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Background: Compared with the West, Hodgkin’s lymphoma in Oriental countries is characterized by a lower incidence rate and a higher proportion of mixed cellularity histology. Both environmental and genetic factors may be involved.

Patients and methods: The incidence and pattern of pathology of Hodgkin’s lymphoma in the migrant Chinese population (0.4 million) in British Columbia (population 3.2 million) were studied. From a computerized database, all Hodgkin’s lymphoma cases diagnosed in British Columbia from 1970 to 1997 were identified. Chinese descent was determined using patient surname by standard methodology and verified from the treatment record or by patient interview. The corresponding figures from the Chinese population in Hong Kong were used for comparison. For incidence rates, the age-specific incidence of Hodgkin’s lymphoma in Hong Kong was obtained from the government cancer registry. For comparison of histology subtypes, 200 Hodgkin’s lymphoma records from a Hong Kong regional referral center for the same time period were reviewed. Crude and age-standardized incidence rates were calculated by 5-year intervals in terms of age and calendar year, and relative rates were compared between the three populations.

Results: From 1970 to 1997, Hodgkin’s lymphoma was diagnosed in 34 Chinese patients in BC, with 24 cases diagnosed from 1970 to 1994. Thus, the crude and age-adjusted incidence rates from 1970 to 1994 were 0.91 and 1.14 per 100 000 per year in the British Columbia Chinese migrant population. Within the same period, 1862 cases of Hodgkin’s lymphoma were diagnosed in British Columbia, giving a provincial background crude and age-adjusted incidence rates of 5.2 and 4.87 per 100 000 per year. The number of cases in the Hong Kong Chinese population (1970–1994) was 404, giving crude and age-adjusted incidence rates of 0.32 and 0.31 per 100 000 per year, respectively. Corrected for age and calendar year trends, the observed 25-year incidence of Hodgkin’s lymphoma in British Columbia Chinese was significantly lower than expected from the British Columbia background population [24 observed versus 71 expected cases; standardized incidence ratio (SIR) = 0.34; 90% confidence interval (CI) 0.24–0.48; P <0.0001]. On the other hand, it is higher than that expected by extrapolating from the Hong Kong Chinese population (24 observed versus 8.5 expected cases; SIR = 2.81; 90% CI 1.94–3.95; P <0.0001). The difference is mainly accounted for by young patients with nodular sclerosis type disease in the migrant population.

Conclusions: Although any conclusion about the impact of migration on Hodgkin’s lymphoma incidence and types in the Chinese population must be considered tentative due to the small number of observed cases and confounding variables such as age, changing diagnostic standards and secular trends in Hodgkin’s lymphoma rates, our data demonstrate a tendency for the Chinese population of British Columbia to take on a Western pattern of Hodgkin’s lymphoma. This observation provides additional evidence that both genetic and environmental influences play a role in the pathogenesis of this lymphoma, and that environmental factors can exert their influence over a relatively short period of time.

Key words: Chinese, Hodgkin’s lymphoma, incidence, migration

Introduction

Although Hodgkin’s lymphoma has been a recognized entity for over a century and is one of the most curable malignancies, its pathogenesis and etiology have largely remained unknown. From
International Agency for Research on Cancer (IARC)-published cancer incidences (2000; http://www-dep.iarc.fr/globocan/globocan.html), the incidence of Hodgkin’s lymphoma in Western countries is significantly higher than that in Asia, South America and Africa [1–3]. The pattern of disease is also different in Western society, where nodular sclerosing histology is much more common than mixed cellularity [1]. The relative contributions of genetic and environmental factors to such differences are unknown [4]. Such differences are not likely to be due to different diagnostic standards, since similar variations have been observed in societies of mixed racial composition [5, 6]. Asian migrant populations in Western countries often take on Western epidemiological characteristics. This has been documented in cases of carcinoma of the stomach [7], colon [8], breast [9] and prostate [10], where the background epidemiological differences are marked, and large migrant populations with adequate follow-up have been studied. This is taken as evidence that at least part of the epidemiological differences are due to environmental factors. To investigate the relative contribution of these factors, we surveyed the incidence and pattern of the pathology of Hodgkin’s lymphoma in the Chinese migrant population in British Columbia, Canada, from 1970 to 1997, and compared them with those seen in the background (mainly Caucasian) population of British Columbia and the Chinese population of Hong Kong.

Patients and methods

Information for lymphoma patients in British Columbia was cross verified from two separate population-based databases of all lymphoma patients and cancer patients in the province since 1960, maintained separately by the Lymphoma Tumor Group and the Cancer Control Strategy section of British Columbia Cancer Agency (BCCA). Over 95% of all cases of Hodgkin’s lymphoma are registered. All potentially Chinese patients in the lymphoma database were identified by surname characteristics. The accuracy of such methodology has been estimated to be 73–85% [11, 12]. The racial origin of all selected cases and their year of migration to British Columbia were verified mostly from the treatment records and, in a few cases, by telephone interview after informed consent. All patients with Caucasian or Asian non-Chinese racial descent were excluded.

The age distributions of the British Columbia background population and the Chinese subpopulation of British Columbia were obtained from Statistics Canada from 5-yearly census figures. The Hong Kong Chinese population was taken as a reference population for the incidence of Hodgkin’s lymphoma in individuals of Chinese ethnicity. Hodgkin’s lymphoma incidence figures were obtained from the Hong Kong Tumor Registry, which has a catchment accuracy of ~90%. Population statistics for Hong Kong were obtained from the Census Department of the Government of the Special Administrative Region of Hong Kong, China. Age-adjusted incidence rates were calculated for the British Columbia, Hong Kong and Chinese migrant populations using World Health Organization world age-standardized rates [13]. The Queen Mary Hospital (QMH) is the major referral center for Hodgkin’s lymphoma in Hong Kong. Histology records of all Hodgkin’s lymphoma cases from BCCA (n = 203) and QMH (n = 200) from 1970 to 1997 were reviewed to provide background information on histology distribution.

Standardized incidence ratios (SIRs) were used to compare the Hodgkin’s lymphoma incidence in the British Columbia Chinese population with that of the British Columbia and Hong Kong general populations. SIRs of Hodgkin’s lymphoma were calculated by 5-year age groups and 5-year calendar periods. Since census figures in Hong Kong and British Columbia and the incidence of Hodgkin’s lymphoma in the Hong Kong population have only been published for the years 1970–1994, only this period was used for statistical calculations. Tests of significance for the differences in the SIRs were calculated assuming the observed number of cases followed a Poisson distribution, with the mean given by the expected number of cases of Hodgkin’s lymphoma based on British Columbia and Hong Kong population rates [14]. One-sided t-test and 90% confidence intervals (CIs) corresponding to a 5% significance level were used.

Results

The background age-specific incidence rate of Hodgkin’s lymphoma, as shown by time periods, for the entire British Columbia population is shown in Figure 1. Among 2013 cases of Hodgkin’s lymphoma (crude incidence rate of 5.2/100 000/year; age-adjusted rate 4.87/100 000/year) in British Columbia from 1970 to 1997, 34 cases were diagnosed in Chinese patients. These com-
prised 15 men and 19 women (male:female ratio = 0.79:1) with a median age of 26 years (range 4–84 years). Among them 11 patients (34%) were born in British Columbia, and the rest were migrants, mainly from China (29%) or Hong Kong (35%). The median age of arrival in British Columbia among migrants was 15 years (range 1–64 years). The age-specific pattern of distribution of the Chinese population in British Columbia is shown in Figure 2. The rapid increase in population is due to a combination of migration and an increase in second generation Chinese. From 1970 to 1994, the crude incidence rate of Hodgkin’s lymphoma in the British Columbia Chinese population was 0.91 per 100 000 per year, with an age-adjusted rate of 1.14 per 100 000 per year. The age-specific incidence rates of Hodgkin’s lymphoma in Hong Kong Chinese (1970–1994) are shown in Figure 3. The number of cases was 404, and the crude and age-adjusted rates were 0.32 and 0.31 per 100000 per year, respectively. Compared with Figure 1, the incidence is ~10-fold lower for all ages, and a bimodal age distribution is not well defined. The incidence appeared to be stable in both populations over the study period.

The expected and observed numbers of Chinese Hodgkin’s lymphoma cases in British Columbia from 1970 to 1994 are shown in Table 1. Corrected for age and calendar year trends, the observed incidence (24 cases) in the British Columbia Chinese population was significantly lower than expected from the British Columbia background population incidence (71 cases), with an SIR of 0.34 (90% CI 0.24–0.48; P <0.0001). On the other hand it was higher than expected from the Hong Kong Chinese population incidence (8.5 cases), with an SIR of 2.81 (90% CI 1.94–3.95, P <0.0001). In the BCCA cohort, the majority of cases were nodular sclerosing histology (64.9%), which was also the commonest
histology among British Columbia Chinese cases (68%) (Table 2). Other reports have also highlighted an increase in detection of nodular sclerosing histology is much higher [5, 19]. These and other reports have also highlighted an increase in detection of Epstein–Barr virus (EBV) in such cases [16, 20, 21]. Whether such an EBV association is altered in Hodgkin’s lymphoma in migrant populations remains to be studied.

For diseases with significant environmental risk factors, there is a tendency for migrant populations to take on the disease pattern of the country in which they settle. For malignant diseases, such observations are well documented in breast [9] and colon cancer [8] in Asian migrants to the United States. There have been very few studies on the effect of migration on the incidence of Hodgkin’s lymphoma. Studies of Hodgkin’s lymphoma in Asian immigrants to Los Angeles and Hawaii in the United States quoted similar rates to their parent population in China, Japan and the Philippines [1, 3, 22]. However, a study of Indian migrants to the UK showed a two-fold increase in risk [23]. Our study in Chinese migrants to British Columbia showed a three-fold increase in crude incidence from 0.32 to 0.91 cases per 100,000 per year. These data must be interpreted cautiously, since the incidence of Hodgkin’s lymphoma varies with age and calendar year [1]. In most Western countries, the age-related incidence of Hodgkin’s lymphoma follows a bimodal pattern, whereas the early peak is less obvious in Asians, mainly due to the lower number of young nodular sclerosing cases [2, 3, 16]. In both the Hong Kong and British Columbia populations, the age-adjusted rates of Hodgkin’s lymphoma have not changed significantly over the 25 years. Small rate increases in young adults and decreases in older adults have been observed (Figures 1 and 3). These were statistically controlled for by SIR calculations. Allowing for such variations and sample size, it appears that the increase in rate of Hodgkin’s lymphoma seen in the migrant Chinese British Columbia population is genuine.

The lower median age of disease in the migrant group and the higher proportion of nodular sclerosing disease seem to follow the Western trends. It is unlikely that this is due to variations in diagnostic standards, since morphological diagnosis of nodular sclerosing and mixed cellularity Hodgkin’s lymphoma in tertiary centers usually show high levels of concordance [24, 25]. Unfortunately, the small number of index cases precludes a meaningful statistical analysis of the shift in incidence in terms of histology subtypes, and between first- and second-generation migrants. Any conclusion about the impact of migration on Hodgkin’s lymphoma incidence and types in the Chinese population must be considered tentative due to the small number of observed cases, differences in case ascertainment and reporting, inaccurate population estimation, and confounding variables such as age, changing

| Table 1. Expected incidence of Hodgkin’s lymphoma in the Chinese population of British Columbia projected from the Hong Kong and British Columbia population-age and calendar-year standardized disease incidences |
|---|---|---|---|---|--- |
| Population model, 1970–1994 | Crude incidence rate | Cases of Hodgkin’s lymphoma expected by 5-year age and calendar year standardization | Standardized incidence ratio | 90% confidence intervals | P value |
| Observed migrant | 0.91/100,000/year | 24 (observed) | 1.00 | NA | NA |
| BC Chinese/HK model | 0.32/100,000/year | 8.539 (expected) | 2.81 | 1.94–3.95 | <0.0001 |
| BC Chinese/BC model | 2.65/100,000/year | 70.648 (expected) | 0.34 | 0.24–0.48 | <0.0001 |

BC, British Columbia; HK, Hong Kong; NA, not applicable.

| Table 2. Histology subtype distribution of Hodgkin’s lymphoma in the three cohorts |
|---|---|--- |
| Histology | BC, n (%) | BC Chinese, n (%) | HK, n (%) |
| NS | 1306 (64.9) | 23 (68) | 76 (38) |
| MC | 446 (22.2) | 3 (9) | 71 (35.5) |
| LP-D | 91 (4.5) | 3 (9) | 10 (5.0) |
| LD | 40 (2.0) | 1 (2.9) | 23 (11.5) |
| LP-N | 9 (0.4) | 1 (2.9) | 2 (1) |
| NOS/others | 121 (6.0) | 3 (9) | 18 (9.0) |
| Total | 2013 | 34 | 200 |

HK, Hong Kong; BC, British Columbia; NS, nodular sclerosis (include syncytial, classical, interfollicular variants); MC, mixed cellularity; LP-D, lymphocyte predominant; LD, lymphocyte depleted; LP-N, lymphocyte predominant nodular; NOS, not otherwise specified.

Discussion

It is known that the incidence and pattern of pathology of Hodgkin’s lymphoma in Oriental countries is different from that in the West [1–3]. Based on the information collected by the IARC, the crude incidence in Chinese populations in Hong Kong, Singapore and mainland China has been estimated to be between 0.3 and 0.6 per 100,000 per year [2, 3, 15]. These figures were similar to those reported in Japan, Korea and South-East Asia [16, 17], and were one order of magnitude lower than those found in the West. It is uncertain whether this is due to genetic or environmental factors, including diet, economic background or infection [4]. Also, there is epidemiological evidence that Hodgkin’s lymphoma represents a mixture of disease entities [5, 18]. It is well recognized that in Oriental and Latin American countries, the ratio of mixed cellularity to nodular sclerosing histology is much higher [5, 19]. These and other reports have also highlighted an increase in detection of Epstein–Barr virus (EBV) in such cases [16, 20, 21]. Whether
diagnostic standards and secular trends in Hodgkin’s lymphoma rates. To study such issues further, a larger study cohort would be required, with the collaboration of several cancer registries. Pending qualification from such larger studies, our data are consistent with the hypothesis that Chinese migrants to a Western country such as Canada rapidly acquire a higher risk of Hodgkin’s lymphoma and a tendency to develop the same histological subtypes of disease seen in the host country. This observation provides additional evidence that both genetic and environmental influences play a role in the pathogenesis of this lymphoma and that such environmental factors can exert their influence in a relatively short period of time. If verified, such observations strengthen the evidence for environmental factors playing a major role in Hodgkin’s lymphoma causation.

References