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ORIGINAL ARTICLE

Mantle cell lymphoma: a report of 31 nodal and extranodal fine-needle aspirates

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KEYWORDS

Mantle cell lymphoma; Fine needle; Malignant lymphoma; Flow cytometry; Aspiration biopsy; FISH **Introduction** This study reports our experience using aspiration cytopathology coupled with various auxiliary tests in achieving diagnostic accuracy in cases of mantle cell lymphoma (MtCL) from both nodal and extranodal sites.

Materials and methods Specimens retrieved from our cytology database used search codes for MtCL. Tissue files were searched for any cases of MtCL that had corresponding fine-needle aspiration biopsy (FNAB) cytopathology. FNAB was performed using the standard technique.

Results Thirty-one aspirates of MtCL were recovered: 11 primary and 20 recurrent examples over a wide age range (x = 63 years). All had histologic confirmation. Nearly one-half were from extranodal sites (14; 45%), mostly representing skin/soft tissue masses. Microscopic examination showed a monotonous proliferation of small-medium lymphocytes in a dispersed pattern with dendritic cells and rarely tingible-body macrophages. Flow cytometry (FCM) performed on all but 6 aspirates demonstrated light chain clonality. In 12 aspirates, ancillary testing in addition to FCM consisted of fluorescence in situ hybridization only (6 cases), fluorescence in situ hybridization plus immunohistochemical (IHC) (2), and IHC only (4). One case had cell block IHC alone without FCM. A specific diagnosis of MtCL was made from 45% of primary and 89% of recurrent MtCL cases. No examples of a correct, specific FNAB diagnosis of MtCL were made without the use of some form of auxiliary testing.

Conclusions Aspirates of MtCL are characterized by nonspecific relatively uniform small-sized to medium-sized lymphocytes. A specific diagnosis of MtCL is achievable in nodal/extranodal sites, but only when a combination of auxiliary studies is judiciously employed.

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Introduction

Patients with mantle cell lymphoma (MtCL), an uncommon form of non-Hodgkin lymphoma (NHL), suffer from one of the lowest overall survival rates among lymphoproliferative

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neoplasms. Because a variety of diagnostic terms were used for this type of NHL over the years due to ever-changing pathologic classifications, epidemiologists could not accurately assess its incidence until hematopathologists could finally agree on the diagnostic term MtCL in 1992. A study examining the years 1992 to 2004 has recently shown an increase in the incidence of MtCL over this 13-year period mainly due to an increase in patients presenting with stage IV disease. Unlike most other forms of NHL, extranodal involvement is common in MtCL. Prior reports on the fine-needle aspiration biopsy (FNAB) of MtCL have focused primarily on aspiration of enlarged lymph nodes. Only 11 extranodal aspirates (11%) were found in a total of 97 FNAB cases of MtCL from 7 different articles where the anatomic site could be determined. 2-8

In this study, we present our experience with FNAB of extranodal as well as nodal disease and highlight the necessity of employing auxiliary tests, sometimes a combination of these tests, to specifically recognize MtCL.

Material and methods

We reviewed our files for all cases diagnosed as MtCL using FNAB. In addition, our surgical pathology files were examined for any cases of MtCL that may have had corresponding aspiration cytopathology.

Percutaneous FNAB biopsy was performed on superficial and deep mass lesions using standard technique with 21-gauge or 22-gauge needles. Typically, 3 to 4 passes were made into each lesion, and each needle pass was rinsed into Roswell Park Memorial Institute (RPMI)-1640 balanced salt solution after expelling material onto glass slides to create conventional smears. All smears were air-dried. Slides were stained using both Papanicolaou and Romanowsky stains. Papanicolaou -stained slides underwent rehydration and alcohol fixation prior to staining. When performed, formalin-fixed, paraffin-embedded (FFPE) cell block sections were made using the plasma-thrombin technique and stained with hematoxylin and eosin. Immunohistochemical (IHC) staining of cell blocks used standard heat-induced epitope retrieval methodology and commercially available antibodies.

All cases had immediate assessment for adequacy performed by an attending cytopathologist. In most cases, if malignant lymphoma was suspected upon immediate microscopic examination, the specimen was submitted for flow cytometry (FCM) from the RPMI-rinsed sample. In some examples, the rinsed RPMI sample was split so that one-half was sent for FCM, and the other one-half for FFPE cell block preparation. Four-color FCM using a standard antibody panel was performed on needle rinses preserved in RPMI. Subsequent to FCM being performed, a subset of cases had the remaining aliquot of fluid submitted for interphase fluorescence in situ hybridization (FISH) analysis after knowing the results of FCM. A commercially available

LSI break-apart probe set was used to detect translocations involving the *CCND1-IgH* gene at 11q13 (Abbott Molecular Inc, Des Plaines, Ill). A positive result was interpreted as demonstrating numerous break-apart signals in the majority of lymphoid cells.

Results

Thirty-one examples of MtCL were recovered from our files; 19 men and 12 women (M:F = 1.6:1). Patient age ranged from 44 to 92 years (x = 63). All patients had histologically confirmed tissue biopsy diagnoses of MtCL independently interpreted by the hematopathology division (Table 1). Tissue specimens were obtained before, simultaneously with, or subsequent to obtaining an FNAB specimen. Seventeen aspirates were obtained from lymph nodes in a variety of anatomic locations, mostly the head/neck region (14 cases). On the other hand, 14 aspirates (45%) were obtained from extranodal sites. Of these, 8 (57%) were from cutaneous/soft tissue masses. Other extranodal sites included the oral cavity (3 cases), the salivary gland proper (2), and the liver (1).

Eleven aspirates were from patients with no known history of lymphoma, and 20 were from known MtCL patients. A specific cytologic diagnosis of MtCL was made in 22 of 31 patients (71%). Most of these were from patients with recurrent disease (17 of 22, 77%), and 5 (23%) were from individuals without no known history of NHL. A specific and correct cytopathologic diagnosis of MtCL was made in all 5 of these cases in a primary setting before a tissue biopsy was attempted. Confirmatory tissue diagnosis of all 5 came after the FNAB results were already known. In 3 of the 14 patients (21%) with extranodal FNAB, a specific diagnosis of MtCL was the initial recognition of their disease. The remaining 9 patients for whom a specific MtCL diagnosis was not issued had other, less specific interpretations of NHL, or even an incorrect NHL subclassification. These diagnoses included diffuse large B-cell lymphoma (1 case), B-cell NHL (2), or not otherwise specified NHL (6). Five of the 6 cases diagnosed as not otherwise specified NHL had only light microscopic examination without ancillary testing of any sort. The single aspirate diagnosed as diffuse large B-cell lymphoma turned out to be an example of MtCL, blastoid variant (case 3). In contrast, whenever combined FCM-FISH-cytomorphology, FCM-IHC-cytomorphology, FCM-cytomorphology, or IHCcytomorphology testing was performed, a specific diagnosis of MtCL was made in all 22 cases, regardless of their primary or recurrent clinical disease status.

Cytologic features were similar in nearly all cases. Smears were highly cellular except for 3 hypocellular cases. Smears had lymphocytes scattered in a single cell (dispersed/dissociated) pattern; 35% showed cells in clusters in addition to single cells. The diffuse, nodular, or mantle zone patterns seen in tissue sections could not be appreciated in aspirate smears. Singly dispersed dendritic cells or

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