Nasopharyngeal Carcinoma: Present Status Of Knowledge1

Brian E. Henderson

University of Southern California School of Medicine, Department of Pathology, Los Angeles, California 90033

Introduction

Nasopharyngeal carcinoma has been the subject of considerable recent interest (6, 15). A rare neoplasm in many parts of the world, nasopharyngeal carcinoma remains one of the leading cancer problems in southeast Asia. This report focuses on the relative importance of genetic and environmental factors in the etiology of the disease.

The Possible Role of Genetic Factors

A relatively high rate (10 to 20/100,000) of nasopharyngeal carcinoma among the Southern Chinese (Kwangtung, Kwangsi, and Fukien Provinces) is present whether they live in China, the nearby islands of Formosa and Hong Kong, or migrate to Australia, New York, Hawaii, or California (5, 6, 10, 15, 16, 22, 25, 26). The nasopharyngeal cancer rates are considerably lower among Chinese from the more northern provinces of China (5, 6, 15). In contrast, nasopharyngeal carcinoma is relatively rare in Japan and India (18, 19). The greater the admixture of Chinese blood in an ethnic group, the more likely it is that the nasopharyngeal carcinoma incidence rates will be elevated (19). Thus, in Thailand, those of mixed Chinese-Thai blood have a frequency of nasopharyngeal carcinoma less than that of pure-blood Chinese and greater than that of the Thais (17).

The nasopharyngeal cancer rates in Chinese who immigrate to California decline somewhat in the 1st generation but remain considerably above that of the white population (1, 26). As pointed out by Buell (3), the study of the Chinese population in California may yield important clues toward a primarily genetic or environmental view of the pathogenesis of nasopharyngeal carcinoma. Based upon the California mortality rate data, there is a strong suggestion that successive generations of Chinese born in the United States are at decreasing risk to nasopharyngeal carcinoma.

Recent work by Simons et al. (24) suggests that an increased frequency of histocompatibility antigen HL-A2 may be a marker of genetic susceptibility to nasopharyngeal carcinoma in the Chinese population. These important observations provide needed insights into the epidemiological characteristics of nasopharyngeal carcinoma.

The Role of Environmental Factors

It has been suggested that the high incidence of nasopharyngeal carcinoma in Chinese may be related to such factors as poorly ventilated housing (11), smoke from exotic trees (7), opium (9, 23), incense (14, 23), antimosquito coils (23), and cigarettes (23). However, subsequent epidemiological studies have failed to link any of these with an increased risk to nasopharyngeal carcinoma. More recently, Ho (15) proposed that nitrosamines from dry salted fish might be an etiological factor. There was no association between occupation, socioeconomic level, and nasopharyngeal carcinoma in Hong Kong and Singapore (15, 21, 23), although Buell reported a 2-fold risk of nasopharyngeal carcinoma among the poorer classes of Chinese in California (1).

The most interesting environmental factor to emerge has been the EBV.2 As reviewed in detail in this volume by de-Thé and Geser (8), virtually 100% of nasopharyngeal carcinoma cases have elevated antibody titers to EBV regardless of the racial or geographical location of the cases (8, 13). The EBV genome has been demonstrated by nucleic acid hybridization in biopsies from nasopharyngeal carcinoma although it is not clear whether the EBV genome is present in the epithelial carcinoma cells or the lymphoid tissue associated with the tumor (20, 27). Whether EBV is a necessary cofactor for the development of nasopharyngeal carcinoma or a "passenger" virus remains unresolved. EBV can be regularly isolated from the pharynx of normal individuals (4, 12) and probably is a common resident of the lymphoid tissue of the pharynx. As nasopharyngeal carcinoma invades the pharynx, the carcinoma cells can invoke both an immunological and nonspecific type of lymphocytic response, and proliferation of such lymphoid tissue may well lead to expression of latent EBV. On the other hand, the finding that EBV transforms lymphocytes into immortal cell lines, and the established etiological association of the herpesvirus group with naturally occurring cancers in chickens, monkeys, rabbits, and frogs, suggest that herpesvirus might play a vital role as an oncogenic cofactor in humans.

Conclusions

Over the past 20 years, a progressive accumulation of information on nasopharyngeal carcinoma has begun to sharpen the focus on possible etiological factors. Evidence now indicates that the high rates of nasopharyngeal carci-

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2 The abbreviation used is: EBV, Epstein-Barr virus.
nomas observed in the southern Chinese are not exclusive to this group; other racial groups such as the Philipinos and Tunisians also have elevated rates (3, 8, 19). The lowered rate of nasopharyngeal carcinoma in 3rd-generation Chinese in California (3) and the finding that children born in southeastern Asia, of parents who are Caucasians from the United States, have an increased risk to nasopharyngeal carcinoma (2) suggest that the Chinese population is not at a unique genetic risk to nasopharyngeal carcinoma; presumably some environmental factor associated with being Chinese is responsible for their high risk.

The age curve of nasopharyngeal carcinoma in the Chinese population peaks at 40 to 54 years (15) and declines thereafter. Such an age distribution could be compatible with exposure to an environmental agent during late childhood and early adolescence, with a variable incubation period (exposure must occur before a certain time, or disease will not occur) or chronic exposure over a prolonged period of time to an environmental agent, assuming the population of susceptibles is being exhausted. At present there is no firm evidence to support either alternative, although the HL-A data would be compatible with the latter hypothesis.

If the former hypothesis is true, it should be possible to identify other associated risk factors that occur during late childhood or early adolescence, such as tonsillectomy or specific childhood infections.

If the latter hypothesis is true, either the agent is repeatedly used and the susceptible population is used up by late adult life or the exposure to the agent is age dependent, being discontinued or altered among older individuals. Whatever the type of environmental agent involved, it may be more easily identified among populations with a lower rate of nasopharyngeal carcinoma, where presumably exposure to the agent is less common or less intense. For this reason detailed study of nasopharyngeal carcinoma in United States Caucasian and Negroid populations should provide valuable information on the epidemiology of nasopharyngeal carcinoma. Such studies are currently underway in several major urban areas.

References

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