Registry of CMPD Variant Forms: So-Called Essential Thrombocythaemia with Ringed Sideroblasts (Refractory Anemia with Marked Thrombocytosis)

Introduction

There is increasing evidence that bone marrow ringed sideroblasts (RS) are not confined to refractory anemia with ringed sideroblasts (RARS) (1), but may also be observed in other MDS types including refractory anemia with excess blasts (RAEB), RAEB in transformation /acute myeloid leukemia and in a rare subset of patients presenting with thrombocythaemia (2-5). This condition formerly known as "essential thrombocythaemia (ET) with RS" remains an ill-defined disease of the WHO classification mentioned in the categories" (ET)" (6) as well as „myelodysplastic/ myloproliferative disease, unclassifiable (MDS/MPD, U)"(7). According to our experience, the "ET/RS" group is now fracturing into clearly defined haematological disease entities which can be categorized either as true ET/RS, CIMF/RS or various MDS categories with RS and thrombocythaemia (8). The presence of RS suggests that a spectrum of myeloproliferative and myelodysplastic disorders may share mitochondrial defects which may contribute to BM dysfunction. A discrimination of the distinct entities, i.e. true ET, CIMF and lower- or higher- risk MDS subtypes within the "ET/RS" group is needed to choose an appropriate treatment approach for individual patients.

Registry of „ET/RS" Patients

The purpose of this registry is to list clinical, laboratory, molecular, cytogenetic and survival data in addition to morphological findings from patients presenting with thrombocythaemia associated with RS in bone marrow smears. The criteria for inclusion in the registry are the presence of ≥15% RS with >5 Prussian blue-positive granules surrounding at least 30% of the nucleus and of persistend thrombocythaemia with a platelet count ≥500 x 10^9/L. Although this platelet level does not strictly conform with the WHO criteria (>600 x 10^9/L) this lower level was in accordance with data obtained from patients with early ET. Patients with a Philadelphia chromosome and BCR/ABL fusion gene, a previous well defined chronic myeloproliferative disorder or a del(5q) must be excluded. In addition, vitamin B12 or folate deficiency, alcoholic or medical intoxication and metabolic disordered should be excluded. Peripheral blood, bone marrow (BM) smears and at least one BM biopsy should be available

in all patients. Evaluation focusses on clinical, cytogenetic and follow-up data and cytological, histological and immunohistochemical examination of primary and, if possible, sequential BM trephines. The aim is to determine whether an individual patient belongs to the categories true ET associated with RS, CIMF with RS or MDS with RS.

Follow-up biopsies may provide additional informations to permit a more precise designation in previously unclassifiable cases. Moreover, they help to document the evolution of the disease.

We hope that the classification of this initially unclassifiable myeloproliferativ/myelodysplastic disease designated as ET/RS may be significantly advanced by this registry. The data should be discussed by a panel of WP9 members.

Studies of a larger patient' cohort may provide predictive factors for the biologic course of the disease, the response to therapy, and help to define the best treatment strategies.

Standardized reporting of patient data in the ET/RS registry

Following ethical guidelines, all patient data have to be strictly anonymous. For each case the clinical and laboratory informations, including age, sex, peripheral blood cell count, cytogenetic/molecular data and spleen size at initial presentation as well as follow-ups and survival data should be documented and sent to the registry. For the standardized evaluation of bone marrow biopsies, the Cologne bone marrow evaluation sheet (see WP9.6) should be used.

Estimates of survival are evaluated from the date of initial diagnosis before therapy to the date of death or last follow-up.

Clinical , laboratory and morphological findings at initial presentation („ET/RS“ registry)

Gender (female/male)	
Age (years)	
Initial symptoms	
Spleen size	
Thrombocytes (x10^9/L)	
Erythrocytes (x10^{12}/L)	
Haemoglobin (g/dl)	
MCV (µm^3)	
Reticulocytes	
Erythrocyte morphology	
Leukocytes (x 10^9/L)	
Blasts in blood smears	
Circulating $CD34^+$ cells	
Bone marrow cytology	
Ringed sideroblasts (% of marrow cells in smears)	
Bone marrow histology*	
Genetics	

* reported on the Cologne bone marrow evaluation sheet (see WP9.6)

Follow-up data documented in the „ET/RS“ registry

Follow-up (months)	
Therapy	
Bleeding	
Thromboembolic events	
Extramedullary haematopoiesis	
Increased spleen size	
Thrombocytes (x10^9/L)	
Erythrocytes (x10^{12}/L)	
Haemoglobin (g/dl)	
Leukocytes (x 10^9/L)	
Increased circulating blast count	
Bone marrow cytology	
Bone marrow histology*	
Leukemic transformation	
Additional genetic abnormalities	
Cause of death	

* reported on the Cologne bone marrow evaluation sheet (see WP9.6)

References

1. Germing U, Gattermann N, Aivado M et al. Two types of acquired sideroblastic anemia (AISA): a time-test distinction. Br J Heamatol 2000; 108: 724-728.

2. Carroll AJ, Poon MC, Robinson NC, et al. Sideroblastic anemia associated with thrombocytosis and a chromosome 3 abnormality. Cancer Genet Cytogenet 1986; 22: 183-187.

3. Bain BJ. The relationship between the myelodysplastic syndromes and the myeloproliferative disorders. Leuk Lymphoma 1999; 34: 443-9.

4. Neuwirtova R, Mocikova K, Musilova J, et al. Mixed myelodysplastic and myeloproliferative syndromes. Leuk Res 1996; 20: 717-26.

5. Gupta R, Abdalla SH, Bain BJ. Thrombocythosis with sideroblastic erythropoiesis: a mixed myeloproliferative myelodysplastic syndrome. Leuk Lymphoma 1999; 34: 615-9.

6. Imbert M, Pierre R, Thiele J, Vardiman JW, Brunning RD, Flandrin G. Essential thrombocythemia. In: ES Jaffe, NL Harris, H Stein, JW Vardiman , eds, Pathology and Genetics of Tumors of Haematopoietic and Lympoid Tissues. World Health Organization Classification of Tumours. IARC Press Lyon 2001

7. Bain B, Vardiman JW, Imbert M, Pierre R. Myelodysplastic/myeloproliferative disease, unclassifiable. In: ES Jaffe, NL Harris, H Stein, JW Vardiman , eds, Pathology and Genetics of Tumors of Haematopoietic and Lympoid Tissues. World Health Organization Classification of Tumours. IARC Press Lyon 2001

8. Schmitt-Graeff A, Thiele J, Zuk I, Kvasnicka HM. Essential thrombocythemia with ringed sideroblasts: a heterogeneous spectrum of diseases, but not a distinct entity. Haematologica 2002; 87: 393-400.