Best Practice & Research Clinical Haematology 28 (2015) 200–207

Contents lists available at ScienceDirect

Best Practice & Research Clinical Haematology

journal homepage: www.elsevier.com/locate/beha

Bone marrow and splenic histology in hairy cell leukaemia

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Keywords:
Hairy cell leukaemia
Histology
Spleen
Lymphoma
Bone marrow

A B S T R A C T

Hairy cell leukaemia is a rare chronic neoplastic B-cell lymphoproliferation that characteristically involves blood, bone marrow and spleen with liver, lymph node and skin less commonly involved. Histologically, the cells have a characteristic appearance with pale/clear cytoplasm and round or reniform nuclei. In the spleen, the infiltrate involves the red pulp and is frequently associated with areas of haemorrhage (blood lakes). The cells stain for B-cell related antigens as well as with antibodies against tartrate-resistant acid phosphatase, DBA44 (CD72), CD11c, CD25, CD103, CD123, cyclin D1 and annexin A1. Mutation of BRAF −V600E is present and antibody to the mutant protein can be used as a specific marker.

Bone marrow biopsy is essential in the initial assessment of disease as the bone marrow may be inaspirable or unrepresentative of degree of marrow infiltration as a result of the tumour associated fibrosis preventing aspiration of the tumour cell component. Bone marrow biopsy is important in the assessment of therapy response but in this context staining for CD11c and Annexin A1 is not helpful as they are also markers of myeloid lineage and identification of low level infiltration may be obscured. In this context staining for CD20 may be used in conjunction with morphological assessment and staining of serial sections for cyclin D1 and DBA44 to identify subtle residual infiltration. Staining for CD79a and CD19 is not recommended as these antibodies will identify plasma cells

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http://dx.doi.org/10.1016/j.beha.2015.10.019

and can lead to over-estimation of disease. Staining for CD20 should not be used in patients following with anti-CD20 based treatments. Down regulation of cyclin D1 and CD25 has been reported in patients following BRAF inhibitor therapy and assessment of these antigens should not be used in this context.
Histologically, hairy cell leukaemia needs to be distinguished from other B-cell lymphoproliferations associated with splenomegaly including splenic marginal zone lymphoma, splenic diffuse red pulp small B-cell lymphoma and hairy cell leukaemia variant. This can be done by assessment of the spleen but as this is now rarely performed in this disorder distinction is almost always possible by a combination of morphological and immunophenotypic studies on bone marrow trephine biopsy, which can be supplemented by assessment of BRAF-V600E mutation assessment in borderline cases.

Introduction

Hairy cell leukaemia (HCL), originally described in 1958 as leukaemic reticuloendotheliosis [1], is a rare chronic leukaemia of mature B-cells representing approximately 2% of all leukaemias [2–4]. This lymphoproliferative disorder has unique morphologic, cytochemical and immunologic characteristics that allow accurate diagnosis and distinction from other haematological malignancies in most cases [5]. Unequivocal diagnosis is essential as, in most cases, this is a curable disease, although refractory cases do occur.

Morphology

Tumour cells tend to primarily involve blood, bone marrow (BM) and spleen. Other commonly involved sites include the liver, lymph nodes and sporadically the skin [4,6].

Bone marrow

Bone marrow (BM) examination by histology is advised in all newly diagnosed cases especially those with dry marrow aspirates, which is not an infrequent occurrence. Histological assessment will provide not only a more accurate diagnosis but will allow a better estimate of the extent of involvement and provide a baseline for the assessment of treatment response [7].

Histologic sections of the BM show a distinctive patchy or diffuse neoplastic infiltrate with ill-defined aggregates that may blend imperceptibly with surrounding haematopoiesis with focal preservation of fat lobules [5,8] (Fig. 1). In keeping with other lymphomas presenting with splenomegaly and leukaemia, HCL may show an intrasinusoidal component to the infiltrate better appreciated with immunostains such as CD20 and DBA44 [9,10]. The sinusoidal infiltration is usually not as marked as is seen in the patterns that are typically encountered in other lymphoid neoplasms that may show some immunophenotypic and/or morphologic overlap with HCL. Although usually hypercellular, the infiltrate may less commonly be inconspicuous/hypocellular at an initial presentation [5,11].

Hairy cells are more commonly seen in a paratrabecular and intramedullary distribution with an extremely monotonous appearance. The cells appear widely spaced owing to a clear and abundant cytoplasm, which renders characteristic ‘fried-egg’ morphology. Hairy projections are usually not seen in routine histological preparations [3,12].

At high power the nuclei are usually round, but may look reniform, horseshoe-shaped or bilobed. The nuclear membrane is virtually always smooth and thickened. The chromatin looks partially condensed and evenly granular [13]. Nucleoli tend to be single and inconspicuous with round and