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MYELOPROLIFERATIVE SYNDROMES***Bone Marrow Biopsy Revision* According to
WHO Criteria in 272 Patients of the
Registro Italiano Trombocitemia (RIT):
Preliminary Report On Clinical and
Histopathological Implications.**Luigi Gugliotta, MD¹, Stefano Ascani, MD^{*2}, Silvia Asioli, MD^{*3},
Emanuela Boveri, MD^{*4}, G. Fraternali Orcioni, MD^{*5},
Umberto Gianelli, MD^{*6}, Elena Sabattini, MD^{*7},
Francesco Passamonti, MD^{*8}, Franca Radaelli, MD^{*9},
Alessia Tieghi, MD^{*10}, Claudio Tripodo, MD^{*11},
Riccardo Valli, MD^{*12}, Nicola Vianelli, MD^{*13} and
Vito Franco, MD^{*11}¹ Department of Hematology, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy,² Istituto DI Anatomia Patologica, OSPEDALE S. MARIA, Terni, Italy,³ Anatomia Patologica, Ospedale GB Morgagni, Forli, Italy,⁴ Department of Pathology, Fondazione IRCCS Policlinico S. Matteo, University of Pavia, Pavia, Italy,⁵ Azienda Ospedaliera Universitaria San Martino, Division of Hematology/BMT Unit, Genova, Italy,⁶ Department of Pathology, San Paolo Hospital, University of Milan, Milan, Italy,⁷ Anatomia Patologica, Istituto L e A Seragnoli, Bologna, Italy,⁸ Hematology Department, Fondazione IRCCS, Istituto Policlinico San Matteo, Pavia, Italy,⁹ U.O. Ematologia 2, Fondazione IRCCS Ospedale Maggiore Policlinico Mangiagalli e Regina Elena, Milano, Italy,¹⁰ Department of Hematology, Arcispedale S. Maria Nuova, Reggio Emilia, Italy,¹¹ Human Pathology, University of Palermo, Palermo, Italy,¹² Pathology Unit, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy,¹³ Hematology Unit, Istituto L.A. Seragnoli-Bologna, Bologna, Italy**Abstract 4974**

Background: The bone marrow trephine biopsy (BMB) has a crucial role for the diagnosis of essential thrombocythemia (ET), both according to the PVSG and the WHO criteria. The WHO 2001 criteria enhanced the role of BMB also by distinguishing the true-ET (ET) from the prefibrotic and the early fibrotic chronic idiopathic myelofibrosis. The WHO 2008 criteria, in the JAK2 era, confirmed the diagnostic and prognostic relevance of the histopathological features in ET as well as in the other Ph-neg myeloproliferative neoplasms (MPN). Otherwise, only few validated data are presently available, and the reproducibility in the evaluation of some morphological details is still controversy.

Objective: To validate ET diagnosis in a large registry-based series of patients by revising the BMB specimens according to the WHO criteria and to evaluate the potential relationship between the histopathological and the clinical parameters at presentation.

Methods: The hematological centers of the Registro Italiano Trombocitemia (RIT) were invited to participate to this study by sending the BMB specimens (hematoxylin-eosin, Giemsa and silver stains) obtained at diagnosis. The clinic-pathological panel of the RIT (with three hematopathologists as permanent members coordinated by a chairman) performed a centralized revision of the BMB specimens, concomitantly (multihanded microscopy) and blindly (only patient sex and age were known). The panel described for each case the morphological features and gave a diagnostic conclusion according to WHO criteria as follows: true-ET (ET); or initial primary myelofibrosis (i-PMF) distinguished in prefibrotic PMF (pf-PMF/MF-0) and early fibrotic PMF (ef-PMF/MF-1); or advanced PMF (MF-2 and MF-3); or early polycythemia vera (e-PV); or MPN unclassifiable (MPN-U); or diagnosis other than MPN (No MPN).

Results: Thirteen centers sent the specimen of BMB at diagnosis of 272 patients registered into the RIT and diagnosed in the years 1986-2002 (group A, cases 66, 24.3%), 2003-2005 (group B, cases 95, 34.9%) and 2006-2008 (group C, cases 111, 40.8%). The patients, 104 (38%) males and 168 (62%) females, had at diagnosis: age over 50 in 64% of cases (median 58); PLT count ($10^9/L$) >1000 in 16% and ≤ 600 in 24% of cases (median 789); Hgb level (g/dL) >17 in 1% and ≤ 9 in 5% of cases (median 14.3); WBC count ($10^9/L$) >9 in 44% of cases (median 8.6); splenomegaly in 18% of cases. Disease symptoms, thrombotic and

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hemorrhagic events were reported in 40%, 21%, and 7% of cases, respectively.

During the follow-up (median 2.7 years) 65% of patients received cytoreductive drugs (Hydroxyurea 59%, Anagrelide 20%, Interferon 14%, Pipobroman 6.5%, Busulfan 0.5%).

The revision of the 272 BMB specimens allowed to the following diagnosis: ET 142 cases, 52.2%; i-PMF 72 cases, 26.5% (distinguished in pf-PMF 19 cases, 7% and ef-PMF 53 cases, 19.5%); e-PV 13 cases, 4.8%; MPN-U 16 cases, 14.3%; No MPN 8 cases, 2.9%. In the patients of groups A, B, and C the rate of ET was increasing (from 44%, to 50% and to 59%, respectively) while the rate of i-PMF was decreasing (from 34%, to 31% and to 18%, respectively); moreover, the rate of e-PV was 0%, 6%, and 6%, respectively.

The ET patients compared with the i-PMF patients showed at diagnosis a lower rate of splenomegaly (16/142, 11.3% vs 24/72, 33.3%, $p < 0.0001$), of age > 50 years (84/142, 59.2% vs 53/72, 73.6%, $p < 0.03$), and a higher rate of PLT count ($10^9/L$) ≤ 600 (39/142, 27.5% vs 11/72, 15.3%, $p < 0.04$); no significant differences were found between the two groups for sex, Hgb level, WBC count, symptoms, thrombotic and hemorrhagic events. The treatment rate was lower in ET than in i-PMF (ratio 0.7).

Conclusion: This preliminary report on the revision of the BMB at diagnosis in 272 patients of the Registro Italiano Trombocitemia (RIT) shows that: the rate of true ET is continuously increasing (from 44% before 2003 to 59% in the period 2006-2008), with i-PMF rate concomitantly decreasing (from 34% to 18%); the ET patients, compared with the i-PMF ones, were younger, with lower PLT count and with lower rate of splenomegaly, and received a less intensive cytoreductive treatment.

Disclosures: No relevant conflicts of interest to declare.

Footnotes

* Asterisk with author names denotes non-ASH members.



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