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論 文 内 容 の 要 旨

〔　目　　的　〕

Sinonasal NK/T-cell lymphoma (NKTCL) is a lethal midline granuloma that produces necrotic and granulomatous lesions in the upper respiratory tract, especially in the nasal cavity. Epidemiological studies have revealed that the disease occurs much more frequently in Asian countries such as Japan, China, and Korea and Latin American countries than in Western countries and is closely associated with Epstein-Barr virus (EBV) infection. Meanwhile, different frequencies of p53 and c-kit gene mutations among patients with sinonasal NKTCL in Japan, China, and Korea were reported. These findings might suggest a causative role for some genetical, environmental, and life-style factors in sinonasal lymphomagenesis. Therefore, we conducted an epidemiological study to elucidate whether socio-environmental ambient factors contribute to the development of sinonasal NKTCL.

〔　方法ならびに成績　〕

Eligible cases were defined as new patients who were diagnosed with NKTCL at age twenty years or older, and admitted to the hospitals of Osaka University, University of Ryukyus, Asahikawa Medical College, and St. Marianna University in Japan, Yonsei University in Seoul, Korea, and China Medical University in Shenyang, China. As a result, 88 eligible cases were accumulated：65 from Japan, 15 from Korea, and 8 from China during the period from March 2000 to March 2005. Controls were obtained by a consecutive series, i.e., from subjects aged twenty years or older with inflammatory diseases, hearing problems, benign cystic diseases, and medical check up in the otolaryngological regions who were admitted to the same hospitals and during the same period as the NKTCL patients. They were selected at random for the present study. They were tried to obtain so that the number of controls should be 3-4 times the number of NKTCL cases. A total of 305 controls including normal individuals were accrued. A structured self-administered questionnaire was filled out by the

NKTCL patients and the controls at the time of admission. The questionnaire contained information on the following items：past medical history, familial medical history, history of alcohol drinking and cigarette smoking, occupation, cultivation of crops, pesticide use (herbicide, insecticide, fungicide), and environment of residence. The software package STATA (Stata Corp., College Station, TX) was used for statistical analysis. Statistical significance and the 95% confidence interval (CI) of the odds ratio (OR) were calculated using an unconditional logistic regression model adjusted for age, sex, and country and judged by using a 2-sided test.

The odds ratio (OR) of NKTCL obtained after adjustments of age, sex, and country was 4.15 (95% confidence interval (CI)：1.74-9.87) for farmers, 2.81 (CI：1.49-5.29) for producers of crops, 4.01 (CI：1.99-8.09) for pesticide users, 11.65 (CI：1.17-115.82) for residents near garbage burning plants, 2.95 (CI：1.25-6.95) for former drinkers, and 0.49 (CI：0.23-1.04) for current smokers. The ORs for crop producers who minimized their exposure to pesticides by using gloves and glasses, and sprinkling downwind at the time of pesticide use, 3.30 (95% CI；1.28-8.54), 1.18 (95% CI：0.11-12.13), and 2.20 (95% CI：0.88-5.53), respectively, were lower than for producers who did not take these precautions. There was no association between tobacco smoking, self-employment and special work and NKTCL development, however, the risk of NKTCL was increased in former drinkers, but not in current drinkers.

〔 総　　括 〕

Cultivation of crops was associated with NKTCL, which was more prominent in individuals who had been cultivating crops for more than five years. Exposure to pesticides and chemical solvents could be causative factors for NKTCL. This was further supported by the following findings：pesticide users were at greater risk and this risk was reduced with the use of protective equipment and careful sprinkling of pesticides. The residents near a garbage incineration plant showed a marked increase in risk for NKTCL. Taken together, environmental factors might be involved in the occurrence of NKTCL, an aggressive lymphoma.

論文審査の結果の要旨

鼻腔 NK/T 細胞性リンパ腫（NKTCL）は、鼻腔を中心とした上気道領域を侵す予後不良の疾患である、その発生には地理的な偏よりが見られ、日本を含めた東アジア地区及び中南米に好発することから、モンゴロイドに多い疾患と考えられている。本研究の目的は NKTCL 発生における、生活習慣、環境因子の関与を明らかにすることである。このため、日本、韓国、中国における症例対照研究を行った。大阪大学など日本の４施設、韓国の延世大学（ソウル市）、中国の中国医科大学（瀋陽）で調査を行った。調査期間は 2000 年３月から 2005 年３月までの５年間で、自記式アンケート調査方式を用い、STATA を用いた多変量解析を行った。NKTCL 症例 88 例、対照例 305 例につき解析した。農業従事者（オッズ比（OR）：4.15）、農作物の栽培群（OR：2.81）では NKTCL の発症率（OR）が上昇していた。特に農薬使用群はオッズ比が高い（OR：4.01）。農薬使用時に防護眼鏡を使用しない群（OR：4.52）、風向きを注意しない群（OR：8.45）ではオッズ比の上昇を認めた。母数は少ないものの、居住地がゴミ焼却場に近い群ではオッズ比（OR：11.65）が有意に上昇していた。

以上の結果は鼻腔 NK/T 細胞性リンパ腫発生に農薬を中心とする生活習慣、環境要因が関与していることを示している。予後不良の本疾患の発症要因を明らかにした本研究は、疾患発生予防への手がかりを与えるものであり、博士（医学）の学位授与に値するものと認める。