ras Gene Mutations in Malaysian Leukemia Patients

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ras gene mutation studies were performed at random on 30 acute myeloid leukemia (AML), 6 acute lymphoblastic leukemia (ALL), 6 chronic myeloid leukemia (CML), 1 hybrid acute leukemia (HAL), and 3 myelodysplastic syndrome (MDS) patients, admitted to the University Hospital, Kuala Lumpur, from July 1988 to October 1989. Results of the French-American-British (FAB) classification of the 30 AML patients were as follows: 6 M1, 1 M2, 8 M3, 12 M4, and 3 M5. The AML and ALL patients were at presentation of the disease. The deoxyribonucleic acid isolated from the bone marrow or peripheral blood of these leukemia patients were subjected to in vitro amplification at regions around codons 12, 13, and 61 of the three ras genes; the H-ras, K-ras, and N-ras by the polymerase chain reaction. The amplified products were then hybridized with oligonucleotide probes to detect point mutations at codons 12, 13, and 61 of the three ras genes; the H-ras, K-ras, and N-ras.

ras gene mutations were detected in 4 (13.3%) of the 30 AML patients. The incidences of ras gene mutations in the M3 and M4 subgroups of AML were 37.5% (3 out of 8) and 8.3% (1 out of 12), respectively. The median age of the 30 AML patients was 35 years and the 4 patients with ras mutations were below 35 (7-32) years. ras gene mutation was not detected in CML, HAL, and MDS patients. Only 1 (aged 14 years; FAB classification: L2) of the 6 ALL patients had a ras gene mutation. Of the 5 ras mutations detected, 4 were N-ras and 1 was K-ras. All the 5 ras mutations resulted in different amino acid substitutions. Table 1 shows the distribution of the ras mutations in the 5 leukemia patients.

The reason for the high incidence of ras gene mutations in M3 AML patients and a young age group (below 35 years) in Malaysian leukemia patients is unknown, and these findings have not been reported in Western countries before [1-3]. Exposure to particular environmental mutagens and irradiation may be one of the factors. It may be worthwhile to extend the research with a larger sample size not only to study the clinical significance but also the geographical and ethnic significance of ras gene mutations in leukemias.

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