Epidemiology of Aplastic Anaemia in the State of Sabah, Malaysia.

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Summary

Aplastic anaemia is a rare disease which is more prevalent in the Far East. In Malaysia, it appears to be unusually common in the state of Sabah. A retrospective analysis of all cases of aplastic anaemia diagnosed between January 1993 and March 1996 was undertaken. The criteria of the International Aplastic Anaemia and Agranulocytosis Study (IAAAS) was used. In this 39 month period, 31 cases were confirmed by marrow trephine biopsy to be aplastic anaemia. The male-to-female ratio was 3.4. Median age of diagnosis was 23 years. There were 24 patients (77%) who were from the Kadazan-Dusun ethnic group, which forms 18% of the population of Sabah. The incidence of aplastic anaemia in Sabah appears to be higher than that reported elsewhere in the Far East, at 4.8 per million population per year. Peak incidence is in the elderly group at 8.6 per million followed by a second peak in young people aged 15 to 24 (7.9 per million). The aplastic anaemia to total acute leukaemia ratio is 0.37. The marked male preponderance and apparent susceptibility of the Kadazan-Dusun people are also notable. A further prospective study to address the true incidence of aplastic anaemia and possible aetiologic factors accounting for these observations is necessary.

Key Words: Aplastic anaemia, Leukaemia

Introduction

Aplastic anaemia is a rare and serious disease in Europe and the United States[1]. The prospective International Agranulocytosis and Aplastic Anemia Study (IAAAS) conducted in Europe and Israel from 1980 to 1984 found an overall annual incidence of 2 per million population with some regional variations ranging between 0.6 to 3.0 per million[2,3]. This low incidence has been confirmed by further prospective studies in France between 1984 and 1987 (1.5 per million)[4] and the United Kingdom in 1985 (2.3 per million)[5].

Aplastic anaemia appears to be more prevalent in the Orient[6]. There have been few prospective studies conducted in Asia on the incidence of aplastic anaemia. Data from national and provincial surveys have suggested the prevalence of aplastic anaemia to be 31 to 48 per million in Japan[7] and 19 to 21 per million in China[8,9]. A prospective study of the incidence of aplastic anaemia in Thailand revealed an overall incidence of 3.7 per million population, which is significantly higher than that in previous western studies[10]. There is also association of the increased incidence with low socio-economical background[11].

A retrospective analysis was conducted in Sabah as the high incidence of aplastic anaemia in this state was noted by local and visiting physicians for many years.

Materials and Methods

Identification and ascertainment of cases: All cases of suspected aplastic anaemia diagnosed between January 1993 and March 1996 were traced from the Central Pathology Laboratory records at Hospital Queen Elizabeth, Kota Kinabalu, Sabah. This laboratory handles all pathological specimens from the whole state

of Sabah, thus ensuring the most accurate way of tracing all cases with diagnostic confirmation. Cases were screened by blood counts, and eligible patients were required to meet at least two of the following three criteria: white blood cell count $\leq 3.5 \times 10^9$/L, platelet count $\leq 50 \times 10^9$/L, and haemoglobin concentration $\leq$ 100g/L or haematocrit $\leq$ 30%. If the latter criterion was one of the two fulfilled, a reticulocyte count $\leq 30 \times 10^9$/L was also required. Patients who received chemotherapy, immunotherapy, or radiotherapy were excluded. The bone marrow aspirate and trephine biopsy was examined and reviewed by at least two pathologists or haematologists. Final acceptance of inclusion of cases into the study required a hypocellular bone marrow trephine biopsy without gross marrow fibrosis, and absence of infiltration by leukaemic, lymphomatous, or carcinomatous cells. These definition criteria are identical to that used by the IAAAS.

Population statistics: The population figures were provided by the Sabah State Statistics Department. Over the period of the 39 months between January 1993 and March 1996, the population of Sabah was estimated to have been relatively stable at around 2 million.

Results

There were 65 cases identified initially which fulfilled clinical, peripheral blood and bone marrow aspirate criteria of hypoplastic anaemia. Of these, 31 cases were confirmed by bone marrow trephine biopsy as aplastic anaemia. 34 patients were excluded from the analysis. One had been diagnosed prior to the study period, 16 did not have a bone marrow trephine biopsy done, 15 had inconclusive bone marrow trephine biopsies due to inadequate sampling, and two had reactive hyperplastic marrows.

There were 24 male and 7 female patients (ratio 3.4). The annual incidence of aplastic anaemia in the state of Sabah was 4.8 per million. The median age at diagnosis was 23 years (range 8-72) with 26 patients (84%) under the age of 40 (Figure 1). The age specific rate is shown in Table I. Peak incidence is in the elderly group at 8.6 per million. The next highest incidence is in those aged 15 to 24 (7.9 per million) and those aged 25 to 39 (6.2 per million). There were

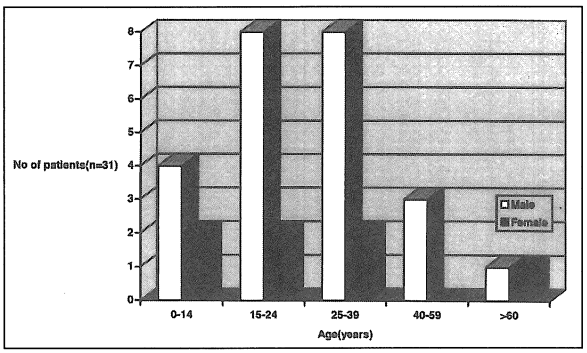

Fig. 1: Age and sex distribution of Aplastic Anaemia in Sabah (January 93 - March 96)

Table I
Incidence of Aplastic Anaemia in Sabah
(January 1993 – March 1996)

Age(years)	Population	Cases	Incidence (per million/year)
0-14	803,250	6	2.3
15-24	391,800	10	7.9
25-39	500,350	10	6.2
40-59	240,300	3	3.9
>60	71,950	2	8.6
Total	2,007,650	31	4.8

24 patients (77%) who were from the Kadazan-Dusun ethnic group.

The ratio of aplastic anaemia to acute myeloid leukaemia diagnosed in the study period is high at 31 : 34 cases (Ratio 0.91). The aplastic anaemia to total acute leukaemia ration is 0.37 (Table II).

Discussion

The state of Sabah is relatively isolated from its neighbouring state Sarawak, and the Kalimantan province of Indonesia, with which it shares its borders. The population is quite contained and the catchment area is well-defined for geographical reasons. This is an important consideration when epidemiological studies are done. Hospital Queen Elizabeth, Kota Kinabalu provides the pathological service for Sabah. All bone marrow aspirates and trephine biopsies are reported there.

The incidence of confirmed cases of aplastic anaemia in Sabah at 4.8 per million population is higher than that reported elsewhere in the South East Asian region. The increased incidence in younger people is notable (Figure 2). This susceptibility of younger patients has also been noted in the Bangkok study[10]. This pattern suggests an environmental factor which may be related to occupation. The peak incidence in old age similar to Western studies was also present.

Incidence studies of aplastic anaemia ideally should be prospective. It has to be taken into account that the

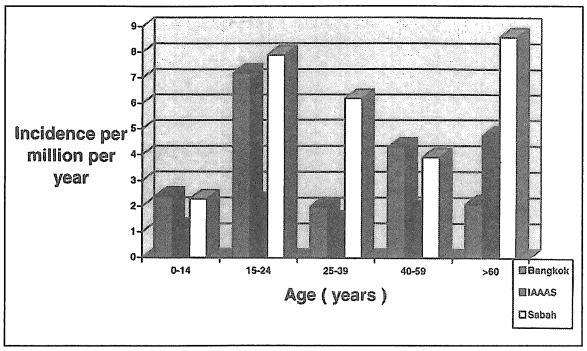

Fig. 2: Incidence of aplastic anaemia in three studies according to age

earlier retrospective studies of the epidemiology of aplastic anaemia in the West also had higher incidence figures : 5.4 to 7.1 per million population in Baltimore, MD from 1970 to 1978[12] and 6.8 per million in the northern region of the United Kingdom from 1971 to 1978[13]. These results were from the analysis of medical records or death certificates. Our study was based on pathologically confirmed cases and thus avoids the pitfalls of misdiagnosis of other haematological diseases for aplastic anaemia. Unfortunately half of the initially identified cases had to be excluded as the bone marrow trephine biopsy was not performed or was inadequate. As a result, the true incidence of aplastic anaemia in Sabah may be underestimated.

The high ratio of aplastic anaemia to acute myeloid leukaemia at 0.91 during the study period and similarly high aplastic anaemia to total acute leukaemia ratio of 0.37 indicate that there is significantly

Table II
Number of patients with aplastic anaemia, de novo acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL)

	1993	1994	1995	1996 (Jan-Mar)	Total
Aplastic anaemia (AA)	12	10	5	4	31
AML	8	12	13	1	34
ALL	17	10	22	2	51
Total acute leukaemias (AL)	25	22	35	3	85
Ratio AA:AML	1.5	0.83	0.38	4.0	0.91
Ratio AA:AL	0.48	0.45	0.14	1.3	0.37

increased incidence of aplastic anaemia in Sabah. In most western centres, acute leukaemia is five to ten times more common than aplastic anaemia[14].

The male-to-female ratio of 3.4 is also higher than that reported previously, although a male preponderance has been noted. This again could reflect an environmental occupational factor in aetiology.

The ethnic distribution of patients with 77% Kadazan-Dusun needs further investigation. This is an ethnic group indigenous to the state of Sabah and forms 18% of the total population. Majority of these peoples are rural dwellers with an agricultural background and of lower socio-economic status. The observed increase in incidence among these peoples suggest a common ethnic environmental factor or genetic predisposition. Environmental aetiologic possibilities include traditional treatments, agricultural toxins and soil-related marrow-suppressive pathogens.

Aplastic anaemia has a high morbidity and is associated with significant mortality. Further detailed prospective case-control studies are indicated in the state of Sabah to identify the true incidence of aplastic anaemia and the aetiologic factors accounting for these observations.

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