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Original contribution

Dyspoietic changes associated with hepatosplenic T-cell lymphoma are not a manifestation of a myelodysplastic syndrome: analysis of 25 patients☆

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Summary Hepatosplenic T-cell lymphoma (HSTCL) is a rare T-cell lymphoma commonly associated with cytopenias. The pathogenesis of cytopenias in patients with HSTCL is not well defined, although the presence of dyspoietic hematopoietic cells and the common association with trisomy 8 raise the possibility of an associated myelodysplastic syndrome (MDS). In 25 bone marrow specimens involved by HSTCL, we systematically assessed for morphologic features of dyspoiesis and correlated the findings with peripheral cytopenia(s), cytogenetic findings, and detection of chromosome 8 by fluorescence in situ hybridization. The median patient age was 33 years. One patient had a history of MDS diagnosed 1 year prior to the diagnosis of HSTCL. Thirteen (54%) patients had anemia less than 100 g/L, 10 (53%) of 19 had neutropenia less than 1.8×10^9/L, and 15 (60%) had thrombocytopenia less than 100×10^9/L. Dyspoietic features were identified in 1 to 3 hematopoietic cell lineages in 20 (80%) of 25 patients. Cytogenetic analysis identified trisomy 8 in 7 cases. Patients with trisomy 8 had a lower platelet count, but trisomy 8 was not associated with cytopenias, dyspoietic features, or cytogenetic abnormalities. Combined morphologic and fluorescence in situ hybridization analysis showed that

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trisomy 8 was restricted to the lymphoma cells, except in the 1 patient with a history of MDS. In conclusion, dyspoietic changes are common in the bone marrow of patients with HSTCL. These changes are not associated with cytopenias or chromosomal abnormalities, suggesting that dyspoiesis in patients with HSTCL is not a manifestation of a MDS.

1. Introduction

Hepatosplenic T-cell lymphoma (HSTCL) is a rare and aggressive extranodal T-cell lymphoma that usually presents in adolescents and young adults. Patients typically present with hepatosplenomegaly and bone marrow involvement, and a subset of patients have a history of immunosuppression [1]. These neoplasms are commonly associated with isochromosome 7q and trisomy 8 [2,3].

Patients with HSTCL commonly present with cytopenia(s) or pancytopenia; however, the pathogenesis of the cytopenia(s) in these patients is not well defined [2]. One hypothesis is that cytopenias in patients with HSTCL reflect an underlying myelodysplastic syndrome (MDS). Evidence to support this concept includes sporadic case reports of HSTCL associated with myelodysplastic features [4,5]. In addition, a subset of patients with HSTCL have trisomy 8, a finding considered in the World Health Organization (WHO) classification to support MDS when associated with morphologic evidence of dyspoiesis provided, a secondary cause of dyspoiesis is excluded [6]. However, dyspoiesis in HSTCL is not formally established as a cause of myelodysplasia, and a systematic assessment of dyspoietic features in bone marrows of patients with HSTCL is not available in the literature.

In this study, we conducted a systematic analysis for morphologic evidence of dyspoiesis in patients with HSTCL and evaluated the possible association between cytopenias and evidence of cytogenetic features that may be associated with MDS.

2. Materials and methods

2.1. Study group

We searched the files of the Department of Hematopathology at The University of Texas MD Anderson Cancer Center and the Departments of Pathology at The University of Texas Southwestern Medical Center and Columbia University Medical Center for cases diagnosed with HSTCL between January 1, 2001, and December 31, 2014. Data were collected according to protocols approved by the institutional review boards of all institutions. The diagnosis of HSTCL was based on criteria in the WHO classification [7]. Clinical data were collected by review of the medical records.

2.2. Histopathologic assessment

Bone marrow specimens obtained at initial diagnosis were evaluated. Hematoxylin and eosin–stained slides of core and/or clot specimens, with corresponding Wright-Giemsa–stained aspirate smears and/or touch imprints, were reviewed. An iron stain was performed on aspirate smears to assess storage iron as well as the presence of ring sideroblasts.

2.3. Assessment of dyspoiesis

Assessment of dyspoiesis was performed using bone marrow core biopsy and/or clot specimens for megakaryocytic lineage, and bone marrow aspirate smears and/or touch imprints for myeloid, erythroid, and megakaryocytic lineages. The possibility of an associated MDS was assessed following parameters recommended by the WHO [6]. All hematopoietic cell lineages were assessed for morphologic features of dyspoiesis and scored as 0-3+ (0; no dysplasia, 1+, dyspoiesis present <5% of cells: 2+, dyspoiesis present <10% of cells; 3+, dyspoiesis present ≥10% of cells).

2.4. Immunophenotypic analysis

The methods used for immunohistochemical studies and flow cytometry immunophenotypic analysis have been reported elsewhere [8]. The tumor burden was semiquantified based on CD3 immunohistochemistry performed on bone marrow core biopsy and/or clot specimens [8,9].

2.5. Cytogenetic analysis

Conventional chromosomal analysis was performed on G-banded metaphases on bone marrow aspirate specimens as described previously [10]. All karyotypes were written based on the 2013 International System for Human Cytogenetic Nomenclature [11]. A karyotype was considered as "complex" when at least 3 abnormalities were identified [12]. Fluorescence in situ hybridization (FISH) analysis was performed using air-dried slides of bone marrow smears or formalin-fixed, paraffin-embedded tissue sections on a subset of cases to assess for trisomy 8, using a CEP8 probe (Abbott Molecular/Vysis, Downers Grove, IL). A total of 200 interphases were analyzed. The cutoff for a positive result of trisomy 8 established in our laboratory is 2.4%.

Combined morphologic and FISH analysis was performed as described previously [13] with minor modifications. In brief,