EXPERIENCE WITH PRIMARY MYELODYSPLASTIC SYNDROMES IN A UNIVERSITY HAEMATOLOGY UNIT: REPORT OF FIVE CASES

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ABSTRACT

Myelodysplastic syndromes apper to be a rare group of blood disorders in Malaysia. It usually affects the elderly and some of the cases were reported to evolve into acute leukemia. We describe our experience with five cases, seen and managed by us over a 5-year period. All patients receiving supportive therapy died with one of them definitely known to transform to acute leukemia. The patient who survives till the time of writing received low dose continuous cytosine arabinoside infusion.

INTRODUCTION

The myelodysplastic syndromes (MDS)[1] denote a group of blood disorders chracterised by peripheral blood cytopenia(s) in the presence of hypercellular bone marrow with features of ineffective haemopoiesis. The French-American-British (FAB)[2] group classified them into five subtypes: Refractory Anaemia (**RA**); Refractory Anameia with Ring Sideroblasts (**RARS**); Refractory Anaemia with excess of Blasts (RAEB); Chronic Myelomonocytic Leukaemia (CMML); and RAEB in Transformation to Acute Myeloid Leukaemia (RAEB/Tr). This has generally been accepted and found to have useful prognostic implications. Various aspects of MDS have been reviewed recently[3]. We describe our experience With five such cases.

MATERIALS AND METHODS

The clinico-pathologic features of five cases of primary myelodysplastic syndrome seen and managed by us between January 1981 and December 1985 were reviewed. We manage on an average about 50 new cases of malignant haematologic disorders every year. Blood count was performed by Coulter S and Coulter thrombocounter. Wright's stain was used for peripheral blood films and May-Grunwald-Giemsa stain for bone marrow smears. Bone marrow biopsy findings and chromosome analysis were omitted in the review as not all cases had the date. The diagnosis was established according to the FAB classification.

RESULTS

The patient characteristics and clinical findings at presentation are summarised in Table I; and their haematologic features in Table II. Prognostication of the cases was made using Multi's method[4]. The results of "predicted median survival" by this method and actual survival of the patients are tabulated in Table III.

TABLE I
PRIMARY MDS – PATIENT CHARACTERISTICS

Patient	GCK	KKL	TM	ARAW	MM
Age (yr)	36	52	60	33	76
Sex	F	M	F	M	F
Race	Chinese	Chinese	Malay	Malay	Malay
Reason for Admission	pallor	fever	fever	pallor	pallor
Hepatomegaly*	nil	4 cm	4 cm	nil	3 cm
Splenomegaly*	nil	1cm	2cm	nil	2cm
Lyrphadenopathy	nil	nil	nil	nil	nil
Duration of illness before diagnosis (wk)	4	4	3	3	12

*(Below costal margin at mid-clavidular line.

TABLE II
PRIMARY MDS-HEHMATOLOGIC FEATURES AT PRESENTATION

Patient	GCK	KKL	TM	ARAW	MM
PERIPHERAL BLOOD					
Twbc (10^9/l)	4.0	27.2	2.3	8.6	5.2
Neutro (10^9/l)	1.2	11.4	O.6	2.2	1.8
Monocyte (10^9/l)	0.2	1.1	0.1	0.4	0.2
Trbc (10^9/l)	3.45	2.81	2.26	2.45	2.20
Hb (g/dl)	9.9	8.2	6.2	6.5	6.1
Hct ratio	0.31	0.28	0.20	0.21	0.19
MCV (fl)	89	102	109	101	84
MCH (pg)	28.3	29.2	28.7	33.0	32.0
MCHC (g/dl)	31.7	29.5	26.2	37.8	32.4
Retic (%)	0.1	0.1	0.5	0.7	0.1
Platelet (10^9/l)	139	91	23	23	70
Blood film	occ blasts	occ blasts & NRBC; L shift in Neutro	occ blasts	occ blasts & NRBC	10% blasts
BONE MARROW					
Cellularity	hyper	hyper	hyper	hyper	hyper
Erythropoiesis (% of erythroid precursors amongst total nucleated cells)	megaloblastic (> 60%)	normoblastic (< 5%)	normoblastic (< 5%)	megaloblastic (> 60%)	normoblastic (< 5%)
Granulopoiesis	abnormal	abnormal	abnormal	abnormal	abnormal
Megakaryocytes	abnormal	abnormal	abnormal	abnormal	abnormal
Blast cells	18%	1%	15%	15%	25% (Auer rods +)
Iron store	normal	normal	excess	normal	excess
Ring sideroblasts	nil	nil	nil	nil	nil

TABLE III
PRIMARY MDS SURVIVAL STUDY

Patient	GCK	KKL	TM	ARAW	MM
Diagnosis (FAB)	RAEB	CMML	RAEB	RAEB	RAEB/TR
Mufti's method	B	B	C	C	C
Predicted median survival (months)	13	11	9	9	3
Actual survival (months)	9	8	7	–	5
Treatment	conservative	conservative	conservative	low dose Cytosar	conservative
Outcome	died in hospital; transformed to AML	died at home; cause of death unknown	died at home; cause of death unknown	still alive (32 months)	died at home; cause of death unknown

DISCUSSION

Myelodysplastic syndromes are not new diseases. Over the last 30 years, observers have described various haematological disorders some of which progressed to overt leukemia. Terms such as "sideroblastic anaemia", "refractory anaemia", "refractory anaemia with excess of blasts", and "preleukemia" have been used. When the French-American-British (FAB) cooperative group proposed the morphological classification of acute leukemias in 1976, they also recognised that, apart from the group of acute leukemias which presented with rapid onset of symptoms and signs, there was a range of disorders that were often subacute and chronic in nature and showed some of the morphological features of acute myeloid leukemias. Since immediate therapy was rarely indicated and the majority of patients were elderly people over the age of 60 years, the term "myelodysplastic syndrome" was used to describe them. Since not all of them evolve into leukemia, the term "preleukemia" has been dropped. Five morphological subtypes are recognised by the FAD group[2].

Many studies based on the FAB classification have demonstrated its usefulness in predicting survival and leukemic transformation. Median survivals range from four years for RARS, three years for RA, about one year for RAEB or CMML, and less than one year for RAEB/Tr. The rate of leukemic transformation is under 15% for RARS or RA, 30–40% for RAEB or CMML, and over 50% for RAEB/Tr.[5] The predicted median survival as suggested by Mufti and co-workers appears to be a useful guide to survival for patients on supportive treatment.

In comparison to the series reported by various authors[6,7,8] over the same period, it appears that our series is very small indeed. MDS occurs mainly in the elderly population and is rare in Malaysia. It may be that Malaysia still has a small elderly population. RA and RARS were not encountered in our series. The reason is not known. It is unfortunate that chromosome data is available for only one case (GCK) whose marrow karyotype shows polyploidy and deletion of the long arm of chromosome (5q-). Based on several large series of study, 37 – 51% of patients with MDS show chromosomal abnormalities. A deletion of 5q is the most common chromosomal abnormality seen in RAEB and MDS in general. Patients with a deletion of 5q usually have a relatively stable refractory anemia with a median survival of 28 months and a leukemia transformation rate of 12.5%.[9] However, patient GCK who had this lesion had a short survival.

FAB classification of the myelodysplastic syndrome together with a simple scoring system based on bone marrow blasts, platelet count, neutrophil count and hemoglobin level (Mufti's method) serves as a useful prognostic tool for counselling and planning treatment. It appears to predict poor survival for GCK even though she has a favourable 5q- chromosomal abnormality.

Patient ARAW, who had been treated with low-dose Cytosine arabinoside, which has been reported to be beneficial in these conditions,[10], has prolonged survival. He is still alive at the time of writing. This mode of treatment, though widely employed, is not yet fully "validated". It remains an experimental approach and should not be routinely used.

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