

Basic Investigations**POPULATION CHARACTERS IN HIGH RISK PEDIGREES OF NASOPHARYNGEAL CARCINOMA (NPC)**

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Abstract

Objective: To investigate population characters in high risk pedigrees of NPC in Guangdong area and to explore the effect each other between tumor genetic susceptibility and infection of EB virus on pathogenic mechanism. **Methods:** Pedigree investigation, examination of DNA fingerprint, multi-antibodies of EB virus and nasopharyngeal cavity were done for all of the members in each high risk pedigree. **Results:** High positive rate of EBV VCA/IgA (23.22%), high percentage of high risk population of NPC (6.53–10.40%), high detected rate of malignant tumor (9552.59/10⁵), and high detected rate of NPC (8464.32/10⁵) were discovered and NPC was most common in first degree relative of a pedigree. **Conclusion:** Tumor genetic susceptibility, infection of EB virus might play a role in coordination of reinforced effect on occurrence of NPC.

Key words: Nasopharyngeal carcinoma, Pedigree, Genetic susceptibility, EB virus.

The etiology of NPC is not clear until now, genetic factor, infection of EB virus and nitrosamine in food were know to be associated with occurrence of NPC.^[1-3] One of the characters on epidemiology in Guangdong is assembly of patients with NPC in pedigree.^[4] There were 10% family cancer history in 1000 new cases of NPC in cancer hospital, Sun Yat-

Sen University of Medical Sciences. A prospective study in high risk area showed that the level of EB virus infection and the habit of life style and diet were similar,^[5,6] but the level of incidence was big difference. The difference of genetic character in population might play an important role, EB virus infection and tumor genetic susceptibility might play a role in coordination of reinforced effect on occurrence of NPC.^[5] The members of cancer pedigrees were recognized as the high risk population of NPC.^[7] We studied systematically population characters in nasopharyngeal carcinoma pedigrees as show as following.

MATERIALS AND METHODS**Source of High Risk Pedigrees of NPC**

There are two or more cases of NPC in a pedigree as to say high risk pedigree of NPC. 25 pedigrees were collected by us from 1986 to 1995 in high risk area of NPC Guangdong Province, China.

Objects of Observation

All of members in high risk pedigrees were the objects observed. Total 827 members in 25 high risk pedigrees, 448 for male and 379 for female. The average age of members was 30, the oldest one was 89 years and the youngest one was 3 months at collection time.

Items of Observation

Investigation for pedigree, physical examination of head and neck, examination of multi-antibodies of EB virus for every member, examination of naso-

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pharyngofibroscopy, biopsy and pathology for some high risk population of NPC and examination of DNA fingerprint for blood and nasopharyngeal tissue were done.

The Standard of Diagnosis for High Risk Population and Precancerous Lesion of NPC

According to the suggestion by Cancer Center, Sun Yat-Sen University of Medical Sciences, the diagnostic standard was used in this research.^[7]

RESULTS

The Positive Rate of Reaction of EB Virus Multi-antigen and Antibody

EB virus VCA/IgA (virus cover antigen/antibody IgA), EA/IgA (early antigen/antibody IgA) and EDAb (EB virus special DNase antibodies) were examined for every member of pedigree, the results show as Table 1.

High Titer Positive, Double Positive and Three Positive Rate

According to the diagnostic standard of high risk population and precancerous lesion of NPC,^[7] the positive rates show as Table 2.

Table 3. Nasopharyngeal mucosa epithelia cell heterotype hyperplasia in 827 members of pedigrees

Pathological type	1		2		3		4	
	No.	%	No.	%	No.	%	No.	%
	19	15.7	3	2.5	1	0.83	0	0

1. Chronic inflammation 2. Mild heterotype hyperplasia/metaplasia

3. Middle heterotype hyperplasia/metaplasia 4. Severe heterotype hyperplasia/metaplasia

Detected Rate for Malignant Tumor

Total 79 cases were diagnosed as malignant tumor in whole members of pedigrees, the detected rate was 9552.59/10⁵ person year. Nasopharyngeal carcinoma, lung cancer, breast cancer, liver cancer, stomach cancer and esophagus cancer were detected in this series, nasopharyngeal carcinoma was the most common one, accounted for 88.60% for whole malignant. There were at most 7 cases and at least 2 cases in a pedigree.

Detected Rate of Nasopharyngeal Carcinoma

Total 70 cases of NPC in 25 pedigrees, detected rate was 8464.32/10⁵ person year, 46 of 70 cases were male (10267.85/10⁵ person year) and 24 of 70 cases

Heterotype Lesion at Nasopharyngeal Mucosa Epithelia Cell

Total 121 persons were diagnosed as high risk population of NPC in all members, examination of nasopharyngofibroscopy, biopsy and pathology were done for them. The results show as Table 3.

Table 1. Positive rate of EB virus multi-antibodies in 827 members of pedigrees

Items	VCA/IgA (≥1:5)	EA/IgA (≥1:5)	EDAb (≥30%)
Positive No.	192	17	91
Positive rate (%)	23.22	2.06	11.00

Table 2. Positive rate of high risk population in 827 members of pedigrees

Item	VCA/IgA (≥1:80)	VCA/IgA, EA/IgA, EDAb double or three positive
Positive No.	54	86
Positive rate (%)	6.53	10.40

were female (6332.45/10⁵ person year). The average age at occurrence was 42 years old, the youngest one was 26 years and oldest one was 81.

The Relationship between the Cases of NPC in a Pedigree

Between the cases of NPC, the relationship was shown as Table 4. It shows that occurrence of NPC was most common between parents and children or brothers and sisters, accounted for 92.23% (23/25) in all of pedigrees and 92.85% (65/70) in all cases.

DISCUSSION

One of the characters on epidemiology of NPC in

Guangdong Province, China is assembly of patients with NPC in pedigree, these characters were discovered by Cancer Center, Sun Yat-Sen University of Medical Sciences in past decades,^[4] 10% new cases of NPC have cancer history in pedigree.^[8] These research results show that genetic susceptibility may be an important factor in etiology of NPC. There is serious significance to grope clearly the characters in this special population for genetic susceptibility of NPC, and induce mechanism of cancer of EB virus and their coordination of reinforced effect on occurrence of NPC.

Through this research to 25 cancer pedigrees, there are some characters for these special populations as following:

High Detected Rate of Malignant Tumor in Members of Pedigree

The detected rate of malignant tumor was up to 9552.59/10⁵ person year in this special population, it is higher than Poland (145.90/10⁵) that is a country of high mortality rate of malignant and Fujian Province, China (156.55/10⁵), the difference is significant. If the incidence is more in the relatives of patient than in general people, it means the disease has pedigree assembly. Pedigree cancer history is not a fortuitous phenomena in NPC, because several epidemiological investigations in Guangdong Province showed that pedigree cancer history is an important factor in occurrence factors of NPC.^[8]

Table 4. Relationship of patients with NPC and percentage in all cases in 827 members of pedigrees

1			2			3*			4		
Pedigree	Cases	%	Pedigree	Cases	%	Pedigree	Cases	%	Pedigree	Cases	%
12	35	50	11	30	42.85	1	2	3.6	1	3	5.45

1. Parents and children 2. Brothers or sisters 3. Husband and wife 4. Uncle or aunt and nephew

*Husband and wife of the pedigree suffered from NPC in same year, but they belong to two different cancer pedigrees.

High Detected Rate of Nasopharyngeal Carcinoma in Members of Pedigree

The detected rate of NPC was 8464.32/10⁵ person year (10267.85/10⁵ person year for male and 6332.45/10⁵ person year for female), it is same with the detected rate of high risk population that was suggested by us before.^[7] The sex ratio is 1.89:1, it is same with Zhongshan (2.31:1) and Sihui (2.0:1) they are the high risk area in Guangdong.^[9] The average

age at occurrence was 42, the tendency of younger at occurrence was not seen.

Most Patients with NPC in Pedigree Occurred in First Degree Relationship

Most patients with NPC in pedigree occurred in parents and children, brothers or sisters, accounted for 92.23% of all cases, 42.85% for brothers or sisters. The typical cases show as Figure 1 and 2.

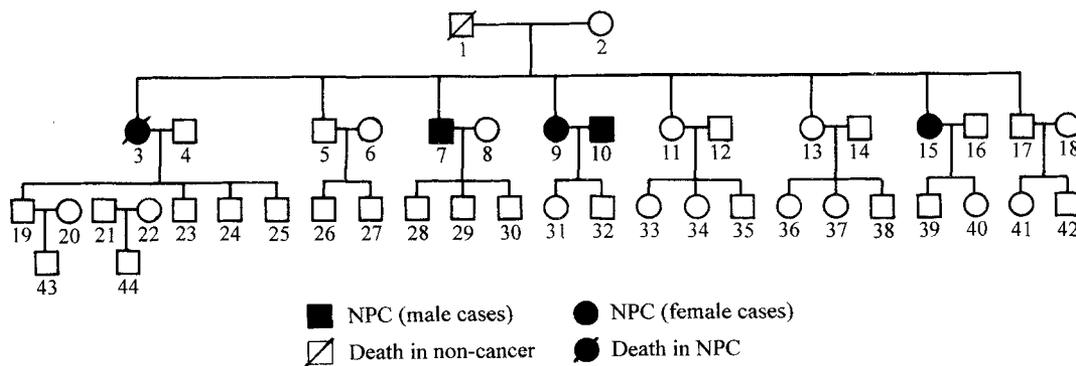


Fig. 1. Wu's pedigree

High Positive Rate of EB Virus VCA/IgA in Members of Pedigree

The positive rate of EB virus VCA/IgA was 23.22% in this special people, it is higher than in

general people in Guangdong Province (8.15%).^[10] The detected rate of NPC in positive persons is 40.7 times to negative persons.^[10]

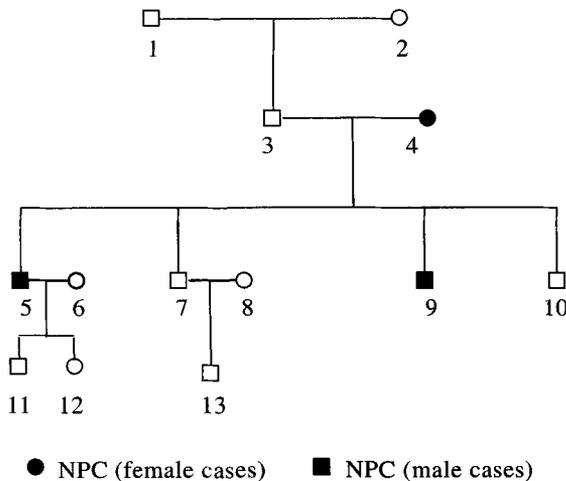


Fig. 2. Huang's pedigree

High Detected Rate of High Risk Population of NPC in Members of Pedigree

The diagnosed standard of high risk population of NPC was suggested by us through prospective study for 100,000 persons past ten years,^[7] the detected rate of NPC in these people was 1794.00–7305.90/10⁵ person year. Coincident the diagnosed standard persons accounted for 6.53–10.40% in this series.

The level of infection of EB virus is coincident with the level of incidence of NPC in members of pedigree. Recent years, more researches about the effects of genetic tendency and EB virus infection on etiology of NPC were reported,^[6,11–13] EB virus exist not only in cell of NPC but also in heterotype hyperplasia of nasopharyngeal epithelia cell and primary situ cancer cell,^[11,12] there is expression of transformation active LMP1 in most biopsy samples of nasopharynx, abnormal expression of LMP1 may initiate the process of heterotype hyperplasia of nasopharyngeal epithelia cell,^[12] EB virus may promote cell hyperplasia in the early process of cell malignant transformation. All of above research results suggest seriously that EB virus plays the role of initiation in multi-steps occurrent process of

nasopharyngeal cancerous. We think that the genetic susceptibility and infection of EB virus play a role in coordination of reinforced effect on occurrence of NPC in members of cancer pedigree.

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