 cells were found in association with large numbers of macrophages. Three mice had Hodgkin’s-like lesions and the rest had anaplastic large-cell lymphoma (ALCL)-like lesions. Immunohistochemical analysis of SCID mouse infiltrated tissues showed the tumor cells to express a phenotype identical to that of SBH-1 cells (Fig 4).

**DISCUSSION**

Studies on the biology of RS cells have been hampered by the low number of these cells in HD tissues and the paucity of established cell lines, of which only one has been established from patients before treatment. Consequently, the biologic properties of RS and H cells have, for the most part, been inferred from tissue studies using in situ hybridization or immunohistochemistry. We have characterized a new cell line, SBH-1, which shows the morphologic, immunophenotypic, and karyotypic features of RS and H cells, derived from a patient not treated with chemotherapy or radiation therapy. Unfortunately, no tissue was available for diagnostic histologic assessment and, consequently, we do not claim that the SBH-1 cell was derived from a case of HD. However, extensive characterization of SBH-1 cells shows that they have the features of RS and H cells, hence the designation of the SBH-1 cell line as composed of RS-like cells.

Some non-Hodgkin’s lymphomas (NHLs) may contain cells that fit the morphologic description of RS cells and

<table>
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<th>Table 1. Immunophenotypic Profile of SBH-1 Cell Line</th>
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<tr>
<td>CD45</td>
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<td>HLA-DR</td>
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<td>CD15</td>
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<td>CD30 (cyt)</td>
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<tr>
<td>EMA</td>
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<td>CD25</td>
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<td>CD19</td>
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<td>CD10</td>
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<td>CD71</td>
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cases of advanced HD may be indistinguishable from cells in certain high-grade NHLs, particularly ALCL, with current diagnostic methods. In the absence of a tissue diagnosis, the origin of SBH-1 cells from HD or NHLs such as ALCL cannot be conclusively determined. Indeed, even with a tissue biopsy it is not always possible to distinguish ALCL from HD with all the currently available diagnostic methods because there are no specific markers of HD. Until specific markers of HD become available, disagreement over the classification of some lymphomas as HD or NHL will exist. This point is most dramatically illustrated by the current debate over the classification of some lymphomas as the syncytial variant of nodular sclerosis HD or ALCL Hodgkin’s-like or Hodgkin’s-related. SBH-1 cells expressed an immunophenotype and contained cytogenetic abnormalities characteristic of RS cells and, even more importantly, had...
the appearance of diagnostic RS cells in tissue sections obtained from tumors developed in SCID mice. Hence, SBH-1 cells will be of value to the study of RS cells biology and the relationship between HD and NHL, especially if more specific markers of HD become available.

SBH-1 cells had the same cytologic and immunophenotypic properties as the patient’s tumor cells. Cells obtained from the patient’s initial pleural effusion and SBH-1 cells both showed an RS and H cell appearance on Rontanowsky and Papanicolau-stained preparations. Initial immunophenotypic analysis of the cells taken directly from the patient's initial pleural effusion and SBH-1 cells.

Table 2. Constitutive mRNA Expression of Cytokine and Cytokine Receptors by the SBH-1 Cell Line, as Assayed by RT-PCR Technique

<table>
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<th>Receptor</th>
<th>Expression</th>
<th>RS Cells</th>
<th>HD Cells</th>
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<tr>
<td>IL-1R (type 1)</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IL-2R</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IL-3R</td>
<td>+</td>
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<td>IL-4R</td>
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<td>IL-6R</td>
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<td>GM-CSFR</td>
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<td>GM-CSF</td>
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<tr>
<td>γ-IFN</td>
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Abbreviations: GM-CSF, granulocyte-macrophage colony-stimulating factor; SCF, stem cell factor; γ-IFN, γ-interferon.

lymphoblastoid cells selected from the patient’s pleural effusion, because monoclonal, aneuploid karyotypes are found in those cells only after prolonged cultivation. This claim is supported by PCR analysis of SBH-1 DNA that was found to be negative for EBV genome.

Nonrandom cytogenetic abnormalities that have been reported in HD tissues support a clonal origin of the atypical cells. Structural rearrangements involving 1q23, 6q11-21, 14q32, 13p11-13, and 4q35 have been reported commonly. The SBH-1 cell line exhibits a number of these chromosomal changes, including breaks at 6q21, 1q23, and 14q32. The 14q32 abnormality found in SBH-1 is of particular interest because it is reminiscent of the translocation t(14;18) of follicular lymphoma. Initial reports based on PCR analysis suggested that this translocation occurred in up to one third of HD cases. Subsequent studies by other groups reported much lower frequencies. It has been suggested that positive PCR findings may represent amplification of bystander lymphocytes bearing the t(14;18) or cases of com-posite lymphoma. In a recent cytogenetic study of 28 HD patients, a case of lymphocyte depletion HD (LDHD) was reported in a patient with no history of follicular lymphoma in which an aneuploid karyotype with the t(14;18) translocation was seen. Despite the t(14;18) translocation present in SBH-1, there was no molecular evidence of a bcl-2–IgH fusion gene. PCR amplification of SBH-1 DNA using primers specific for JH and the MBR or MCR regions of the bcl-2 gene failed to produce amplification products. Southern blot analysis using probes for MBR, MCR, and a cDNA probe to sequences in exon 1 upstream of these breakpoint regions showed the bcl-2 gene to be in germline configuration.

FVT-1, a novel transcription unit located 10 kb upstream of the bcl-2 locus, was recently cloned from a case of follicular lymphoma that overexpressed bcl-2 oncoprotein and contained a variant t(2;18) translocation. This translocation was found to involve the Ig k light chain locus without Southern blot evidence of a bcl-2–IgH gene rearrangement. Overexpression of bcl-2 was attributed to juxtaposition of the bcl-2 gene to the Ig k light chain gene enhancer sequences. We performed Southern analysis using three probes capable of detecting rearrangements of FVT-1; in all instances a germline pattern was seen.

Although the frequency of the t(14;18) translocation and its associated bcl-2 gene rearrangement in HD is still undefined, bcl-2 oncoprotein expression by RS and H cells is a common finding. LeBrun et al recently reported bcl-2 protein expression in RS cells of 20 of 32 (63%) cases of HD using paraffin-embedded tissue. Only 2 patients in that study had PCR evidence of a t(14;18) translocation and both had a prior history of follicular lymphoma. The finding of bcl-2 oncoprotein expression by SBH-1 is therefore consistent with the results of this and other studies that have shown bcl-2 protein expression by RS and H cells in 37% to 60% of HD cases. RS and H cells, both in culture and in tissues, produce a number of cytokines, including IL-1, IL-4, IL-5, IL-6, IL-9, granulocyte colony-stimulating factor (G-CSF), macrophage-CSF (M-CSF), TNFα, and TGF-β. Additional cytokines, such as IL-2, are produced by the SBH-1 cell line.
Fig 4. Histologic sections of tissues obtained from SCID mice injected with SBH-1 cells. Diagnostic RS cell in bone marrow; H&E stain (A). Binucleate and multinucleate RS cells in tumor tissue. Immunostain for CD15, avidin-biotin-peroxidase complex method (B and C).
reactive cells in HD lesions. Cytokine networks likely contribute to the unique histopathologic appearance of HD and may influence the proliferation and differentiation of RS and H cells. The presence of cytokine receptors, including c-fms, IL-2R, IL-4R, IL-6R, IL-9R, and CD30 on RS and H cells, suggests that autocrine and/or paracrine pathways may modulate the proliferation of these cells. According to our RT-PCR data, SBH-1 cells produce messages for a number of cytokines and cytokine receptors known to be expressed by RS and H cells, including IL-1β, TNFα, TGFβ, IL-2R, IL-4R, and IL-6R. We are currently investigating whether these cytokines and cytokine receptors play a role in the growth regulation of SBH-1.

By serial transplantation of primary HD-derived tissue into SCID mice, it was recently shown that these animals can provide a microenvironment suitable for in vivo growth of RS and H cells. Lymphoproliferative disease-like (LPD) and ALCL lesions occurred most frequently. A few tumors consisted of large multinucleated CD30+ cells surrounded by macrophages and were defined as HD-like lesions (HDDL). The H&E appearance and antigen profile of SBH-1 cells in SCID mouse tumors were characteristic of RS and H cells. Analysis of the histologic patterns of SBH-1 tumors showed that ALCL lesions occurred much more frequently than HDDL, similar to the results with primary HD-derived tissue. There were no lesions that resembled LPD. This finding is not surprising because the LPD seen with transplantation of primary HD-derived tissue was felt to reflect proliferation of normal EBV-infected bystander lymphocytes.

Establishment of a SCID mouse model using SBH-1 cells should be of great value for understanding the biologic attributes of RS and H cells and for testing novel therapeutic interventions in vivo. The fact that SBH-1 was established from a patient who was not treated with potentially mutagenic therapies makes this cell line particularly useful for these purposes.

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