MYELOBLASTIC SYNDROMES IN THE MALTESE ISLANDS: A 5 YEAR STUDY

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INTRODUCTION

MYELODYSPLASTIC SYNDROMES/MDS/ are heterogenous group of haemopoietic stem cell disorder characterized by increasing bone marrow failure with quantitative and qualitative abnormalities of all three myeloid cell lines.

In 1982 the FBA group introduced classification of the MDS and defined five groups:

1. Refractory anaemia/RA/2. RA with ringed sideroblast/ RAS/
3. RA with excess of blast/ RAEB/
4. RAEB in transformation/ RAEBT/
5. Chronic myelomonocytic leukaemia/CMML/

These groups are separated according to:

- proportion of blast cells
- whether or not ringed sideroblast are frequent in the marrow
- the proportion of the monocytes in the peripheral blood

Typically the patients are over 50 years old, of either sex, but with male predominance in most series. Presenting clinical features are those of anaemia, infection, or of easy bruising, or bleeding. However the disease may be found by chance when a patient has a blood count done for some unrelated reason.

The range of clincal features and haematological findings consistent with diagnosis of MDS is very wide, but there are also many features in common.

PATIENTS AND METHODS

The study covers a 5 year period from 1990 -1994.
Subclassification of MDS was made according to FAB criteria.
Our minimal haematological criteria for the diagnosis of MDS were:

- in the peripheral blood: single or multiple cytopenias or just macrocytosis without anaemia
- in the bone marrow:

clear morphological evidence of dysplasia in one or more cell line (this criterion being fulfilled by one or more of the following:

micromegakaryocytes, percentage of myeloblasts between 5% and 30%, hypogranultion of promyelocytes and myelocytes, pseudo - Pelger cells, abnormal monocytes precursors, ringed sideroblasts). Histological specimen was available to rule out aplastic anaemia.

Before diagnosis of MDS was made other clinical and laboratory features were reviewed. In particular we looked for exclusion criteria for primary MDS, such as Vitamin B12

and folic acid deficiency, alcoholism, hypersplenism, antibody-mediated cytopenia, paroxymal noctural haemoglobinuria, solid tumours, chronic inflammatory diseases, severe metabolic disorders, and acute toxicity from myelotoxic substances or ionizing radiation.

RESULTS

Among a total of 1919 different patients entered into the bone marrow register between 1990 - 1994, 37 cases of MDS (1.9%) were identified. MDS was diagnosed with increasing frequency.

However in 1993 the decline was observed. As the annual number of BM has been constant as shown in Table II the proportion of MDS cases rose almost constantly 0.9% to 3.5%.

The sex ratio (male / women) was balanced for (1.7) RAS and (1.0) RAEB, RAEBT and CMML were characterised by a high male to female ratio of 3.0. The series as a whole yielded a sex ratio 1.05.

MDS patients showed the well-known preponderance of the elderly.

Average annual crude incidences and age-specific per 100,000 population of Maltese Island incidences

Age	
< 49 yr	0.3
50-69 yr	2.12
≥ 70 yr	16.5
All ages *	2.4

* children excluded

DISCUSSION

The incidence of MDS show a substantial increase in recent years. For example Oscier (1987), who examined the frequency of MDS in the Bournemouth area with population of about 200,000 reported 137 new patients over a period of only 5 years with more than a third of his cases diagnosed during the last year of study.

Reizenstern and Dabrowski (1991) conducted an international opinion poll in which 91% of 41 haematologists accepted that the prevalance and incidence of the myelodysplastic syndromes have increased at least 100% during the past 10-20 years. This observation may be attributed to several factors including demographic changes, increased exposure to leukaemogenic agents and improvements in geriatric medical care and diagnosis.

In our studies changing demographics are unlikely to explain the raising frequency of MDS, because the age composition of population remained rather constant. It is our impression that improved knowledge of MDS coincided with an increasing willingness on the part of physician to perform bone marrow biopsies in elderly patients in order to arrive at a plausible explanation for abnormal haematological findings. This impression is supported by our data showing an increase in the proportion of bone marrow specimens from elderly patients.

We would therefore suggest that a raise in MDS is at least partly

due to increased physician awareness and extended use of diagnostic procedures in the elderly, and also diagnostic accuracy

in general to make case ascertement as complete as possible.
However, reliable estimate of the true incidence of MDS appears difficult to obtain. It would require a screening for abnormal blood counts and performing bone marrow biopsies in all cases of unexplained cytopenia. One should be aware of a phenomenon which is described as the 'greying' of the population; the percentage of people over age 65 is expected almost to double over the next four decades. These changes in the age compositon of population will lead to an increase in all age-related disorders including the myelodysplastic syndromes, which may become one of the most common haematological neoplasias.

ABSTRACT

Reported raising prevalance and incidence of MDS, reliable epidemiological data on these disorders are largely lacking.
Cases of MDS diagnosed and reported in the Haematolgy
Department of St. Luke's Hospital allowed us to assess incidence and age-relation over a 5 year period (1990 -1994) in the Maltese population. Among a total of 1919 different patients registered during 1990 - 1994, 37 cases of MDS (1.9%) were identified. Over the study period the percentage of newly diagnosed cases rose from 0.9% to 3.5%. Only 3 patients were younger than 60 (8%) whereas 34 cases (92%) occured after the age of 60.

We found a strong correlation between the proportion of elderly patients and relative frequency of MDS diagnosis. However, our crude annual incidence (all age groups 2.4 / 100,000) compared with data reported by Gattermans (1992), Oscier and others is significantly lower.

We conclude that MDS incidence continues to raise into very old age and nomber of newly diagnosed cases rose significanlty, which may reflect increased awareness on the part of physician and extended use of diagnostic procedures in elderly patients.

TABLE 1: Numbers and FAB type distribution of MDS cases in the Maltese Island population (1990-1994)

FAB type	No. of cases	%
RA	13	35
RAS	11	29
RAEB	6	16
RAEBT	4	11
CMML	4	11

Abbreviations: FAB - French American British Group, RA - Refractory anaemia, RAS - RA with ringed sideroblast, RAEB - RA with excess of blast, RAEBT - RAEB in transformation, CMML - chronic myelomonocytic leukaemia.

TABLE 2: Relative frequencies of MDS cases in the bone marrow register 1990-1994

	No. of BM specimens	MDS No. of cases	MDS %
1990	405	4	0.9
1991	360	6	1.6
1992	400	10	2.5
1993	365	3	0.8
1994	389	14	3.5

Age distribution of MDS patients 1990 -1994

AGE (years)	No of patients
<40	1
40-49	1
50-59	1
60-69	12
70-79	19
80 +	3