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- Contents -

Study on HLA Types and SCE Frequency in Familial and Sporadic Nasopharyngeal Carcinoma

Nasopharyngeal carcinoma has a higher prevalence rate in Chinese than in other ethnic groups This difference has attracted the attention of many epidemiologists, and many risk factors such as EB virus, smoking, Cantonese salted fish, which containing nitrosamine, occupational exposures, genetic factors, and history of nasal cavity diseases, etc have been suggested No study, however, has yet established the temporality of causal relation between any of these factors and the nasopharyngeal carcinoma Even the most mentioned EB virus, many facts still remain unexplained For instance, the male-female ratio of nasopharyngeal carcinoma is 2-3:1, the infection of EB virus in male and female is about the same Simons et al[1] , therefore, proposed a hypothesis on Human Leukocyte Antigen (HLA) and nasopharyngeal carcinoma However, many studies in different areas with different ethnic groups have so far produced inconsistent findings

On the other hand, many studies have pointed out that the other EB virus-related disease, Burkitt's lymphoma in those patients some find, their No 8 and No 14 chromosomes show a chromosomal exchange This makes one wonder whether there also exists chromosomal exchange in nasopharyngeal carcinoma, which is also EB virus-related disease We find some familial aggregated NPC cases in Taiwan It is suggested that genetic factors may play an important role in the pathogenic mechanism of nasopharyngeal carcinoma With the assistance of the ENT Department of the National Taiwan University Hospital, the authors have identified some family-clustered nasopharyngeal carcinoma cases for study The major purposes of the study are to understand the possible relationship between nasopharyngeal carcinoma and HLA and sister chromated exchange (SCE), and the distribution of HLA in cases and controls

We have identified some family-clustered nasopharyngeal carcinoma cases They are matched by age and sex with some sporadic nasopharyngeal carcinoma cases and healthy controls All cases are pathologically confirmed 171 healthy controls have also been selected from the National Taiwan University Hospital for HLA testings as controls against the nasopharyngeal carcinoma cases

20 nasopharyngeal carcinoma cases, 15 males and 5 females, all above 30 years of age, have been collected. Of them, 10 are family-clustered and the other 10, sporadic A comparison of HLA in 20 cases and 171 healthy controls (Table 1) shows that HLA-A2 is higher in cases (80%) than in controls (40 4%), with OR (odds ratio) = 5 91 (95% confidence interval = 2 1 - 16 6, p = 0 0017) Table 2 shows that HLA-B16 is higher in cases (25%) than in controls (5 3%), with OR=6 00 (95% confidence interval=2 0 - 18 0, p=0 0082) HLA-C shows no significant difference between this two groups Table 3 shows that HLA-DR1 is higher in cases (18%) than in controls (3%), with OR=6 89 (95% confidence interval=1 26 - 37 5, p=0 025) Between the familial and the sporadic cases, no significant differences are noted in HLA-A, B, C, and DR A further haplotype analysis of HLA-A2B16 (Table 4) shows a highest OR of 15 5 (95% confidence interval=4 5 - 52 8) for HLA-A2(+) B16(+) group compared with HLA-A2(−)B16(−) group Though a higher frequency of SCE is found in the cases than in the controls, no statistically significant difference is found between this two groups.

Specific HLA labels are found in the nasopharyngeal caricinoma patients in singapore, Malaysia, Hong Kong, and California[2-4] In Singapore, they are HLA-A2 BW46 and AL9 B17 They are not seen in Caucasians. Though many studies show a relationship between HLA and nasopharyngeal carcinoma, their actual relationship is not clear A more acceptable hypothesis at present is that HLA itself is not a carcinogenic factor, but very close to a "disease-susceptible" gene 5 This hypothesis, however, requires further confirmation. The HLA data of the family-clustered patients are helpful in understanding the hypothesis, however, since the samples in this study are small, no conclusion can be made The findings, however, indicate that more family-clustered

patients should be collected for further study In terms of SCE frequency, though the frequency is higher in cases than in controls, the difference is not statistically significant, a further study of the changes of chromosomal patterns such as chromosomal aberration is necessary Though the number of cases is small, the present study shows a significant relationship between HLA and the nasopharyngeal carcinoma, the hypothesis that genes play an important role in the pathogenic mechanism of nasopharyngeal carcinoma is supported

Note: This report was the abstract of the presentation at the 1988 annual meeting of the ROC Public Health Association, 27 September 1987

Table 1. Distribution of HLA-A locus antigens in 20 Chinese patients of nasopharyngeal carcinome (NPC) and 171 unrelated controls.

Antigen	NPC (N = 20)	Control (N = 171)	OR (95% CI)
A1	0 05	0 05	1 07 (0 13- 9 1)
A2	0 80	0 40	5 91 (2 10-16 6)
A3	–	0 01	–
A9	0 30	0 37	0.72 (0 26- 2.0)
A10	0 10	0 05	2 00 (0 41- 9.7)
A11	0 25	0.52	0 31 (0 11- 0.8)
A19	0 25	0 16	1 70 (0.58- 5 0)
A28	–	0 01	–
A blank	0 05	0 20	

N: number; OR: odds ratio; CI: confidence interval

Table 2. Distribution of HLA-B locus antigens in 20 Chinese patients of nasopharyngeal carcinoma (NPC) and 171 unrelated controls.

Antigen	NPC (N = 20)	Control (N = 171)	OR (95% CI)
B5	0 15	0 13	1 20 (0 32- 4 4)
B7	0 05	0 02	2 95 (0 32-27 0)
B8	–	0 01	–
B12	0.05	0 006	8 95 (0 86-93 5)
B13	0 15	0 14	1 08 (0 29- 4 0)
B14	–	–	–
B15	0.15	0 14	1 08 (0 29- 4 0)
B16	0.25	0 05	6 00 (2 0 -18 0)
B17	0 20	0 23	0 85 (0 27- 2 7)
B27/47	–	0 02	–
B37	–	0 005	–
B40	0 35	0.47	0 61 (0 23- 1.6)
BW21	–	–	–
BW22	–	0 16	–
BW35	0 05	0 03	1 75 (0 20-15 4)
BW46	0 10	0 15	0 62 (0.14- 2.8)
BW48	0.05	0 04	1 45 (0.17-12 6)
B blank	0 34	0 26	

N: number; OR: odds ratio; CI: confidence interval

Table 3. Distribution of HLA-DR locus antigens in 11 Chinese patients of nasopharyngeal carcinoma (NPC) and 96 unrelated controls.

Antigen	NPC (N = 11*)	Control (N = 96)	OR (95% CI)
DR1	0 18	0 03	6.89 (1.26-37.5)
DR2	0.36	0 24	1.81 (0.49- 6 7)
DR3	0 09	0.31	0 22 (0.03- 1.5)
DR4	0 18	0 33	0.44 (0 09- 2.1)
DR5	0 18	0.15	1 30 (0.25- 6 7)
DR6	0 09	0 07	1.27 (0.14-11 5)
DR7	-	0 62	
DR8	0 09	0 06	1 50 (0 16-13 7)
DR9	0 09	0.14	0 64 (0 08- 5.4)
DR10	-	0 02	-
DR blank	0 54	0 43	

* Blood samples of 9 NPC patients were not enough to test antigens of HLA-DR locus.
N: number; OR: odds ratio; CI confidence interval

Table 4. Distribution of HLA-A2 and B16 haplotype among 20 Chinese patients of nasopharyngeal carcinoma (NPC) and 171 unrelated controls

HLA-A2	HLA-B16	Case	Control	OR (95% CI)
−	−	4	99	1 0
−	+	0	1	
+	−	11	63	4.3 (1.4-13.1)
+	+	5	8	15 5 (4 5-52 8)

OR: odds ratio; CI: confidence interval

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