CD56/NCAM-Positive Langerhans Cell Sarcoma: A Clinicopathologic Study of 4 Cases

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Abstract

This report concerns the clinicopathologic features of 4 patients with CD56/neural cell adhesion molecule (NCAM)-positive Langerhans cell sarcoma (LCS). Three of the patients were elderly, between 59 and 62 years of age at presentation, and the other was 35 years old. The presenting symptoms included fever, bone pain, and weakness. The patients shared some clinical findings, such as multiorgan involvement of lymph nodes, skin, lung, bone marrow, and spleen. LCS carries a poor prognosis, and 3 of the patients died of the disease within several years of presentation despite multiagent chemotherapy and radiotherapy. Of special interest is that all of the cases showed CD56 expression on the tumor cells in addition to expression of CD1a, S100, and langerin, the presence of which suggests derivation from Langerhans cells. For control, CD56 was also examined in 8 cases of Langerhans cell histiocytosis (LCH), a single-system unifocal or multifocal disease, and the results of staining of the tumor cells were negative. Our findings indicated that CD56 may be a clinically relevant biologic marker for predicting an intractable course of Langerhans cell neoplasms, although it is often difficult to draw a definite morphologically-based distinction between LCS and LCH.

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Key words: CD56; Langerhans cell sarcoma; Langerhans cell histiocytosis; Langerhans cell neoplasm

1. Introduction

Neoplastic proliferations of Langerhans cells are currently classified by the World Health Organization (WHO) into Langerhans cell histiocytosis (LCH) and Langerhans cell sarcoma (LCS) [1]. LCH always seems to pose diagnostic and therapeutic problems for pathologists and hematologists because of difficulties in identifying the Langerhans cell derivation of a neoplastic cell and in determining whether the neoplasm is aggressive. As recommended by the Histiocyte Society [2], the course of the disease is generally related to the number of organs affected at presentation [3] but may vary greatly from case to case, although the systemic form of the disease (Letterer-Siwe disease) generally has poor prognosis. Furthermore, the histologic features are not necessarily helpful in determining prognosis [4,5].

Expression of CD56 on neoplastic cells has been well documented for a variety of hematolymphoid malignancies [6-11] and has often been shown to be a clinical risk factor in several tumors, such as acute myeloid leukemia (AML) with t(8;21) [12] and t(15;17) [13] and peripheral T-cell lymphoma, including anaplastic large cell lymphoma [10]. To the best of our knowledge, however, there has been no report in the English literature regarding the clinical and prognostic significance of CD56 expression in tumors of histiocytes and accessory dendritic cells.

In this report we describe the clinicopathologic features of cases of LCS characterized by expression of CD56 on tumor cells in biopsy specimens. This expression suggests that CD56...
may function as a clinical risk factor in categorization of LCH and LCS.

2. Materials and Methods

2.1. Case Selection

Four patients with CD56+ neoplastic proliferation of Langerhans cells were entered into this study. The patients were treated at 4 collaborating institutions. All patients underwent initial biopsy between 1997 and 2002, underwent reevaluation according to the WHO classification [1], and were given the diagnosis of LCS on morphologic grounds. All patients had no history of other lymphoproliferative disorders. All specimens for histologic and immunophenotypic studies were obtained at the initial presentation of the patients. The clinical data were obtained from hospital records or supplied by physicians at the collaborating centers. All patients underwent computed tomographic (CT) examination of the chest, abdomen, and pelvis; gallium scintigraphy; biopsy; and routine peripheral blood laboratory studies. Patients were clinically evaluated in accordance with the guidelines of the Histiocyte Society [2].

2.2. Light Microscopy

Tissue samples were fixed in 10% formalin and embedded in paraffin. Sections 5 μm thick were stained with hematoxylin–eosin, elastica–van Gieson, silver impregnation, periodic acid–Schiff, May-Grünwald-Giemsa, and methyl green–pyronine. Imprint smears of the surgically resected specimens were prepared with May-Grünwald-Giemsa stain.

2.3. Immunohistochemistry

The avidin-biotin peroxidase complex method was used for immunoperoxidase studies on formalin-fixed paraffin sections [14]. We used a panel of monoclonal antibodies against CD3, CD8, UCHL-1/CD45RO, L26/CD20, CD21, Ber-H2/CD30, CD68, myeloperoxidase (MPO), and lysozyme (Dako, Santa Fe, CA, USA); CD1a (Immunotech, Mar-selles, France); CD2, CD4, CD5, CD7, CD10, CD56, and langerin (Novocastra Laboratories, Newcastle-upon-Tyne, UK); LeuM1/CD15 and Leu7/CD57 (BD Medical Systems, Sunnyvale, CA, USA); T-cell intracellular antigen (TIA-1) (Coulter Immunology, Hialeah, FL, USA); granzyme B (Monosan, Uden, The Netherlands); and S100β (kindly supplied by Dr. K. Kato, Aichi Human Service Center, Nagoya, Japan). All antibodies were applied after antigen retrieval following heat treatment in a microwave oven. Tumors were considered of Langerhans cell origin when the neoplastic cells expressed CD1a, S100β, and langerin [15].

2.4. Case Presentations

2.4.1. Case 1

A 59-year-old man with diarrhea and leukocytosis was admitted in June 1993. His medical history was essentially normal. He had splenomegaly but not hepatomegaly. Bone marrow biopsy findings led to a tentative diagnosis of myelofibrosis. The patient underwent follow-up evaluations without therapy. During the clinical course from 1998 to 2000, erythematous nodules on the precordia (Figure 1) and lymphadenopathy gradually emerged. In November 2000 the patient was hospitalized for weight loss, fever, and leukocytosis. Bone marrow biopsy showed proliferation of atypical cells with the phenotypic characteristics of Langerhans cells. The patient was treated with combination chemotherapy, that is, 2 courses of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), and attained partial remission. However, the patient’s condition deteriorated over the following 6 months in spite of the chemotherapy. In July 2002 the patient died of acute respiratory failure caused by rupture of the gastrointestinal tract and diaphragm. According to the autopsy findings the rupture was due to multiorgan involvement of LCS.

2.4.2. Case 2

A 35-year-old man presented with lower limb pain in September 1998. X-rays and magnetic resonance imaging (MRI) showed multiple bone lesions in the ilium and left thigh, respectively. Iliac bone biopsy findings led to a diagnosis of neoplastic proliferation of Langerhans cells. Treatment with 10 mg/day of oral prednisone produced some resolution of lower limb pain and reduction of bone lesions. In August 1999 the patient was readmitted because of fever and progressive dyspnea. CT examination of the thorax disclosed mediastinal lymphadenopathy. Three courses of combination chemotherapy (cytosine arabinoside, vincristine, and prednisone) and 6 courses of single-agent chemotherapy (etoposide) were administered, and the lymphadenopathy disappeared. In July 2002, however, mediastinal lymphadenopathy and bilateral pleural effusion were found on chest radiographs. On the 11th day after the last onset, the patient died of acute respiratory failure associated with left pneumothorax. Autopsy showed pleural invasion of the tumor cells.

2.4.3. Case 3

A 62-year-old woman presented in December 2002 with high fever of 1 week’s duration. She had a 2-year history of multiple bone pain. Chest radiography indicated the presence of bilateral hilar lymphadenopathy. Physical and CT