

Bone Marrow Histology in CML: A Continuing Relevance

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Dear Editor,

A Bone Marrow Biopsy (BMB), though not essential for diagnosing Chronic Myeloid Leukemia (CML) in chronic phase, remains a first-line investigation in the work-up, prognostication and follow-up of this disorder. It demonstrates histological and topographic features, proliferation patterns, detects CML metamorphosis and fibrosis and is indispensable in the investigation of unexplained cytopenias during therapy.

Histology of CML

The hypercellular marrow of CML shows panmyelosis and a virtual absence of adipocytes. There is granulocytic and/or megakaryocytic proliferation, eosinophilia and basophilia, occasionally with pseudo-Gaucher / sea-blue histiocytes and fibrosis. Past studies divided CML into two histological subtypes: a commoner granulocytic variant (~66%) showing unilinear granulopoietic hyperplasia, and a bilinear megakaryocytic type (~33%) additionally showing megakaryocytic hyperplasia, altered topology and pleomorphism with ineffective diminished erythropoiesis and grade 2-4 reticulin [1]. The clinical significance of this distinction (apart from the higher grade of fibrosis encountered in the megakaryocytic-type) remains controversial (Figure 1).

Fibrosis in CML

Manifest myelofibrosis is an adverse morphological factor associated with larger spleens, increased circulating blast percentages, lower hemoglobin levels and additional karyotypic abnormalities. Grading of collagen density, whether semi-quantitative or by computerized morphometry, reveals that even slight increase in reticulin (compatible with doubled normal values) is associated with significantly worsened

prognosis [2]. Thiele et al. recommended that myelofibrosis should be included in any staging system in CML relating to survival [3].

Histological changes in therapy

Imatinib mesylate therapy significantly decreases cellularity, neutrophil granulopoiesis, abnormal micromegakaryocytes, microvessel density and cell proliferation indices with regression of myelofibrosis. There is an increase in erythroid precursors and reactive lymphoid nodules with enhanced apoptosis. Myeloblasts, CD34+ cells and immature myelomonocytic cells also decrease in patients who go into complete or partial remission [4]. Imatinib-associated marrow aplasia has been described. Interferon-alpha induces apoptosis, resulting in reduced cellularity, expansion of normal erythropoiesis with increased iron-laden histiocytes and reticulum cells. Busulfan promotes myelofibrosis while hydroxyurea prevents it in a significant number of patients. In a study on 363 BMBs taken sequentially before and after allogeneic bone marrow transplantation, there was a significant correlation of marrow fibrosis, CD61+ cells and peripheral blood platelet counts with delayed haemopoietic reconstitution and leukemic relapse [5].

Ancillary studies on the BMB

Apart from assessing cellularity and fiber content, the BMB is also suitable for immunohistochemistry (angiogenesis, apoptosis, proliferation indices) and morphometric studies as well as Fluorescent In-Situ Hybridization (FISH). Application of FISH to paraffin sections for demonstrating bcr/abl in intact cells, though not recommended for diagnosis, has been used as an adjunct to cytogenetic studies and to demonstrate the common stem cell origin of the CML clone. FISH for bcr/abl on BMBs was also found to be useful to monitor therapeutic efficacy of Imatinib [6].

Conclusion

In conclusion, the BMB remains a valuable investigation in CML, both for the wealth of prognostic information conveyed as well as its usefulness in investigating scientific queries.

References

1. Knox WF, Bhavnani M, Davson J, Geary CG (1984) Histological classification of chronic granulocytic leukaemia. Clin Lab Haematol 6: 171-175.

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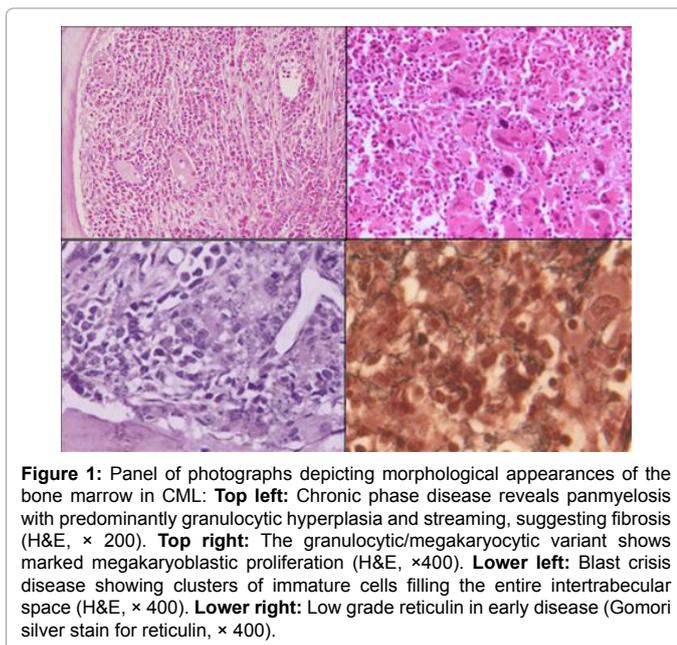


Figure 1: Panel of photographs depicting morphological appearances of the bone marrow in CML: **Top left:** Chronic phase disease reveals panmyelosis with predominantly granulocytic hyperplasia and streaming, suggesting fibrosis (H&E, × 200). **Top right:** The granulocytic/megakaryocytic variant shows marked megakaryoblastic proliferation (H&E, ×400). **Lower left:** Blast crisis disease showing clusters of immature cells filling the entire intertrabecular space (H&E, × 400). **Lower right:** Low grade reticulin in early disease (Gomori silver stain for reticulin, × 400).

2. Kvasnicka HM, Thiele J, Schmitt-Graeff A, Diehl V, Niederle N, et al. (2003) Impact of bone marrow morphology on multivariate risk classification in chronic myelogenous leukemia. *Acta Haematol* 109: 53-56.
3. Thiele J, Kvasnicka HM (2006) A critical reappraisal of the WHO classification of the chronic myeloproliferative disorders. *Leuk Lymphoma* 47: 381-396.
4. Thiele J, Kvasnicka HM, Schmitt-Graeff A, Kriener S, Engels K, Staib P, Ollig ES, Keller C, Fokkema S, Griesshammer M, Waller CF, Ottmann OG, Hansmann ML (2005) Bone marrow changes in chronic myelogenous leukaemia after long-term treatment with the tyrosine kinase inhibitor STI571: an immunohistochemical study on 75 patients. *Histopathology* 46:540-50.
5. Thiele J, Kvasnicka HM, Beelen DW, Flucke U, Spoer C, et al. (2001) Megakaryopoiesis and myelofibrosis in chronic myeloid leukemia after allogeneic bone marrow transplantation: an immunohistochemical study of 127 patients. *Mod Pathol* 14: 129-138.
6. Thiele J, Kvasnicka HM, Varus E, Ollig E, Schmitt-Graeff A, Staib P, Griesshammer M (2004) Megakaryocyte features and bcr/abl translocation in chronic myeloid leukemia following imatinib mesylate (STI571) therapy--a fluorescence in-situ hybridization study. *Leuk Lymphoma* 45:1627-31.