

Refractory anemia with excess blasts (RAEB)

Identity

Note This disorder is part of the heterogeneous category of [myelodysplastic syndrome](#) (MDS). According to the FAB classification of MDS, RAEB includes those patients with 5-20% blasts in the bone marrow (BM). Because the severity of the disease largely depends on the percentage of blasts in the BM, two categories of RAEB were recognised by the WHO classification, i.e. RAEB-1 and [RAEB-2](#), with 5-9% and 10-19% blasts, respectively. In this card, the FAB classification will be used, because the majority of available data on cytogenetic anomalies was derived from studies published before WHO classification.

Other names RAEB-1 and RAEB-2

Clinics and Pathology

Phenotype / cell stem origin RAEB is a clonal disorder originating from a totipotent stem cell or from a multipotent myeloid progenitor cell, characterized by ineffective hemopoiesis and diserythropoiesis. The blast cell present in the BM are usually CD34+ and express myeloid markers (i.e. CD33 and/or CD13).

Epidemiology There are few data on the epidemiology of RAEB, which may account for 20-30% of all MDS cases. MDS is predominantly diagnosed in the elderly population. The global incidence of all MDS was comprised between 3,5 and 12,6 new cases / year / per 100,000 in some studies. The incidence may rise from 0,5 MDS cases per year in the 40 years age-group to 89 cases per year in the >80 age-group.

Clinics RAEB usually presents with hypercellular bone marrow (BM) with 5-20% blasts (5-9% in RAEB-1 and 10-19% in RAEB-2) and cytopenias of various degree. Blast cells (<20%) can be present in the peripheral blood. The patient may be asymptomatic or, alternatively he/she may suffer from BM failure-related symptoms.

Cytology Criteria for the recognition of dysplastic features of BM cells were published by the FAB group. Dyserythropoiesis includes megaloblastoid changes of erythroid precursors, multinuclearity, nuclear fragmentation, unstained area in the cytoplasm (dysemoglobinization). Dysgranulocytopenias include hypogranular neutrophils, the pseudo-Pelger anomaly of neutrophils. Micromegakaryocytes, large mononuclear forms and multiple separated nuclei are major signs of dysmegakaryocytopenias.

Pathology The bone biopsy may be useful in some cases of MDS with BM fibrosis and allows for the demonstration of the so called "abnormal localization of immature precursors" (ALIP) which may represent a prognostic factor.

Treatment Treatment of this condition in the elderly patient is largely supportive,

including blood transfusion in patients with symptomatic anemia. Anemic patients with low serum erythropoietin (EPO) levels may benefit of the administration of rHu-EPO. Low dose cytarabine can be used to reduce the burden of blasts. Myeloablative regimens including anthracyclines and cytarabine in conventional or high doses can be used in high-risk patients under 60 years. Allogeneic bone marrow transplantation may offer a chance of cure in young patients.

- Evolution This is an oligoblastic leukemia, carrying a 20-40% probability of evolving into leukemia. In a study approximately 25% of the patient developed [acute myeloid leukemia](#) (AML) within 18 months. The probability of RAEB to transform into AML is lower in the RAEB-1 group (approximately 50% of the patients develop acute leukemia within 6 years) than in the RAEB-2 group (approximately 50% at 18 months with overt leukemia).
- Prognosis Median survival of RAEB falls in the 1-2 year range. The best outcome is usually observed in RAEB-1. Chromosomal abnormalities have independent prognostic significance and are to be included in risk assessment at diagnosis. Favourable cytogenetic features are normal karyotype, [5q-](#) or [20q-](#) isolated; unfavourable features are complex karyotype (i.e. 3 or more clonal anomalies) and abnormalities of chromosome 7q; other abnormalities identify patients in the intermediate cytogenetic-risk group.

Cytogenetics

- Cytogenetics There is no specific chromosome marker for patients with RAEB, up to 60% of whom may show an abnormal karyotype. More sensitive techniques such as fluorescence in situ hybridization (FISH) found that a minority of patients with apparently normal karyotype can be shown to carry an occult chromosome defect
- Morphological The 5q- chromosome may be found in up to 40% of the cases, usually in association with additional chromosome aberrations. Approximately 20% of the cases may carry a [-7/7q-](#) or [trisomy 8](#). A chromosome [12p deletion](#) or 11q deletion can be found in 5% of cytogenetically abnormal cases. Those patients with a 17p deletion may display distinctive hematologic features, including dysgranulopoiesis with the pseudo-Pelger anomaly and small vacuoles in the cytoplasm of the neutrophils, p53 mutation and poor outcome. A number of very rare chromosome aberrations were described in some reports. Recurrent deletions are represented by [del\(3\)\(p14p21\)](#), [del\(6\)\(p21\)](#), [del\(9\)\(q13q22\)](#), [del\(12\)\(p13\)](#), [del\(18\)\(p11\)](#). [Monosomy Y](#) may occur more frequently in elderly males. Rare recurrent structural anomalies which can also be found in acute myeloid leukemia include: [t\(6;9\)\(p23;q34\)](#); [t\(3;5\)\(q25;q35\)](#); [t\(1;3\)\(p36;q21\)](#); [t\(3;21\)\(q26;q22\)](#); [inv\(3\)\(q21q26\)](#); [t\(7;11\)\(p15;p15\)](#). Trisomies are represented in <1% of the cases by [+4](#); [+11](#); +13; [+21](#).

Bibliography

Proposals for the classification of the myelodysplastic syndromes.

Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, Sultan C. Br J Haematol 1982; 51: 189-199.

Medline [6952920](#)

Prognostic factors of myelodysplastic syndromes-a simplified 3-D scoring system.

Goasguen JE, Garand R, Bizet M, Bremond JL, Gardais J, Callat MP, Accard F, Chaperon J.

Leuk Res 1990; 14: 255-262.

Medline [2319806](#)

Clinical implications of chromosomal abnormalities in 401 patients with myelodysplastic syndromes: a multicentric study in Japan.

Toyama K, Ohyashiki K, Yoshida Y, Abe T, Asano S, Hirai H, Hirashima K, Hotta T, Kuramoto A, Kuriya S, et al.

Leukemia 1993; 7: 499-508.

Medline [8464227](#)

Life expectancy in primary myelodysplastic syndromes: a prognostic score based upon histopathology from bone marrow biopsies of 569 patients.

Maschek H, Gutzmer R, Choritz H, Georgii A.

Eur J Haematol 1994; 53: 280-287.

Medline [7813708](#)

Myelodysplastic syndrome and acute myeloid leukemia with 17p deletion. An entity characterized by specific dysgranulopoiesis and a high incidence of p53 mutations.

Lai JL, Preudhomme C, Zandecki M.

Leukemia 1995; 9: 370-381

Medline [7885035](#)

Cytogenetics of Myelodysplastic syndromes.

Fenaux P, Morel P, Lai JL.

Seminrs Hematol 1996; 33: 127-138.

Medline [8722683](#)

International scoring system for evaluating prognosis in myelodysplastic syndromes.

Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel P, Sanz G, Sanz M, Vallespi T, Hamblin T, Oscier D, Ohyashiki K, Toyama K, Aul C, Mufti G, Bennett J.

Blood 1997; 89: 2079-2088.

Medline [9058730](#)

Myelodysplastic syndromes: recent advances.

Alessandrino EP, Amadori S, Cazzola M, Locatelli F, Mecucci C, Morra E, Saglio G, Visani G, Tura S.

Haematologica 2001; 86: 1124-1157.

Medline [11694400](#)

Clinical importance of interphase cytogenetics detecting occult chromosome lesions in myelodysplastic syndromes with normal karyotype.

Rigolin GM, Bigoni R, Milani R, Cavazzini F, Roberti MG, Bardi A, Agostini P, Della Porta M, Tieghi A, Piva N, Cuneo A, Castoldi G.

Leukemia 2001; 15: 1841-1847.

Medline [11753603](#)

The World Health Organization (WHO) classification of the myeloid neoplasms.

Vardiman JW, Harris NL, Brunning RD.

Blood 2002; 100: 2292-2302.

Medline [12239137](#)

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