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Maxillary sinus squamous cell carcinoma (SCC) is relatively rare in western countries, but is frequent in Japan. To the best our knowledge, the potential role of immunological events in the pathogenesis and clinical course of this disease has not been investigated. Besides contributing to our understanding of the interactions between patient's immune system and maxillary sinus SCC cells, this information may suggest immunotherapeutic strategies for the treatment of this disease. Therefore in this study, we have investigated the expression of HLA class I and class II antigens in maxillary sinus SCC lesions. These antigens mediate and restrict the recognition and destruction of tumor cells by tumor associated antigen-specific cytotoxic T lymphocytes (CTL). Defects in HLA antigen expression and/or function which are frequently found in malignant lesions, are likely to

provide malignant cell with an escape mechanism from a host's immune system(1). Furthermore, the presence of HLA defects in a malignant lesion is likely to result from two events, i.e. a mutation which causes HLA antigen loss or down-regulation in a clone and selective pressure which results in the expression of the clone which has acquired resistance to immune destruction because of phenotypic changes. Therefore, information about the presence of HLA class I antigen defects in maxillary sinus SCC lesions may contribute to our understanding of the presence of immune response to tumor cells in patients with maxillary sinus SCC.

The study group consisted of 70 Japanese patients with a median age of 67 who were treated in Department of Otolaryngology, Asahikawa Medical College between 1980 and 2000. According to the 1997 UICC TNM staging systems, T1 was not present; T2 was in 8 patients (11%), T3 in 33 patients (47%) and T4 in 29 patients (42%), respectively. Seven patients (10%) had lymph node metastasis (N1 in all cases) at diagnosis.

Formalin fixed, paraffin embedded tissue sections were utilized as a substrate in immunohistochemical staining. These sections were stained with anti-HLA class I heavy chain monoclonal antibody (mAb) HC-10, anti-$\beta_2$microglobulin (β_2m) mAb L368, and anti-HLA class II mAb LGII-612.14. When the percentage of stained tumor cells was <30%,

≥30% and <70% and ≥70%, the lesion was scored as negative, heterogeneous and positive, respectively. The number of infiltrating T cells stained with anti-CD3 mAb EPOS in 500μm^2 of a tumor lesion was counted.

HLA class I antigen expression was down-regulated in 71.4% of the lesions tested with the score being heterogeneous in 38.6% and negative in 32.8%. β_2m expression was down-regulated in 81.4% of the lesions tested with the score being heterogeneous in 35.7% and negative in 45.7%. HLA class II antigen expression was expressed in 18.6% of the lesions tested with the score being heterogeneous in 10% and positive in 8.61%. 8.6 and 10.0% of the lesions with positive and heterogeneous score, respectively. HLA class I antigen expression was significantly correlated with β_2m expression ($p<0.01$) and with the number of infiltrating T cells in carcinoma lesions ($p<0.01$). In 57 patients who had been treated with surgery, the survival of the 20 patients with a negative score was significantly shorter than that of the 16 patients with a positive score ($p<0.05$).

The present study has shown for the first time that HLA class I antigen down-regulation has a high frequency in maxillary sinus SCC lesions. This frequency is higher than that reported by other investigators(2, 3) in head and neck SCC lesions. The latter studies have in general lumped together head and neck SCC lesions located different

anatomic site. Therefore at present we do not know whether the difference between the results in the literature and ours reflects the different types of head and neck SCC lesions investigated and/or differences in the sensitivity of the immunohistochemical methodology used. The high frequency of maxillary sinus SCC lesions with HLA class I defects we have found suggests that a HLA class I restricted TAA specific cellular immunity takes place in large percentage of these patients. Furthermore, the association we have found between T cells infiltrating the lesions and favorable prognosis suggests that an immune response to tumor antigens may play a role in the clinical course of the disease.

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