The French-American-British classification of myelodysplastic syndromes

Moshe Mittelman

Tel Aviv Sourasky Medical Center, Tel-Aviv University, Tel-Aviv, Israel

E-mail: moshemt@gmail.com

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TITLE	Proposals for the classification of the myelodysplastic syndromes.
AUTHORS	Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, Sultan C.
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In 1976, Dr. John M. Bennett and colleagues, the French-American-British (FAB) cooperative group (Figure 1), published a seminal paper, the first classification of acute myeloid leukemia (AML).[1] Interestingly, for decades it had been recognized that many AML patients experience a preleukemic phase. Rhoads & Barker had reported on 100 patients with "refractory anemia" in 1938.[2] Several terms were subsequently suggested, including: "preleukemic leukemia", "smoldering leukemia", "preleukemic syndrome (hemopoietic dysplasia)" and "dysmyelopoietic syndrome". The 1976 paper, summarizing data from 150 patients, was the first to distinguish between common AML of recent onset, requiring immediate treatment, and less acute disorders regarded as "preleukemia", with no need for urgent treatment.[1] The authors also noted that many patients with "preleukemia" never evolve to AML and succumb to the complications of bone marrow failure.

Later on, the FAB group realized that further clarifications of the preleukemic phase were required, especially characterization of blasts, and definition of conditions with excess blasts, monocytosis and leukemic progression. Reviewing slides from an additional 80 patients led to the landmark report, changing the field.

The paper introduced the term "myelodysplastic syndrome (MDS)" and proposed guidelines for its diagnosis and classification based on morphological findings, dysplasia and percentage of blasts in the peripheral blood and bone marrow. Five MDS groups were described (Table 1): (i) refractory anemia; (ii) refractory anemia with ring sideroblasts; (iii) refractory anemia with excess of blasts; (iv) chronic myelomonocytic leukemia (which was included among the MDS, despite controversy); and (v) refractory anemia with excess of blasts 'in transformation' (a new term). A main distinguishing feature of these conditions is the proportion of blast cells in the peripheral blood and/or bone

Figure 1. The French-American-British Leukemia Cooperative Group. Figure provided by Dr. John Bennett, the head of the group. Reproduced with permission.

Table 1. Peripheral blood and bone marrow viariables that the French-American-British cooperative group suggested considering when analyzing a case of myelodysplastic syndrome.

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Table I. Suggested features to record when analysing a case of MDS

Name, age, sex, full blood count		
	Bone marrow	Peripheral blood
(1)	Blast cells (types I and II) <5%, 5–10%, 10–20% 20–30%, >30% Auer rods	0, 1–5%, 5–10%, 10–20%, >20% Auer rods
(2)	Dyserythropoiesis Ringed sideroblasts ≥15% Multinuclearity Nuclear fragments Other nuclear abnormalities Cytoplasmic abnormalities Erythroblasts <5%, >60%	RBC abnormalities Circulating NRBC
(3)	Dysmegakaryocytopoiesis* Micromegakaryocytes Large mononuclear forms Multiple small nuclei Reduced numbers	Large platelets
(4)	Dysgranulopoiesis Nuclear abnormalities Hypogranular cells	
(5)	Monocytes	Monocytes and promonocytes $>1\times10^9$/l
(6)	Cellularity Hyper-, normo- or hypocellular	
(7)	Diagnosis Refractory anaemia (RA) RA with ringed sideroblasts RA with excess of blasts (RAEB) RAEB 'in transformation' Chronic myelomonocytic leukaemia (CMML)	

* Examine at least 10 megakaryocytes.

MDS: myelodysplastic syndrome; RBC: red blood cells; NRBC: nucleated red blood cells. Table with permission from Bennett *et al.* Br J Haematol 1982.

marrow. The morphological features of blasts were redefined and over 30% bone marrow blasts were proposed to diagnose AML.

Several aspects made this original report a landmark paper. First, the proposed term, MDS, was new and descriptive but also reflected the biology, i.e., syndromes (not a single disease) of the bone marrow ("myelo"), characterized by defective production (dysplasia). Second, clear guidelines, with some objectivity and quantitation, although arbitrary, for MDS diagnosis were described. The diagnostic criteria are based mainly on peripheral blood and bone marrow morphology, still the backbone of diagnosis even today, despite the developments of novel tools (cytogenetics, immunophenotyping, molecular analysis). Third, this allowed the use of a common language and terminology, providing a platform for research, communication, and permitting comparisons between patients, and led to collaborative clinical trials. Finally, this was an academic collaborative international effort, without external funding.

The MDS FAB guidelines soon became the worldwide gold-standard for the diagnosis and classification of MDS. Numerous publications validated it, leading to more research and clinical trials.[3] Not surprisingly, despite new clinical, biological and genetic information that required updated classifications (the World Health Organization classification, Revised International Prognostic Scoring System, Molecular International Prognostic Scoring System), the FAB classification remained the backbone, and all these classifications maintained the structure and philosophy of the FAB proposal.

In summary, the MDS FAB classification manuscript proposed a new term, defined a new disease entity, suggested diagnostic tools and risk stratification and led to a diagnostic, prognostic and therapeutic paradigm change.

Disclosure

No conflicts of interest to disclose.

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